CONTENTS

EFFECT OF DIETARY SALT ON THE MANAGEMENT OF BRONCHIAL ASTHMA PATIENTS

MD. SAYEDUL ISLAM[1], S M MUSTAFA ZAMAN[2], MD. NAIMUL HOQUE[1], BISWAS AKHTAR HOSSAIN[1], KHALEDA BEGUM[1], MIRZA MOHAMMAD HIRON[1], MD. RASHIDUL HASSAN[1]

Abstract

This study assesses the effects of increased in dietary salt consumption on the clinical severity of asthma patients. This prospective study was carried out in the Department of Medicine in the Institute of Diseases of the Chest & Hospital (IDCH), Mohakhali, Dhaka. A randomized placebo controlled, crossover design was employed. Twenty-six mild to severe asthmatic patients were selected and randomized to receive 9 gm (3 capsules 6 hourly, each capsule contains 750 mg of NaCl or Lactose) Sodium Chloride or matched placebo (Lactose) for 7 days, crossing over to the alternative regime for a further 7 days. PEFR (Peak expiratory flow rate) was chosen as a parameter for the monitoring of asthma control, which was recorded daily, along with daily symptom scores. All the patients depending upon their clinical steps were receiving both reliever and preventive anti-asthmatic drugs. Twenty-four patients completed the study with sex and age distribution 15 (62.57%) male, 9 (37.5%) female and age ranging from 5-60 years; mean age 25.08 ± SD 13.56 respectively. Statistical analysis shows that salt loading worsened the symptoms of asthma and increased the use of inhaled antiasthmatic drugs. The effect of salt on lung function specially worsen the Peak expiratory flow rate (PEFR) in Step-II ($P<0.01$), Step-III ($P<0.001$), Step-IV ($P<0.05$). The results on Step-I asthmatic is rather equivocal ($P>0.05$). The Peak expiratory flow rate (PEFR) during placebo therapy remain unchanged or increased in most of the cases. Our result suggests that increase in dietary salt result in physiological deterioration of asthma patients and poor control during management. So dietary salt restriction may improve the management of asthma.

Introduction

Bronchial asthma is an inflammatory disease characterized by an increase responsiveness of the trachea and bronchi to various stimuli manifested by a widespread narrowing of the airways that changes in severity either spontaneously or as a result of therapy.[1] Five characteristic structural alteration are usually observe in the preterminal and terminal bronchiole of fatal bronchial asthma. (a) Plugging of the basophillic polysaccharide rich mucus blocking many of the terminal bronchiole; (b) Goblet cells are increased in size and number; (c) Marked thickening and irregularity of the basement membrane; (d) Smooth muscle of preterminal bronchiole are hypertrophied; (e) Inflammatory infiltrate composed of mononuclear cells, particularly eosinophillic granulocytes is found in the submucosa and between the hypertrophied muscle bundle.[2]

Numerous environmental factor are responsible for these changes in the bronchial tree. As in the case of essential hypertension, there is a marked geographic variation in asthma prevalence and mortality.[3] The regions where bronchial asthma prevalence and mortality are higher in advanced countries, which differ from poorer and technologically less developed regions in several respects. One of these eating habit in particular a higher salt intake.[4] Experimentally, salt intake appears to influence bronchial hyperreactivity. When asthmatic were loaded with sodium, the histamine provocation dose decrease and hyperreactivity increase, when they were receiving a low salt diet, the opposite occurred.[5,6]

As bronchial asthma is a multifunctional disease influenced by both genetic and environmental factors, so dietary change having high level of salt consumption are associated with spastic disorder of smooth muscle i.e. (i) Essential hypertension; (ii) Bronchial asthma. The high salt intake leads to increased bronchial hyperreactivity in asthmatics i.e. enhance contractility of bronchial smooth muscle to spasmogenic stimuli. On the basis of these observations, this study with assesses the effects of increased in dietary salt consumption on the clinical severity of asthma patients.

Materials and Methods

This prospective study was carried out in IDCH, Dhaka from January 1999 to September 1999. Twenty six mild to severe bronchial asthma patients who fulfills the inclusion and exclusion criteria were studied in a randomized placebo controlled, crossover

1. Department of Medicine, IDCH, Mohakhali, Dhaka.
2. Department of Medicine, BSMMU, Shahbag, Dhaka.

method. This study was carried out to find out whether high salt intake worsen asthma symptoms or conversely does salt restriction improve them and also for better management of asthma patients. The study design were as follows:

Study Design

Low salt in diet

Run in period	+ Salt + Placebo	+ Placebo + Salt	Follow-up

Days (-) 7 0 +7 +14 21

* Salt = 9 gm Sodium Chloride

12 capsule/day (each capsule containing 750 mg NaCl)

* Placebo = 9 gm Lactose

12 capsule/day (each capsule containing 750 mg Lactose)

* The salt and placebo (lactose) were supplied by courtesy of General Pharmaceuticals Ltd.

Most of our studied patients were hospitalized, daily PEFR were recorded. All the antiasthmatic drugs were given as per steps of the disease. Drugs were monitored as symptoms improved or deteriorated. The preliminary investigations like chest X-ray, lung function test, ECG and serum electrolytes were done before starting of the study regime.

Results

Twenty four patients completed the study with age sex distribution 15 (62.57%) male, 9 (37.5%) female and age ranging from 5-60 years; mean age 25.08 ± SD 13.56 (Table-I). Depending upon severity of asthma, 6 (25%) patients were Step-I, 7 (29.16%) were Step-II, 8 (33.33%) were Step-III and 3 (12.5%) were Step IV of American Thoracic Society Stepping (Table-II). Out of 24 patients 15 (62.5%) initial regime was salt and 9 (37.5%) patients were stared with placebo, which was crossover after 7 days (Table-III).Statistical analysis showed that increase in dietary salt worsened the asthma reflecting the reduction of PEFR and increase the use of antiasthmatic drugs specially the Step-II ($t=4.08$, $df=5$, $P<0.01$), Step-III ($t=14.78$, $df=6$, $P<0.001$), Step-IV ($t=4.99$, $df=2$, $P<0.05$). The results on Step-I asthmatic is rather equivocal ($t=0.44$, $df=6$, $P>0.05$). The PEFR during placebo therapy remain unchanged or increased in most of the cases (Table-IV).

Table-I

Age and sex distribution of patients (n = 24)

Age range	Male	Female	Total
6-15	4 (16.67%)	1 (4.16%)	5 (20.84%)
16-30	7 (20.16%)	5 (2.80%)	12 (50%)
31-45	3 (12.5%)	2 (8.33%)	5 (20.84%)
46-60	1 (4.16%)	1 (4.16%)	2 (8.33%)
Total	15 (62.57%)	9 (37.5%)	24 (100%)

Table-II

Distribution of patients according to clinical steps (n = 24)

	Male	Female	Total
Step-I	2 (8.33%)	4 (16.67%)	6 (25%)
Step-II	3 (12.5%)	4 (16.67%)	7 (29.16%)
Step-III	7 (29.10%)	1 (4.10%)	8 (33.33%)
Step-IV	3 (12.5%)	0	3 (12.5%)
Total	15 (62.57%)	9 (37.5%)	24 (100%)

Table-III

Stepwise Distribution of Patients According to Initiation of Therapy with Salt/Placebo (n = 24)

	Number	Initial salt	Initial placebo
Step-I	6	3 (12.5%)	3 (12.5%)
Step-11	7	4 (16.67%)	3 (12.5%)
Step-III	8	7 (29.16%)	1 (4.16%)
Step-IV	3	1 (4.16%)	2 (8.33%)
Total	24 (100%)	15 (62.5%)	9 (37.5%)

Table-IV

Results with Statistical Analysis (n = 24)

Steps	No.	Salt		P-value	Placebo	
		PEFR ↓	PEFR ↑		PEFR ↓	PEFR ↑ or No change
Step-I	6	3 (50%)	3 (50%)	P>0.05	0 (00%)	6 (100%)
Step-II	7	7 (100%)	0 (00%)	P<0.01	1 (16.68%)	6 (85.71 %)
Step-III	8	6 (75%)	2 (25%)	P<0.001)	2 (25%)	6 (75%)
Step-IV	3	3 (100%)	0 (00%)	P<0.05	0 (00%)	3 (100%)

Discussion

Bronchial asthma is a ambiguitus disease. It can affect all ages irrespective of sex. As it is not a curable disease, so avoidance of exciting factors and prevention by the antiinflammatory drugs are the mainstay for adequate control.

Epidemiologic and experimental evidence suggests that high levels of salt consumption are associated with spastic disorders of smooth muscle i.e. essential hypertension and bronchial asthma. In hypertensives ß-receptors of smooth muscles are down regulated by salt loading, leading to contraction. Hence, salt sensitivity seems to be a common phenomenon of both disorders, at least in many patients.

The way in which increased salt intake exerts its effects in patients with bronchial asthma is uncleared. However, there are data from in vitro and in vivo experiments that they may explain the mechanism of salt sensitivity. From the work of Sauhrada and Souhrada[8], we know that after renewed antigen contact, sensitized bronchial muscle cell demonstrate an influx of Na+ with consequence stimulation of the electric Na-K+ pump and hyperpolarization. The intracellular increase in Na+ is associated with increase in Ca++ and contraction of muscle cell.

The result of our study obtained in a small number of asthmatic support the hypothesis of salt sensitivity in asthmatics. When asthmatic are subjected to salt loading, asthma symptoms become worse, lung function deteriorated and the use of antiasthmatic drugs increased, which is more marked in Step-II, Step-III, Step-IV. The result is equivocal in Step-I. This may be due to fact that Step-I asthmatics have the mild disease and the airway between two episodes remains completely normal and less sensitive to salt loading.

Conclusion

Our results suggests that increase in dietary salts results in physiological deterioration of asthma patients and poor control during management. So, dietary salts restriction appears to have a favorable effect in patients with asthma and to reduce the need for antiasthmatic drugs.

References

1. David W. Hudgel. Bronchial Asthma. In: Gerald L. Baum (ed. in ch.). Text book of pulmonary disease. 5th edn. Little Brown and Company. 1993; vol-1 : p-647.
2. Kobzik L, Frederick J, Schoen. The lung. In: Ramzi S, Cotran (ed. in ch.). Robin's pathologic basis of disease. 5th edn. W.B. Saunders Company 1994; p-692.
3. Gleiberman L. Blood pressure and dietary salt in human population. Ecol. Food Nutri. 1973; 2 : 143-145.
4. Cookson JB. Prevalence of asthma in developing countries and their comparison with those in Europe and North American. Chest. 1987; 91 (suppl): 9755-10355.
5. Burney PGJ, Neild JE, Twort CHC, Chinn S, Jones TD, Mitchel WD, et al. Effect of changing dietary sodium on the airway response to histamine. Thorax, 1989; 44 : 36-41.
6. David A, Cashley MJ, Bowl MF. Effect of dietary salt on bronchial hyperreactivity in histamine in asthma. BMJ. 1988; 297 : 454.
7. Skrabal F, Kotanko P, Meister B, Doll P, Gruber G. Up regulation of α_2-adrenoceptor, and down regulation of $ß_2$-adrenoceptor by high salt diet in normotensive hypertension, 1986; 4(suppl) : 1366-69.
8. Souhrada M, Souhrada JF. Sensitization induced sodium influx and airway smooth muscle cell. Am. Respir. Dis. 1985; 131 : A356.

COMPARISON OF DAILY VERSUS ALTERNATE DAY THERAPY WITH CORTICOSTEROIDS IN THE TREATMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

MD. KHAIRUL HASSAN JESSY[1], MIRZA MOHAMMAD HIRON[2], MD. SAYEDUL ISLAM[3], ROWSHNE JAHAN[3], AKM MOSTAFA HOSSAIN[3], MD. MOSTAFIZUR RAHMAN[3]

Summary

The study was carried out in the Institute of Diseases of the Chest and Hospital (IDCH), Dhaka, during the period of from December 1996 to June, 1998. It was a two-week prospective case control study. Of the initial 78 patients, 60 completed the study. There was 28 males and 32 females in both daily therapy (DT) and alternate day therapy (ADT) groups. Mean age was 58.83± 1.77 years in the DT group and 58.30 ± 2.19 years in the ADT group. The majority of the study patients were within the range of 51-80 years. All were smokers. Ten healthy nonsmoker subjects of around same age, sex and socioeconomic status (mean age 61 ± 1.99 years) were taken as control for comparison of lung function tests of the patients prior to commencement of therapy.

A standard proforma with questionnaire was designed and filled to select patients with Chronic obstructive pulmonary disease (COPD). The patients were selected according to the predetermined criteria viz. Peak expiratory flow rate (PEFR) < 200 L/min, Forced expiratory volume in one sec (FEV_1) < 1.5 L, FEV_1/FVC% <60%. To establish the diagnosis and for pretreatment evaluation, necessary baseline investigations were done. The patients were then allocated into two treatment groups, viz. daily-therapy (DT) and alternate-day therapy (ADT) group on the basis of simple random technique. DT group of patients were given prednisolone (0.5 gm/kg/day) in a single dose daily and ADT group of patients were given prednisolone every alternate day at doses twice the equivalent daily dose orally in a single dose in the morning for 2 weeks. Daily clinical evaluation and peak expiratory flow rate (PEFR) estimation were done. Post treatment evaluation, including pulmonary function tests were done after 2 weeks. Results were analyzed and compared statistically. Twenty-three (76.66%) out of 30 (100%) cases in the DT group and 21(70%) out of 30 (100%) case in the ADT group were improved and relieved of their symptoms. There were statistically significant improvements in PEFR, FEV_1, FVC and FEV_1 / FVC ratio in both the DT and ADT groups after two weeks of therapy, and no significant difference in the amount of improvement between the two groups was observed. The mean FEV_1 improved more in the ADT groups, while the mean FVC improved more in the DT group. Of the 19 patients (19 / 60, 31.67%) with more than a 25 percent improvement in their FEV_1, 10 were in the DT group and 9 were in the ADT group. This study confirms that the administration of corticosteriods to patients with COPD results in substantial improvement of pulmonary function in 31.67 percent of the patients. In addition, the present study suggests that corticosteriod therapy initiated on an alternate-day basis is as effective as that given on daily basis when the total dose per 48 hours period is the same.

Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of death and disability in the adults worldwide. It is also a common clinical problem in Bangladesh and is increasing in this country like other parts of the world due to urbanization, industrialization and change of profession of people from agriculture and fresh air-based rural communities to industry and smoking-based urban communities.

The administration of corticosteroids to patients with COPD results in substantial improvement in the pulmonary function of 20 to 30 percent of the patients.[1,2] Accordingly, several investigators [2,3,4] have recommended that patients with COPD whose symptoms are not well-controlled while taking inhaled and oral selective (32 adrenergic agonists, inhaled ipratropium bromide (metered dose inhaler [MDI] and oral theophylline be given a short (2-4 weeks) trial of

1. Department of Medicine, Central Police Hospital, Dhaka
2. Department of Medicine, Institute of Diseases of Chest and Hospital, Dhaka
3. Department of Respiratory Medicine, Institute of Diseases of Chest and Hospital, Dhaka

high dose oral corticosteroids. Then the corticosteroid therapy is continued in those who improve and discontinued in those who do not. When corticosteroids are administered on an alternate-day regimen, the side effects are substantially reduced.[5,6] Short acting corticosteroids should be given on alternate 'days but at twice the equivalent daily dose in maintenance therapy, whenever possible. Another study suggested that in patients with COPD, initiation of corticosteroid therapy with an alternate-day regimen is as effective as initiation of therapy with a 6-hourly regimen if the total dose of corticosteroids per 48-hour period is the same.[4] Another study reported that alternate-day corticosteroids therapy adequately controlled symptoms in 84 percent of 30 patients with chronic asthma who had responded to daily corticosteroids.[7]

Since the alternate-day regimen is associated with fewer side-effects and we have frequently encountered difficulty in switching patients from daily to alternate-day corticosteroid regimens, the present two weeks prospective case control study was designed to compare the efficacy of equivalent doses of prednisolone given either daily or every 48 hours to patients with COPD. Then aim of this study was to compare the efficacy of prednisolone given daily or every alternate day to patients with COPD, if the total dose of prednisolone per 48 hour is the same.

Materials and Methods

This prospective case control study was done in IDCH, Dhaka during the period of December 1996 to June 1998. The patients were identified according to the predetermined criteria as well as criteria of inclusion and exclusion. A detailed history was taken and COPD cases were diagnosed on the basis of complains of cough, sputum, dysponea and smoking habits etc. In the second phase, a through physical examination was done for pretreatment assessment of patients and to exclude other causes of cough, sputum, dyspnoea, wheeze etc. Selection criteria of patients were history suggestive of chronic bronchitis and/ or emphysema with suggestive physical findings, Chest X-ray criteria of emphysema and lung function results as PEFR < 200 L/min, FEV_1 < 1.5 L, FEV_1/FVC % <60%. Exclusion criteria to be absent like use of corticosteroids during the 4 weeks preceeding the study for any reason, significantly disabled patients due to COPD, associated life threatening complications of COPD like corpulmonale, spontaneous pneumothorax etc, Chest x-ray showing active tuberculosis, consolidation, bronchiectasis or any mass shadow. The patients were allocated into two groups, viz. daily therapy (DT) groups (n=30) and alternate-day therapy (ADT) group (n=30) on the basis of simple random technique. The patients were assessed both subjectively and objectively before commencement of therapy. These results were taken as baseline control values for the respective groups. Study procedure was on Day 1 to 14 DT group was given prednisolone (0.5 mg/kg/day) orally in a single dose daily in the morning. In ADT (alternate day theraphy) group prednisolone was given orally every alternate day at doses twice the equivalent daily dose in the morning, in a single dose. Daily medical check up and PEFR estimation done. Final post treatment evaluation was done to see the objective and subjective responses of prednisolone. All the investigations including pulmonary function tests were done. All the datas were compilated and statistical analysis was done.

Results

Out of 60 patients, 30 were categorised as daily therapy group and the rest 30 as alternate therapy group. Ten healthy and nonsmoker persons were selected as control for comparison of lung function test of the patients prior to commencement of therapy. Age distribution of the patients are shown in Table-I. Age of the patients ranged 41-80 years (mean ± SE, 58.83 ±1.77) in the DT group and 39-75 years (Mean ± SE, 58.3± 2.19) in the ADT group. In the control group the mean ± SE age was 61.0± 1.99 years, range (45-75 years). All the patients studied in both groups were smokers or ex-smokers with the majority having the history of smoking more than 20 pack years (Table-II). Patients with history of smoking more than 20 pack-years ranked the top of the list. The control (n=10, 100%) were nonsmokers. Cough and dyspnoea were the predominant symptoms in both the groups (Table III). In both the DT and ADT group, cough and dyspnoea were present in all the 30(100%) patients. Duration of cough in the DT group was (Mean ±SE) 16.33 ± 1.49 years (ranges 5-35 years) and in the ADT group, 22.07 (± 1.55) years (range 7-41 years) (Table IV). In the DT group, mean (± SE) duration of dyspnoea was 8.70(±0.88) years (range 5-20 years) and in the ADT group was 13.50(±1.26) years (range 5-25 years). Lung function tests between control, DT and ADT groups were estimated and analysed prior to prednisolone theraphy (Table V and VI). The difference between control and DT & control and ADT groups, regarding pretreatment lung function tests was statistically significant. Lung function test between DT and ADT groups were thoroughly analysed and compared (Table VII).

Table VIII shows complications after completion of theraphy. No significant difference was observed between DT and ADT groups regarding complications.

Table -I

Age distribution of control and cases.

Age groups (Years)	Groups		
	Control(n=10) No. (%)	DT (n=30) No. (%)	ADT (n=30) No. (%)
31-40	0	0	4(13.33)
41-50	3(30.00)	8(26.66)	4(13.33)
51-60	2(20.00)	11(36.66)	9(30.00)
61-70	2(20.00)	6(20.00)	7(23.33)
71-80	3(30.00)	5(16.66)	6(20.00)
Range(years)	45-75	41-80	39-75
Mean± SEM	(16.00±1.99)	(58.83± 1.77)	(58.30±2.19)

Table -II

Smoking habits in control and cases.

Smoking habits	Groups		
	Control(n=10) No. (%)	DT (n=30) No.(%)	ADT (n=30) No.
Smoker	0	3(100.0)	30(100.00)
<10 Pack-year	0	0	0
10-20 Pack-year	0	4(13.33)	7(23.33)
>20 Pack-years	0	21(70.00)	19(63.33)
Ex-smoker (>20) Pack-years	0	5(16.67)	4(13.33)

Table -III

Major symptoms at the start of trial in patients

Major symptoms	Groups	
	DT (a=30) No. (%)	ADT (n=30) No.
Cough	30(100.00)	30(100.00)
Dyspnoea 30(100.00)	30(100.00)	
Productive sputum		
Scanty and mucoid	19(63.33)	17(56.66)
Copious and loose	4(13.33)	7(23.33)
Purulent or mucopurulent	7(23.33)	6(20.00)
Wheeze	17(56.66)	20(66.66)
Chest tightness	3(10.00)	5(16.66)
Fever	7(23.33)	6(20.00)

Table-IV

Analysis of duration of cough and dyspnoea is patients

Cough/ Dyspnoea	Group	
	DT(n=30)	ADT(n=30)
Cough		
Range (years)	5.35	7-41
(Mean± SE)	(16.33±1.49)	(22.07±1.55)
Dyspnoea		
Range (years)	5-20	5-25
(mean ± SE)	(8.70± 0.88)	(13.50 ± 1.26)

Table-V

Comparison of lung function tests between control and daily therapy (DT) group of patients.

Pretreatment Parameters	Control (n=10) Range (Mean ± SEM)	DT(n=30) Range (Mean ± SEM)	't' value	'p' value
PEFR(L/min)	220.00-450.00	70.00-180.00	6.22	<0.001
	(314.00±29.04)	(131.00±4.85)		
FEV_1(L)	1.65-3.29	0.42±1.20	7.47	<0.001
	(2.26±0.20)	(0.76±0.04)		
FVC(L)	2.29-3.83	0.88-3.07	5.68	<0.001
	(2.85±0.20)	(1.62±0.10)		
FEV_1 / FVC	70.80-89.60	32.90-59.20	14.36	<0.001
ratio(%)	(78.63±1.72)	(47.99±1.27)		

Table-VI

Comparison of lung function tests between control and alternate-day therapy (DT) group of patients.

Pretreatment Parameters	*Control(n=10)* Range (Mean± SE)	*DT(n=30)* Range (Mean± SE)	't' value	'p' value
PEFR(L/min)	220.00-450.00	80.00-180.00	6.33	<0.001
	(314.00±29.04)	(128.00±4.41)		
FEV_1 (L)	1.65-3.29	0.42-1.15	7.33	< 0.001
	(2.26±0.20)	(0.79±0.04)		
FVC(L)	2.29-3.83	1.11-3.07	5.35	<0.001
	(2.85±0.20)	(1.73±0.08)	.	
FEV_1 / FVC	70.80-89.60	34.60-55.80	15.56	<0.001
ratio(%)	(78.63±1.72)	(45.92±1.21)		

Table-VII

Comparison of lung function tests between daily therapy and alternate-day theraphy (ADT) group of patients before and after theraphy.

Pretreatment Post treatment	DT(n=30) Range Mean± SE	ADT(n=30) Range Mean± SEM	't' value	'p' value
PEFR (L/min)	70.00-180.00	80.00-180.00	0.46	NS
Pretreatment	(131.00±4.85)	(128.00±210.00)		
One week	90.00-210.00	100.00-210.00	0.29	NS
Post treatment	(154.00±5.40)			
Two weeks	90.00-280.00	90.00-270.00	0.69	NS
Post-treatment	(185.67±7.99)	(177.33±910)		
FEV_1 (L)	0.42-1.20	0.42-1.15	0.58	NS
Pretreatment	(0.76±0.04)	(0.79±0.04)		
Two weeks	0.42±1.50)	0.60-1.60	0.45	NS
Post treatment	(0.91±0.05)	(0.95±0.06)		
FVC(L)				.
Pretreatment	0.88-3.07	1.11-3.07	0.87	NS
	(1.62±0.10)	(1.73±0.80)		
Two weeks	0.86-3.32	1.15-3.07	0.021	NS
Post treatment	(1.84±0.11)	(1.84±0.09)		
FEV_1 / FVC ratio (%)	.90-59.20	34.60-55.80	1.18	NS
Pretreatment	(47.99±1.27)	(45.92±1.21)		
Two weeks	35.30-67.30	36.80-65.80	0.203	NS
Post-treatment	(51.18±1.86)	(51.67±1:60)		

Table-VIII

Comparison of post-treatment complications between daily therapy (DT) and alternate-day therapy (ADT) group of patients.

Complications	Groups		P value
	DT(n=30) No.(%)	ADT(n=30) No. (%)	
Weight gain(kg)	13(43.33)	7(23.33)	NS
[Mean±SE)	[0.96 ±0.105]	[0.93±0.13]	
Dependent	5(16.66)	2(6.66)	NS
Oedema			
Moon face	3(10.00)	1(3.33)	NS
Exacerbated	1(3.33)	1(3.33)	NS
cough			
Insomnia	1(3.33)	1(3.33)	NS
Hypertension	2 (6.66)	1(3.33)	NS
Hyperglycaemia	4(13.33)	2(6.66)	NS

Table-VIII

Comparison of post-treatment complications between daily therapy (DT) and alternate-day therapy (ADT) group of patients.

Complications	Groups		P value
	DT(n=30) No.(%)	ADT(n=30) No. (%)	
Weight gain(kg) [Mean±SE)	13(43.33) [0.96 ±0.105]	7(23.33) [0.93±0.13]	NS
Dependent Oedema	5(16.66)	2(6.66)	NS
Moon face	3(10.00)	1(3.33)	NS
Exacerbated cough	1(3.33)	1(3.33)	NS
Insomnia	1(3.33)	1(3.33)	NS
Hypertension	2(6.66)	1(3.33)	NS
Hyperglycaemia	4(13.33)	2(6.66)	NS

Discussion

Severe COPD is uncommon in persons less than 40 years old, but it becomes increasingly prevalent in patients beyond that age. This is apparent from various survey studies of the general population. Most patients with COPD seek medical attention because of symptoms when they are between 55 and 65 years old[8]. In this study, most of the patients (> 70%) in both the DT and ADT groups fell within the age range of 51-80years. A considerable number of patients were in the 51-60 years age group (36.66% and 30.00% in the DT and ADT group respectively. A negligible number of cases were found below 40 years (13.33%, 4 out of 30 cases in the ADT group only). Various studies showed that it is more prevalent in the late fifth and early sixth decades of life[9]. Cigarette smoking is the principal identified risk factor in the causation of COPD, yet only a minority of persons who smoke develop COPD while an occasional lifelong nonsmoker may develop severe disease. Other factors are clearly operative, but their identity remains largely unknown.[10] Symptoms only associated with COPD include dyspnoea, cough, sputum expectoration and wheezing. Dyspnoea and cough are two universal features of COPD. It was also observed in this study. Cough and dyspnoea were present in all the 60(100%) patients. This result is parallel with study of Hossain.[11] Still cough and dyspnoea must be evaluated in every patient as a cardinal symptom of COPD before treatment and after a short course of prednisolone therapy. After corticosteroid therapy 83.33 percent of patient in the DT group and 80 percent in the ADT group showed, to some extent, improvement of dyspnoea. Cough was also improved in 76.66 and 70 percent patients in the DT and ADT group respectively, at the end of prednisolone therapy.

The present study showed that daily and alternate-day prednisolone therapy is equally effective in the treatment of COPD. Mean duration of cough was 16.33 and 22.07 years in the DT and ADT groups respectively. Mean duration of dyspnoea. was 8.70 and 13.50 years in the DT and ADT group respectively. This finding is parallel with Hossain's study[11], where the mean duration of COPD was 8.5 years. Production of sputum and wheeze are two important symptoms of COPD. In this study, all patients of DT and ADT groups had history of sputum expectoration. The character of sputum varies from scanty and mucoid to copious and loose and purulent or mucopurulent and the patients variably responded to therapy with prednisolone. In the present context, wheeze was the presenting symptom in 56.66 percent cases in the DT group and 66.66 percent in the ADT group. In this study, 23(76.66%) out of 30 (100%) cases and 21(70%) out of 30 (100%) cases were improved and relieved of their symptoms in the DT and ADT group, respectively. That is to say, prednisolone is equally effective in both steroid-treated groups, regarding subjective relief of symptoms. Most centres of the Western World use FEV_1, FVC and FEV1/FVC ratio to measure airflow.[12] But these are less widely used in Bangladesh because many physicians do not have access to spirometer. PEFR is the most widely used lung function test. But PEFR indicates only first 10 millisecond of maximum expiratory flow rate, it indicates only larger airway obstruction, so there was

associated evaluation with spirometry, for the validity of peak expiratory flow measurement in the study.[12,13] The measurement of the PEFR potentially meets this criteria to assess the severity of obstruction & its degree of reversiblity. The criterion of an absolute increase in PEFR of 60 L/min avoids having to make any calculations and seems to be an excellent way of predicting reversibility.[13] In this study, means improvement of PEFR was 23.33 L/min in both steroid-treatment group (23 L/min in the DT group and 23.67 L/min in the ADT group) after 1 week and 52 L/min (54.67 L/min in the DT group and 49.33 L/min in the ADT group) after 2 weeks. This is comparable with Hussain's study,[14] who showed mean improvement of PEFR as 25.6 L/min after 2 weeks treatment in the steroid responder group. Measurement of reversibility of airflow obstruction in response to bronchodilators is often used in clinical studies and research work. Recommended criteria for response to a bronchodilator is 12 percent of baseline FEV_1 and and absolute change of 200 ml, suggested by American Thoracic Society,[14] 25 percent of basline FEV_1 in at least 2 of 3 tests, suggested by American College of Chest Physicians[14] and 15 percent or more improvement in FEV_1[3]. In this study, mean improvement in FEV_1 was 160 ml in both steriod treated groups (150 ml in DT group and 170 ml in the ADT group). It is comparable to Hussain's study (1995)[11], who showed mean improvement of FEV_1 as 150 ml in the steroid-responder group. FEV_1 represents the integrated flow over the first second of expiration. It is relatively independent of effort unlike PEF. Significant difference between control and both steroid-treated groups (DT and ADT groups) were observed regarding pretreatment lung function tests ($P<0.001$). The difference between pretreatment and post-treatment lung function tests were statistically significant within the both steroid-treated groups. There was a highly significant difference between pretreatment and post-treatment PEFR and FEV_1 ($P<0.001$) in both the groups. There was also significant difference between the pre and post-treatment FVC (in the DT group $P<0.001$ and in the ADT group $P<0.05$). The difference between pre-and post treatment FEV_1/ FVC ratio was also significant (in the DT group $P<0.02$ and in the ADT group $P<0.001$). Though statistically significant difference was observed within both steroid-treated groups, before and after therapy, there was no significant difference between the groups regarding pre-and post-treatment values. That is, there was no significant differences in the amount of improvement in the two groups. In other words, prednisolone is equally effective in both the groups. In this study, complications were observed two weeks after prednisolone therapy. There was no significant difference of complications between the two groups. This result is parallel with studies by Albert[15] and Hossain[11]. Weight-gain was the commonest complication in both steroid-treated group. Dependent oedema, moon-face, hypertension and hyperglycaemia were common in the DT group although the results were statistically not significant while there are many variables, it is generally agreed that complications are caused by the duration of treatment and size of the dose. It was not possible to see the complications in the present study - since it was carried out for a short period (2 weeks) of time. Further studies of longer duration are needed to see the complications. No case of intercurrent infection was noted in both steroid treated group during the 14 days study period. In this study, there were significant improvements in the FEV_1 in both the daily therapy and alternate-day therapy groups after 14 days of therapy ($P<0.001$) and no significant differences in the amount of improvement in the two groups. The mean FEV_1 improved more in the ADT group [in the DT group 0.15 (19.74%) and in the ADT group 0.17 L (21.79%)], while the mean FVC improved more in the DT group [in the DT group 0.22 L (13.58%) and in the ADT group 0.11 (6.36%)]. Of the 19 patients with more than 25 percent improvement in their FEV_1, 10 were in the DT group and the rest 9 were in the ADT group. Other authors suggested that steroid -associated increases in FEV_1 of less than 30 percent should be interpreted with caution.[3] The results of the present study suggest that alternate-day theraphy is effective in some patients with COPD who have little or no asthmatic component. This study confirms previous well-controlled studies[2,1,3,4] which concluded that 20-30 percent of patients with severe COPD will have a significant improvement in their flow rates. when they are given corticosteroids. However, it is possible that some patients would respond to daily but not to alternate-day therapy. No significant difference was observed in the occurrence of side-effects between the two groups. This is probably attributable to the short duration of the study. Patients with COPD whose symptoms are not well- controlled while taking inhaled and oral selective $ß_2$ adrenergic agonists, inhaled ipratropium bromide and oral theophylline be given a short trial (2 weeks) of oral corticosteriods. Then the corticosteriod therapy is continued in those who improve and discontinued in those who do not. In view of the lower incidence of side-effects with alternate-day therapy as observed by other workers and equivalent and comparable efficacy of daily and alternate-day regimens, alternate-day therapy with prednisolone at doses twice the equavalent daily dose may be tried initially.

References

1. Herding SM, Freedman SA comparison of oral and inhaled steroid in patients with chronic airways obstruction: features determining response. Thorax 1978; 33: 214-9.
2. Shim C, Stover DE, Williams MH Jr. Response to corticosteriods in chronic bronchitis, J Allergy Clin Immuno1.1978; 62-363-7
3. Mandella LA, Manfreda. J, Warren CPW, Anthonisen NR. Steroid response in stable chronic obstructive pulmonary disease. Ann Intern Med 1982; 96 : 17-21.
4. Blair GP, Light RW. Treatment of chronic obstructive pulmonary disease with corticosteriods: comparison of daily vs alternate-day therapy. Chest 1984; 86 : 524-8.
5. Harter JG, Reddy WJ, Thorn GW. Studies on an intermittent corticosteroid dosage regimen. N Engl J Med 1963; 269 : 591-6.
6. Ackerman GL, Nolan CM. Adrenocortical responsiveness after alternate-day corticosteriod therapy. N Engl J Med 1968; 278 : 405-9.
7. Fanta CH. Clinical aspects of COPD. The ACCP Pulmonary Board Review, 1997; 7-15.
8. Newoehner DE. Clinical aspects of chronic obstructive pulmonary disease, In: Baum GL, Wolnsky E, editors, Textbook of Pulmonary disease. Vol. II, 5th ed. Boston: Little Brown and company 1994; 995-1028.
9. Seaton A, Seaton D, Leitch AG. Chronic bronchitis and emphysema, In: Crofton and Doughlas's respiratory disease. 4th ed. Oxford: Balckwell Scientific Publication 1989; 490-511.
10. Fletcher C, Peto R. The natural history of chronic airflow obstruction Br. Med J. 1977; 1:1645-8.
11. Hossain R. Determination of predictive indices in corticosteriod responders and non-responders suffering from chronic obstructive pulmonary disease [thesis]. Dhaka: University of Dhaka. 1995.
12. Spiro SG, Roberts CM. Lung function tests. Med Intern 1995; 9: 242-9.
13. Dekker Fw, Schrier AC, Sterk PJ, Dijkman JH. Validity of peak expiratory flow measurement in assessing reversibility of airflow obstruction. Thorax 1992; 47:162-6.
14. Gold WM. Pulmonary function testing, In: Murray JF, Nadel JA, editors. Textbook of respiratory medicine. Vol. I, 2nd ed. Philadelphia: WB Saunders Company 1994; 798-881.
15. Albert RK. Martin Tr, Lewis SW. Controlled clinical trial of methylprednisolone in patients with chronic bronchitis and acute respiratory insufficiency. Ann Intern Med 1980; 92: 753-758.

AMBIGUOUS GENITALIA-DUE TO CONGENITAL ADRENAL HYPERPLASIA-A CASE REPORT

MD. ABDUL MANNAN[1], ZAKIR HOSSAIN[2], SK. MD. ABU ZAFOR[3], SHOHAEL MAHMUD ARAFAT[4], HAJERA MAHTAB[5], AK KANDAKER[6]

Summary

A 19 years unmarried, female presented with primary amenorrhoea, under developed breasts, hirsutism and general weakness. She observed gradual enlargement of her clitoris and development of increased body hair. Her voice was low-pitched male type. Physical examination and laboratory investigations substantiated the diagnosis of female pseudohermaphroditism due to congenital adrenal hyperplasia. Synthetic adrenal steroid and female hormones (estrogen and progesterone) were instituted as treatment. This is a rare form of autosomal recessive genetic disorder.

Introduction

Congenital adrenal hyperplasia (CHA) represents a group of autosomal recessive disorders characterized by adrenocortical deficiency or total lack of a particular enzyme involved in the biosynthesis of steroids particularly cortisol.[1-7] Steroidogenesis is then channeled into the pathway leading to increased production androgen that accounts for virilization.[8-9] Simultaneously the deficiency of cortisol results in increased secretion of ACTH resulting in adrenal hyperplasia. Certain enzyme defects may also impair aldosterone secretion causing salt wasting. In female pseudohermaphroditism, affected individuals have normal ovaries and mullarian derivatives associated with ambiguous external genitalia. In the absence of testes, a female will be musculinized if subjected to increase circulating levels of androgens derived from an extragonadal source. There are six major types of congenital adrenal hyperplasia (CAH) all transmitted as autosomal recessive disorders. Among them, 21-hydroxylase deficiency is the commonest form of the enzymatic abnormalities in the pathway of steroid biosynthesis.[10] The incidence of this particular form of congenital adrenal hyperplasia in the USA is believed to be approximately 1:5000 live births. However, the incidence may vary from nation to nation.

Case note

A 19 year unmarried female hailing from a village of Keranigonj was admitted in the Medical unit of SSMC & Mitford hospital, Dhaka in February, 2001 with the complaints of primary amenorrhoea since her puberty, under developed breasts, development of male sexual characteristics i.e beard, moustache, increased pubic, axillary and body hairs. She had generalized weakness. According to the patient's statement about 5 years back she noticed gradual development of her beard, moustache and increased body hair. She also noticed gradual development of her clitoris. She does not have any history of taking drugs related to hirsutism nor had any history of other systemic disorders. On examination, she had increased facial hair (hirsutism), breasts were under developed. Her pulse rate was 82/minute, blood pressure 120/65mm of Hg, temperature 95°F. Skin condition was normal. She had low pitched male type voice. Other systems revealed no abnormalities. General physical examination also revealed increased body hair especially facial hair. Height was 141.7 cms, arm spans 145 cms, pubic hair at stage- PH4, clitoris: enlarged length 5cms and circumference 4cms.

Followings are the investigation reports :

WBC-6300/Cmm.DC:N-56%, L-38%, E-4%, M-2%.S. creatinine -0.7mg/dl S. urea-23mg/dl. Urine for routine examination :Normal finding .Chromosomal Karyotype-46xx, Sex chromatin: +ve (Barr body-present).

USG of the lower abdomen showed uterus of normal in size and shape, anteverted in position. Myometrial echotecture was uniform. Tubo ovarian region was

1. Department of Endrocrinology & Metabolism, SSMC & Mitford Hospital, Dhaka
2. Department of Medicine, SSMC & Mitford Hospital, Dhaka
3. Department of Medicine, SSMC & Mitford Hospital, Dhaka
4. Department of Medicine, SSMC, Mitford, Dhaka
5. Clinical Services, Research and Academy, BIRDEM, Dhaka
6. Department of Medicine, SSMC & Mitford Hospital, Dhaka

normal. No enlargement of adrenal glands could be seen. No definitive testis could be seen in the pelvic cavity. Chest X-ray and ECG were normal. Serum testosterone level was 4.36ng/ml. (Normal level: male; 2.5-10.51ng/ml and famale ; 0.10ng/ml-0.96ng/ml).Serum ACTH Level was 80pg/ml(normal level: 8.3-57.8pg/ml).LH and FSH level were 4.60microU/ml(normal 3-20microU/ml) and 8.12 microU/ml(normal 2-15 microU/ml) respectively. Radiological bone age was 18 years. T3, T4 and TSH level were 2.80 nmol/L,143.2 nmol/1 and 2.45 microU/ml respectively. 17 hydroxyprogesterone was measured after injection of 250 microgram synthetic ACTH (synecthen).After one hour 17 OH progesterone level was 11.81 ngm/ml(normal value : Follicular phase ;0.10.8 ngm/ml, Luteal phase 0.3-2.9 ngm/ml). Serum electrolyte levels were Na + 141mmo1/L,K+4.1 mmol /L,Cl -104 mmol /L, $TC0_2$-25 mmol/L. Laparoscopy revealed normal finding.

Discussion

Congenital adrenal hyperplasia (Female Pseudohermaphroditism) is an autosomal rececive disorder.[1,3,7] This is a rare form of disorder presenting with ambiguous genitalia. Patients may present with early skeletal maturation leading to short final height. In our patient, in addition to the above features, hirsutism, primary amenorrhoea and history of intercurrent infection were present. Clinical findings and investigations substantiated the diagnosis of congenital adrenal hyperplasia. We did not find enlarged (hyperplastic) adrenal gland by ultrasound. CT Scan might detect this, which was not available in this hospital. Patient has excessive facial hair (hirsutism). It is due to defect in the pathway of normal steroid synthesis leading to over production of androgenic hormones. [1,3,7] In our patient, there was increased production of 17 OH progesterone and probably androstenidione and testosterone that indicates abbaration of normal steriodogenic pathway.[1,3,7,11] These high androgens caused hirsutism and male type body habitus as well as ambiguous genitalia. Height of the patient was below 3rd percentile. It is probably due to early fusion of epiphysis with metaphysis. Replacement of glucocorticoid with or without minerelocorticiod in all forms of congenital adrenal hyperplasia is essential.[1,3,7] It corrects metabolisms and lowers ACTH level .It also reduces androgen over production with remission of hypertension and or virilization.[8-10] We started dexamethasone 0.5 mg and estrogen 0.625 mg daily. She was advised to take surgical correction of ambiguous genitalia e.g., Clitoroplasty or clitoral resection rather than Clitoridectomy. For the treatment of hirsutism, oesterogen was given the form of oral contraceptive. She was advised to remove her facial hair (hirsutism) by local therapy like plucking shaving, electrolysis or use of depilatory cream. These patients may be helped leading near normal life if periodically supervised while kept under hormonal therapy.

References

1. Jubiz W. The Adrenals. Endocrinology. A logical for approach for clinicals. Mc Graw-Hill book company. New York, Sydney, Toronto, Tokyo, Singapore. 2nd Edition, Chapter V ; 1987: p168-178.
2. Gordon H, Williams, Robert G and Diuhy. Diseases of the adrenal cortex. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL . Harrison's Principles of Internal Medicine 14th edn. McGraw- Hill. New York, 1998:p-2 105, 2124-2127.
3. Edwards CRW, Taft AD and Walker BR. Endocrine disease. In: Haslett C, Chilvers ER, Hunter JAA and Boon NA . Davidson's principles and practice of medicine 18th edn. Churchill Living Stone, Edinburgh, 1999. P-591-595.
4. Schneider MA and Honour JW. Adrenal cortex, tumour and peripheral production of deoxycorticosterone. Steroids. 1992; 57 : 7-12.
5. Cotran RS, Kumar V and Collins T . Robbins.Congenital adrenal hyperplasia. Cotran RS, Kumar V and Collins T . Robbins Pathologic Basis of diseases. 6th edition, W B Saunder's Company, Philadelphia, 1999. P-1157-1159.
6. Griffing GT and Melby JC. Hirsutism : Causes and treatments. Hospital Practice 1991; 30 : 26 : 43-58.
7. Felix A, Conte MD, Melvin M and Grambach MD. Abnormalities of sexual differentiation. Congenital adrenal hyperplasia. In: Amad CD, Aron DC, Baxter JD, Findling JD, Greenspan FS, Biglieri EG . Basic and Clinical endocrinology, USA. 3'd edition. 1991. P505-509.
8. Aziz R: Non classic adrenal hyperplasia current concepts J.CIin.Endocrinol Metab 1994; 78 : 810
9. White MC and Ginsburg J. The hirsute female .In : Crosignani PG, Rubin BL. Endocrinology of human infertility : new aspects. London,England, Academic Press : New York, Grune and Stratton, 1981. 307-25. Proceeding of the Serono Clinical Colloquia on Reproduction No 2.
10. New MI : Steroid 21 OH (Hydroxylase) deficiency (Congenital adrenal hyperplasia) Am J Med. 1995; 98 : 25.

ISOLATED DUODENAL TUBERCULOSIS - A CASE REPORT AND LITERATURE REVIEW

H. AFTAB[1], M. HASAN[1], M.T. RAHMAN[1], S.M. ISHAQ[1], Z.R. KHAN[2], A.S.M.A. RAIHAN[1]

Introduction

Gastrointestinal tuberculosis (GITB) is not uncommon in our country and its symptoms can mimic that of other GI diseases. Isolated duodenal involvement is rare. Here we report a case of isolated duodenal tuberculosis. The purpose of this report is to heighten clinician's awareness of the varied presentations of GITB. Limitations of clinical evaluation, radiology, endoscopy and value of laparatomy in the diagnosis of GITB is stressed.

Case Report

A 35 year old lady presented with history of upper abdominal pain and vomiting after meals for three months. She used to vomit solid food about $1^1/_2$ to 2 hours after meals, liquids were well tolerated. She had immediate relief of her pain after vomiting. There was no history of fever, cough, jaundice, hematemesis, melena or any bowel alteration. Her appetite was normal. There was no significant weight loss. She had no history of contact with the patient of tuberculosis or any abdominal surgery in the past. Physical examination was unremarkable.

Investigations revealed a haemoglobin of 10 gm/dl, erythrocyte sedimentation rate 25 mm in first hour, complete blood count within normal limit, peripheral blood film showed non specific morphology, blood glucose 2 hours after breakfast was normal, liver function tests were normal. She had a normal chest X-ray. Her mantoux test was 10 mm. Endoscopy of upper GI tract was done on three occasions and showed mucosal irregularly, nodularity, surface ulceration and contact bleeding in whole of the second part of duodenum (Fig.-1). Repeated endoscopic biopsy revealed evidence of chronic inflammation only, no granulomata or evidence of malignancy seen.

Ba meal study of stomach, duodenum and follow through of small gut showed persistent narrowing of the 3rd and 4th part of the duodenum with proximal dilatation of the 2nd part of the duodenum, rest of the gut was normal (Fig.-2). Ultrasonography of whole abdomen revealed para-aortic lymphadenopathy.

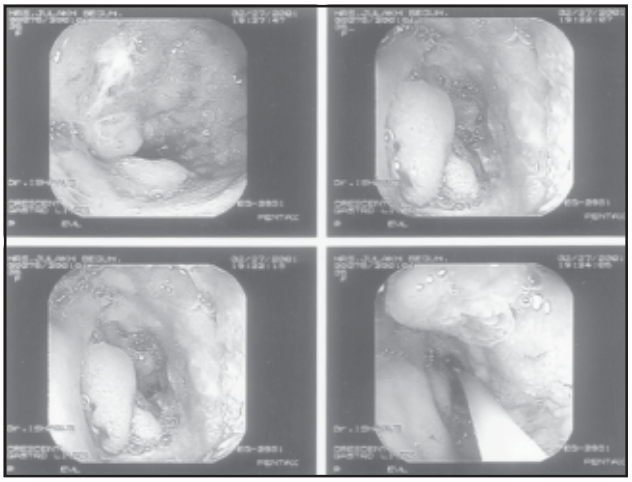

Fig.-1 : *Endoscopic picture of Duodenal tuberclosis*

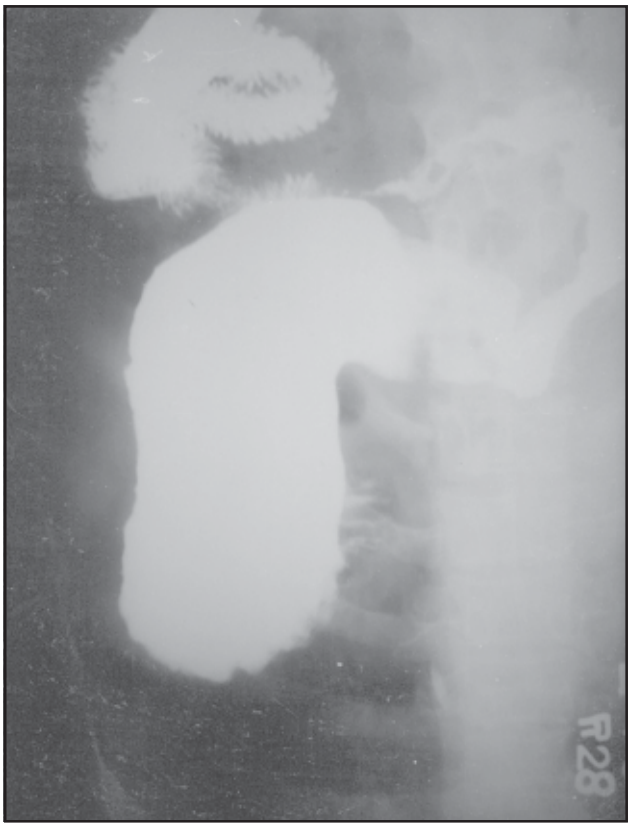

Fig.-2 : *Barium meal showing pepsistent narrowing of duodenum*

1. Department of Gastrointestinal, Liver and Pancreatic Diseases, BSMMU, Dhaka.
2. Department of Surgery, BSMMU, Dhaka.

Bangladesh J Medicine 2002; 13 : 31-33

Later on she had laparatomy. At laparatomy, stomach was dilated, 1st, 2nd and 3rd part of the duodenum appeared normal, duodenojejunal flexure was compressed by one mesenteric lymphnode. Multiple tubercles were seen on the serosal surface of the duodenojejunal flexure. Ileocaecal area was also thickened. Rest of the gut was normal. Mesenteric lymphnodes were enlarged. Antecolic gastro-jejunostomy was done. Histopathology of the mesenteric lymphnode showed caseating glanulomatous lymphadenitis consistent with tuberculosis (Fig.3). Postoperative period was uneventful and antituberculous chemotherapy was started.

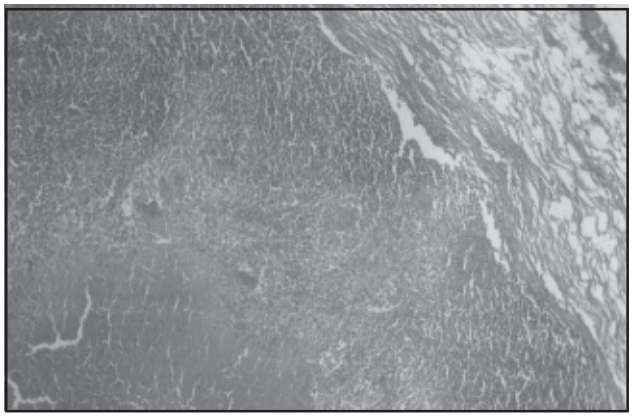

Fig.-3 : *Histopathology of biopsy showing tuberculous granuloma*

Discussion

Tuberculosis is the leading cause of infectious death and approximately 2 million death occurs annually and one half of the world population is infected with Mycobacterium tuberculosis at present.[1] Upto 5% of patients with M.tuberculosis have GI involvement and GI tract is reported to be the sixth most common extrapulmonary site.[2] Within the GI tract, the ileocaecal area is the most common site of involvement. The trophism is thought to be due to the relative physiologic stasis in this area and the increased density of lymphoid tissue for which bacilli have an affinity.[2,3]

Duodenal involvement accounts for only 2.5% of TB enteritis.[4] The disease may be extrinsic, intrinsic or both.[4] In extrinsic type there can be either primary duodenal involvement or compression due to enlarged periduodenal lymphnodes. With intrinsic involvement lesions are ulcerative, hypertrophic and ulcerohypertrophic. In our case both were present, external compression from surrounding lymphnodes as well as ulcerohypertrophic mucosal lesion.

The clinical manifestations of duodenal TB are non specific. Abdominal pain and vomiting are common presentation of duodenal TB, fever and weight loss may be present, some patients may present with upper GI bleeding. Palpable epigastric mass is found in 33% of patients of duodenal TB.[6] Upto 60% may have active pulmonary TB.[7] Our patient had features of outlet obstruction and did not have any evidence of pulmonary TB.

Radiographic studies may be helpful but they are non specific. Endoscopy may not be diagnostic as in our case and biopsies obtained show only inflammatory changes. Ultrasonography and CT scan has limited utility as diagnostic test but these can give a supportive evidence as ultrasonogram of our case revealed para-aortic lymphadenopathy.

Laparatomy with biopsy is often needed to confirm the diagnosis.[8] When resection of the affected part is difficult, a bypass procedure followed by antituberculous treatment should be the treatment of choice.[8]

Upper GI bleeding, perforation and fistulation with other parts of GI tract and even the kidney and aorta[8,9,10,11] and obstructive jaundice,[12] are recognized complications of duodenal TB.

Conclusion

Without a high index of suspicion duodenal tuberculosis being the rarest form of intestinal tuberculosis poses great difficulty in diagnosis. Suspicion supported by endoscopy, radiological investigation, exploratory laparatomy and histopathological examination of the tissue biopsy can only lead to a definitive diagnosis. Treatment is surgical as well as medical with antituberculous therapy.

References

1. Marshall JB. Tuberculosis of gastrointestinal tract and peritoneum. Am J Gastroenterol 1993 88 : 989-99.
2. Richter JM. Case records of the Massachusets General Hospital. N Engl J Med 1983 309 : 96-104.
3. Moss JD, Knauer CM. Tuberculous enteritis: A report of three patients. Gastroenterology, 1973; 65 : 959-66.

4. Paustin FF. Marshall JB. Intestinal tuberculosis. In : Berk EJ, Haubrich WS, Kalser MH, et al editors. Gastroenterology, Philadelphia : WB Saunders, 1985; 3 : 208-36.

5. Misra D, Raj RR, Nandy S et al. Duodenal tuberculosis presenting as bleeding peptic ulcer. Am J Gastroenterol 1988; 83 : 203-4.

6. Geeason T, Prinz RA, Kirsch EP et al. Tuberculosis of duodenum. Am J Gastroenterol 1979; 72 : 36-40.

7. Shakil AO, Korula J, Kanel BC, Mussay NGB. Reynolds TB Diagnostic features of tuberculous peritonitis in the absence and presence of chronic liver disease : a case control study. Am J Med 1996; 100 : 179-85.

8. Gupta SK, Jain K, Gupta AP et al. Duodenal tuberculosis. Clin Radiol 1998 159-61.

9. Smith DR. Kidney infections. In : Smith DR, ed, General Urology. Lange Medical Publications, 1978 : 387-8.

10. Schwartz PT, Garner HA, LaHimer JK et al. Pyeloduodenal fistula due to tuberculosis. J Urol 1970 104 : 373-5.

11. Edie DGA, Pollock DS. A complicated aortoduodenal fistula. Br J Surg 1968; 55 : 314-7.

12. Shah P, Ramakantan.R, Deshmukh H. Obstructive jaundice - unusual complication of duodenal tuberculosis. Indian Journal of Gastroenterology, April 1991; 10(2) : 62-3.

REVIEW ARTICLE

PROGNOSTIC FACTORS OF HEPATOCELLULAR CARCINOMA (HCC)

A K AZAD, P K ROY, M T RAHMAN, M HASAN

Hepatocellular carcinoma is the most common primary malignant hepatic neoplasm.[1,2] It is the fourth most common cause of death worldwide.[3,4] HCC ranks as the seventh most common cancer in men and the ninth most common in women and eighth commonest when both sexes are combined.[5] HCC frequently has a rapidly progressive clinical course, low rate of respectability, poor response to non-operative treatment and hence a grave prognosis. To prognosis of HCC patients is determined not only the HCC stage (number and size of the nodules, vascular invasion, extrahepatic spread, presence of symptoms), but also by the functional status of the underlying liver.[6] The prognosis of patients with advanced HCC is poor. In 83.5% of patients, death occured within 6 months of the onset of symptoms, if untreated.[7] HCC is a continuously progressive tumour, leading to death from tumour growth, tumour recurrence, extrahepatic metastasis or underlying liver cirrhosis. Progressive hepatic failure with hepatic coma and cachexia are the main causes of death, gastrointestinal bleeding, rupture of the tumour with fatal haemorrhage and severe infection are other frequent causes. Different studies have shown the following prognostic factors

Age

Age of onset of HCC varies in different parts of the worlds.[8] The incidence of hepatocellular carcinoma (HCC) generally rises progressively with age although it tends to level off in the oldest age group.[9] Advanced age is usually associated with reduced survival. In a study by Collier et al[10] shows significantly worse prognosis in those aged >65 years compared with patients less than 65 years (10.5 vs 18.5 weeks).

Sex

Hepatocellular is more common in males all over the world. The greater susceptibility of males may be related to hormones or genetics or to a greater exposure to carcinogenic environmental factors such as HBV infection, higher rates of cirrhosis in males, smoking and alcohol drinking.[11] Male sex shows adverse effect on survival. The five years survival after onset of symptoms in developing countries is 0.8% in men and 4.4% in women.12 Female sex is associated with prolonged survival (Sutton et al).[13] Study by Falkson et al[14] in patients of HCC from North America and South Africa, male sex showed adverse effect on survival. In another study by Ng IO et al[15] showed the following in females (i) lower incidence of tumour recurrence, (ii) increased median survival (36.5 months vs 12.4 months in male), (iii) tumour encapsulation was higher than in males (80% vs 45%), (iv) tumours were less invasive (37%) in women than in men (61 %).

Geographical variation

The prognosis also varies depending on the geographical location. The course seems to be rapid in Southern Europe, South Africa and Honkong. Study by Falkson et al[14] found no difference in survival between white and black patients within North American but North American patients survived longer than South African patients.

Clinical stage

Prognosis of HCC depends upon the clinical stage of the patient. Presence of cirrhosis, low albumin, high bilirubin and advanced stage were associated with short survival. Onodera et al[16] also found short survival with advanced stage. Okuda et al[17] found median survival 8.3 months for stage-1, 7 months for stage-II and 2 months for stage-III, with an overall median survival of 1.6 months. Severe jaundice and ascites are invariably associated with a poorer prognosis.

Tumour size

Onodera et al[17] and Hsu HC et al[18] confirmed tumour size is an important prognostic factor and ominous sign is a large tumour. Another study shown small tumours (<3 cm) are associated with a 1 year survival of 90.7%, a 2 years survival of 53% and 5 years survival

Department of Gastrointestinal, Liver and Pancreatic Diseases, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka

Bangladesh J Medicine 2002; 13 : 26-28

of 12.8%. Study by DiCarlo-V et al[19] published 10 years experience in surgical treatment of HCC in 122 cirrhotic patients. Probability was significant for tumour size.

Cirrhosis

Cirrhosis of liver of any cause is an important risk factor for the development of hepatocellular carcinoma (HCC) which is the principal cause of death in patients with cirrhosis.[20,21] Male sex, age and duration of cirrhosis are the main risk factors for HCC in cirrhotic patients. Nzeako et al[22] found patients of HCC with cirrhosis i) were older, ii) had high grade tumour, iii) portal vein invasiveness was more, iv) had high AST and bilirubin levels and low albumin had a poorer prognosis and HCC without cirrhosis were found to be more capsulated and those patients had prolonged survival. Sutton et al[13] showed that without cirrhosis presence of the lesion in the left lobe was associated with prolonged survival and shorter survival with presence of cirrhosis. In a study by Smalley et al[23] also found survival significantly more favourable in noncirrhotic HCC than in cirrhotic HCC. Cirrhotic patients presented with a single hepatic mass or a dominant primary with satellite lesions in contrast to the usual multinodular or diffuse disease seen in cirrhosis.

Invasiveness

Infiltrating tumours have a worse prognosis than expanding ones. The presence of intact capsule is a good sign. Haratake et al[24] found portal vein with or without hepatic vein invasion was associated with poor prognosis. In both small and large HCC, invasive tumours were accompanied by high mortality from tumour recurrence even when the tumour was small indicating that intrahepatic spread may start very early during the growth of HCC.

Histologic findings

The degree of cancer cell differentiation varies from case to case and area to area in the same liver. According to the degree of differentiation, HCC is classified into (i) well differentiated, (ii) moderately well differentiated and (iii) undifferentiated (pleomorphic). Low histologic grade, mild mitotic activity and the presence of some fibrosis within the specimen were associated with a favorable outcome within noncirrhotic HCC[24]. Lee et al[25] followed 51 patients of HCC <5 cm underwent hepatic resection. In group A, cancer cells were confined within the capsule. Seven years survival rate was 100%. In group B, there was extracapsular extension and survival (7 years) was 47.5%. In group C, there was PV thrombosis and survival was 47.5%. Group D had no capsule and survival was 37.5%. Sonoda et al[26] reported two patients of HCC who were treated surgically. The tumours consisted of a broad area of dense collagenous stroma that embedded the nodules of HCC. Microscopically, nodules of cancer cells were separated by the dense fibrous stroma with lymphocytic infiltration. These patients survived for 10 years and 8 years.

Viral marker

HBV has the strongest association with the development of HCC in patients who are hepatitis 'B' carriers, whereas HCV related HCC only occurs after development if cirrhosis. HCC with positive HBsAg was somewhat associated with portal vein invasion and HBsAg positivity is one ominous sign from the prognostic point of view (Harataka et al.[24]

Ploidy pattern

The ploidy pattern of nuclear DNA may serve as a useful prognostic marker for hepatocellular carcinoma. In a study by Omagari et al[27] measured nuclear DNA content of 41 cases of HCC measured by flow cytometry. Twenty five were diploid and 16 were aneuploid. In the aneuploid cases, the serum AFP level were found to be higher and stage more advanced. Patients with aneuploid tumours had a poorer prognosis than those with diploid tumours.

P^{53} gene mutations

P^{53} gene mutation at codon 249 have been reported in HCC from China and South Africa, a phenomena shown P^{53} mutations on HCC might be an independent prognostic predictor. In a study by Hayashi et al[28] found p^{53} mutations were significantly associated with the degree of differentiation of HCC. The mutation was found in 35.9% cases of poorly differentiated HCC and 66.7% cases of anaplastic HCC. P^{53} mutations were an unfavourable prognostic factor related to recurrence.

Management

Survival of patients depend on the management. Without treatment, most of the patients die within 3-6 months (Isselbacher et al)[29]. Survival also depends upon the modality of treatment. In a study by Onodera et al[16] showed 5 years survival was 53.7% for hepatic resection, 38.7% for PUT and 13.5% for TAE. Sutton et al[13] also showed longer survival of patients who underwent resection. In a retrospective study by Stuart et al[30] found significantly shorter survival of untreated groups and systemic chemotherapy groups. Okuda et al found median survival of 229 patients without specific treatment 1.6 months. Median survival of surgically treated group was 12.2 months, for small HCC 29 months. Medical treatment did prolong survival in stage II and III patients.

References

1. Molmenti EP, Marsh JW, Dvorchik I, Oliver JH-3rd; Madariaga J; Iwatsuki S et al. Primary hepatic neoplasms. Surg Clin North Am 1999; 79 : 43-57.
2. El Serag HB; Mason AC. Rising incidence of hepatocellular carcinoma in the United States. N Engl J Med 1999; 340: 745-50.
3. Fernandez MP; Redvanly RD. Primary hepatic malignant neoplasms. Radiol Clin North Am 1998; 36 : 333-48.
4. Wolfgang H; Caselman. Pathogenesis of hepatocellular carcinoma. Digestion 1998; 59(Suppl.2): 60-63.
5. R Idilman; N DeMaria; A Colantoni and DH Van Thiel. Pathogenesis hepatitis B and C induced hepatocellular carcinoma. J Viral hepatitis, 1998, 285-299.
6. Calvel X, Bruix J, Gines P, Bru C, Sole M; Vilana R et al. Prognostic factors of hepatocellular carcinoma in the West. A multivariate analysis in 206 patients. Hepatology; 12 : 753-760.
7. Jen-pei Lee. Hepatoma presenting as craniospinal metastasis: analysis of 16 cases. Journal of Neurology, Neurosurgery and Psychiatry 1992; 55 : 1037-39.
8. Martin P. Hepatocellular carcinoma. Risk factors and natural history. Liver Transpl Surg 1998; 4(Suppl.1): 87-91.
9. Lai CL, Gregory PB, Wu PC, Lok AS, Wong KP, Ng MM. Hepatocellular carcinoma in Chinese males and females. Possible causes for the male preponderance. Cancer 1987; 60: 1107-10.
10. Collier JD, Curless R, Bassendine MF, James OF. Clinical features and prognosis of hepatocellular carcinoma in Britain in relation to age. Age Ageing 1994; 23: 22-7.
11. Hepatitis Viruses, IARC Monographs on the evaluation of carcinogenic risks to humans, vol 59. Lyon. International Agency for Research on Cancer, 1994. p. 202.
12. Sakamoto M, Hirohashi S. Natural history and prognosis of adenomatus hyperplasty and early hepatocellular carcinoma. Upn J Clin Oncol 1998; 28 : 604-8.
13. Sutton FM, Russel NC, Guinee VF, Alpert E. Factors affecting the pronosis of primary liver carcinoma. J Clin Oncol 1988; 6 : 321-8.
14. Falkson G, Cnaan A, Schutt AJ, Ryan LM, Falkson HC. Prognostic factors for survival in hepatocellular carcinoma. Cancer Res 1988; 48 : 7314-8.
15. Ng 10, Ng MM, Lai EC, Fan ST. Better survival in female patients with hepatocellular carcinoma. Possible causes from a pathologic approach. Cancer 1995; 75: 18-22.
16. Onodera H, Ukai K, Minami Y. Hepatocellular carcinoma cases with five year survival and prognostic factors affecting the survival time. Tohoku J Exp Med 1995; 176 : 203-11.
17. Okuda K, Ohtsuki T, Obata H, Tomimatsu M, Okazaki N, Hasegawa H et al. Natural history of hepatocellular carcinoma and prognosis in relation to treatment study of 850 patients. Cancer 1995; 56 : 918-828.
18. Hsu HC, Wu TT, Wu MZ, Sheu JC, Lee CS, Chen DS. Tumor invasiveness and prognosis in resected hepatocellular carcinoma. Clinical and pathogenetic implication. Cancer 1988; 61 : 2095-9.
19. Di Carlo V, Ferrari G, Castoldi R, Nadalin S, Marenghi C, Molteni B et al. Surgical treatment and prognostic variables of hepatocellular carcinoma in 122 cirrhosis. Hepatogastroenterology 1995; 42 : 222-9.
20. Kew MC; Yu MC; Kedda MA; Coppin A; Sarkin A, Modkinson J. The relative roles of hepatitis B and C viruses in the aetiology of hepatocellular carcinoma in south Africans blacks. Gastroenterology 1997; 112 :184-7.
21. Shiratori Y; Shiina S; Zhang PY; Ohno E; Okudoira T, Payawal DA et al. Does dual infection by hepatitis B and C viruses play an important role in the pathogenesis of hepatocellular carcinoma in Japan : Cancer 1997; 80 :2060-7.
22. Nzeako UC, Goodman ZD, Ishak KG. Hepatocellular carcinoma in cirrhotic and noncirrhotic livers. A clinico histopathologic study of 804 North American patients. Am J Clin Pathol 1996; 105 : 65-75.
23. Smalley SR, Moertel CG, Hilton JF, Weiland LH, Weiland HS, Adson MA. Hepatoma in the noncirrhotic liver. Cancer 1988; 62 : 1414-24.
24. Haratake J, Harie A, Takeda S, Hisawomi K, Tokudome S. A clinical pathological study involving a consecutive series of 75 primary liver carcinomas with resection. Gan No Rinsho 1988; 34 : 759-63.
25. Lee CS, Hwang LY, Beasley RP, Hsu HC, Lee HS, Bin TY. Prognostic significance of histologic findings in resected small hepatocellular carcinoma Acta Chir Scand 1988; 154 : 199203.
26. Sonoda T, Shirabe K, Kanematsu T, Takenaka K, Sugimachi K. Long term surviving patients with hepatocellular carcinoma comprised of dense collagenous stroma. Am J Gastroenterol 1989; 84 :1087-91.
27. Omagari K, Imanishi T, Morikawa S, Nishihata S, Kamiya T, Hayashida K, Tanioka H et al. Prognostic implications of the ploidy pattern of the nuclear DNA in hepatocellular carcinoma. Gan No Rinsho 1990; 36 : 121-6.
28. Hayashi H, Sugio K, Matsumata T, Adachi E, Takenaka K, Sugimachi K. The clinical significant of p53 gene mutation in hepatocellular carcinoma from Japan. Hepatology 1995; 22 : 1702-7.
29. Isselbacher KJ, Dienstage JL. Tumors of the liver. In: Harrison's principles of Internal medicine. 13th edition. Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci As, Karper DL. eds. McGraw Hill Inc. 1994; 1495-98.
30. Stuart KE, Anand AJ, Jenkins RL. Hepatocellular carcinoma in the United States. Prognostic features, treatment outcome, and survival. Cancer 1996; 77 : 2217-22.
31. Okuda K. Clinical aspects of hepatocellular carcinoma-analysis of 134 cases. In: Okuda K, Peters RL. Editors.Hepatocellular carcinoma, New York: Wiley, 1976 : 387-436.

EFFECT OF LOW DOSE ALFACALCIDOL ON RADIAL BONE MINERAL DENSITY IN POSTMENOPAUSAL OSTEOPOROSIS

M MATIUR RAHMAN, S A HAQ, M N ALAM, M A JALIL CHOWDHURY, M A RAHIM, M A HASANAT

Summary

Vitamin D has antiosteoporotic activity in both postmenopausal and senile osteoporosis. Besides hormone replacement therapy, bisphosphonate, salmon calcitonin, ipriflavone and some other agents are found to have antiresorptive effect in postmenopausal osteoporosis. This study was undertaken to find out the effect of one-year low dose vitamin D in the form of 1a-(OH)D_3 (alfacalcidol) on bone mineral density (BMD) of patients with postmenopausal osteoporosis. Twenty-two women with postmenopausal osteoporosis were assigned to this study. Alfacalcidol was given at the dose of 0.25 mg daily. Distal radial BMD was measured for assessment of the effect of the drug on bone mineral density. Serum calcium, phosphate, 24-hour urinary calcium & phosphate were measured to study its effect on calcium metabolism. Twenty patients completed the trial. BMD of the distal radius decreased from 0.311±0.033 to 0.307±0.036 g/cm^2 (not significant) after one year of treatment with alfacalcidol. The parameters of calcium metabolism did not change significantly. The study showed that long-term effect of alfacalcidol at the daily dose of 0.25 mg does not increase bone mass.

Introduction

According to consensus conference definition, osteoporosis is defined as a systemic disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in fragility and susceptibility to fracture.[1] Bone mineral density (BMD) measurements form the basis for a more practical and operational definition of osteoporosis with better clinical utility.[2] By current definitions, osteoporosis is defined as BMD >2.5 standard deviation (SD) below the young adult mean value.[3] The aim of treatment of osteoporosis is to maintain and to restore the bone mass density, so as to prevent fractures and immobility in late life.[2] Physical exercise, adequate calcium intake and avoidance of smoking and alcohol are important general measures for treatment and prevention of osteoporosis. Several studies have shown the beneficial effect of estrogens, bisphosphonates and calcitonin in increasing the BMD and in reducing the incidence of fractures.[4-5]

Classically vitamin D deficiency has been associated with a failure to mineralize the organic matrix of skeleton, giving rise to two diseases : rickets in children and osteomalacia in the adult.[6] Recently, it is assumed that vitamin D supplement might have beneficial effect on osteoporosis. Vitamin D deficiency may cause decreased bone mass and imposes increased risk of femoral neck fracture among elderly individuals.[6-7] The role of vitamin D in regulating postmenopausal bone metabolism and prevention of osteoporotic vertebral fracture and its beneficial effect on the BMD has recently been stressed.[7-8] The agents most widely used are parent vitamins, 1,25$(OH)_2D_3$ (calcitriol) and alfacalcidol.[6-7] Some studies suggested that the effect of calcitriol or alfacalcidol on the BMD of patients with osteoporosis are dose dependent.[8-12] Alfacalcidol is a synthetic analogue of calcitriol that is metabolized to calcitriol by its 25-hydroxylation in the liver.[13]

The present study was undertaken with a view to evaluating the effect of 1a-$(OH)D_3$ on BMD in a one-year period of treatment in postmenopausal osteoporotic women.

Materials and Methods

This open, prospective clinical trial was conducted in the department of Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. Patients presenting with postmenopausal osteoporosis in the Rheumatology clinic, department of Medicine, BSMMU, between June and November 1998 were included in the study.

All patients were assessed clinically. Body mass index (BMI) was calculated. Following laboratory tests were carried out routinely : complete blood counts including ESR, alkaline phosphatase, ALT, serum calcium, serum inorganic phosphate, serum

Department of Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka

creatinine, routine urinalysis, 24 hours urinary calcium & phosphate, X-ray of thoracic and of lumbar parts of the vertebral column in antero-posterior and lateral views and BMD measurement. Densitometry of the distal radius of the non-dominant arm was done with the help of single x-ray absorptiometry. Women with age ³50 but £70 years, BMI <30 kg/m^2, with osteoporosis confirmed by BMD value of distal radius of non dominant arm lower than -2.5 SD (T-score) were included in the study. Those with serious co-morbidity, or known hypersensitivity to alfacalcidol, with substantial scoliosis, moderate to severe osteophytosis or spinal fusion (determined by antero-posterior dorsal and or lumber spine X-ray), with secondary osteoporosis, were excluded from the study. Informed consent was obtained before entry into the trial.

Alfacalcidol was given at the dose of 0.25 mg once daily after meal. The subjects were instructed to keep an account of number of tablets used during the whole period of treatment. All patients were followed up 2 monthly for the first 6 months and then at the end of the study- after one year. In addition to this routine follow up, the subjects were advised to visit any time if they found any difficulty during the whole course of the study. For assessment of drug safety, history of any new symptom was taken and following laboratory tests were performed : routine urinalysis, complete blood counts, Hb%, ESR, serum calcium, phosphate, alkaline phosphatase, ALT, serum creatinine. For assessment of the effect of alfacalcidol on bone mass, distal radial BMD was measured at the end of one year. Serum calcium, inorganic phosphate, 24-hour urinary calcium & phosphate were measured at one year to assess the effect of the drug on calcium metabolism.

Statistical analysis

Data were collected in a structured questionnaire and analyzed using SPSS PC 7.5 version. The significance of the differences between pre and post treatment values was estimated by Wilcoxon signed rank test.

Results

A total of 22 female patients were included in the trial. Two patients discontinued the study due to loss of interest. Eventually, 20 patients completed the study. Baseline data of these patients are shown in table-I. Data of these 20 valid completers were finally used in all subsequent analyses.

BMD decreased from 0.311±0.033 to 0.307±0.036 g/cm^2 after one year of treatment. This decrease was not significant. Serum calcium, phosphate, alkaline phosphatase as well as twenty-four hour urinary calcium and twenty-four hour urinary phosphate excretion were not changed significantly (table -II).

Six patients developed adverse effects (table-III). All of them developed gastrointestinal symptoms. Anorexia, constipation, abdominal discomfort and nausea were the common adverse effects. No serious or life threatening events occurred during the study.

Table-I

Baseline characteristics of patients.

Parameters	Patients (n-20)
Age (year)	63.23± 3.89
Body mass index (Kg/m^2)	22.37 ± 3.22
Bone mineral density (BMD) g/cm^2	0.311±0.033
Hb% (gm%)	11.18 ± 0.65
ESR (mm)	30.72 ± 8.12
TC (K/µL)	7.93 ± 1.37
Alkaline phosphatase (U/L)	206.70 ± 27.69
Serum creatinine (mg/dl)	0.85± 0.10
Serum calcium (mg/dl)	9.08 ± 0.24
Serum inorganic phosphate (mg/dl)	4.07 ± 0.27
24 hours urinary calcium mg/24h	173.42 ± 45.23
24 hours urinary phosphate (mg/24h)	569.43 ± 173.70

Table-II

Treatment response after 12 months (n=20).

Parameters	Month 0	Month 12	P
Bone mineral density (BMD) (g/cm^2)	0.311±0.033	0.307±0.036	NS
Alkaline phosphatase (U/L)	206.70 ± 27.69	194.60 ± 21.56	NS
Serum calcium (mg/dl)	9.08 ± 0.24	9.17 ± 0.26	NS
Serum inorganic phosphate (mg/dl)	4.07 ± 0.27	4.10 ± 0.43	NS
24-hour urinary calcium mg/24h	173.42 ± 45.23	182.83 ± 54.36	NS
24-hours urinary phosphate (mg/24h)	569.43 ± 173.70	547.55±166.59	NS

Table-III

Adverse effects

Symptom	No of patients
Gastrointestinal disturbances	6
Headache	1
Vertigo	1
Insomnia	1

Discussion

The mechanism of action of vitamin D in treating postmenopausal osteoporosis is not exactly known. The primary insult, in menopause-induced osteoporosis, is not related to vitamin D but rather related to a lack of estrogen. The lack of estrogen has an important effect on bone, allowing it to be easily mobilized. Calcium coming from the skeleton then floods into plasma compartment, suppressing parathyroid hormone, which in turn suppresses production of $1,25(OH)_2D_3$. This results in low calcium absorption and also suppresses other actions of $1,25(OH)_2D_3$. Low calcium absorption is associated with osteoporosis in the postmenopausal women. Whether plasma levels of $1,25(OH)_2D_3$ are low or not in these conditions is still controversial, but since calcium absorption is low, it is likely that plasma $1,25(OH)_2D_3$ levels are insufficient to stimulate the intestine. Finally, a decrease in the receptor for vitamin D that can account for reduced calcium absorption has not been found consistently. Thus in post-menopausal osteoporosis the vitamin D endocrine system is probably involved as a secondary factor in the pathogenesis of the disease.[6-7, 13]

Alfacalcidol, now available in Bangladesh, is a costly drug. The aim of this study was to determine the effect of one-year treatment with low dose alfacalcidol on bone mineral density in postmenopausal osteoporosis. The BMD at the end of the study period was not significantly different. The effect of $1,25(OH)_2D_3$ or $1a\text{-}(OH)D_3$ (alfacalcidol) on the bone mass of patients with postmenopausal osteoporosis appears to be dose dependent.[8-12] It has been claimed that a daily dose of 0.25 µg, 0.50 µg or at an average daily dose of 0.43 µg $1,25(OH)_2D_3$ have no significant effect on bone mass.[9-10, 12] Similarly, no effect was observed with a daily dose of 0.25 µg of $1a\text{-}(OH)D_3$.[8, 11] Results of this present study also support these observations. Due to lack of facilities, measurement of serum vitamin D level was not possible in the present study. Baseline data and data after one year showed insignificant increases in serum calcium and phosphate and an insignificant reduction of 24 hours urinary phosphate level. During the same period 24 hours urinary calcium level increased insignificantly. Because of the lack of laboratory facilities, we could not measure serum bone Gla-protein, calcitonin, parathyroid hormone, osteocalcin and urinary hydroxyproline.

Finally, it may be concluded from this limited study that daily low dose alfacalcidol (0.25µg) does not have beneficial effect on BMD in post-menopausal osteoporotic women. Long-term use of this agent at a higher dose (>0.75µg) with larger sample size and comparison with well-matched controlled group is needed to assess its favorable effect, if any, on BMD.

Acknowledgement

We are grateful to Dr. Tasmin, Department of Gynaecology and Obstretics, BSMMU, for measuring the BMD of these patients. We are also indebted to the doctors of the Rheumatology clinic, BSMMU, for their sincere efforts to run the work smoothly.

References

1. Consensus development conference. Diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 1993; 94 : 646-50.
2. Christiansen C. The strategy for the treatment of osteoporosis. Osteoporosis Int 1997; 7 (Suppl. 3) : S147-S49.

3. World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. WHO Technical Report Series 843. Geneva : WHO,1994 : 1-129.

4. Macodo JM, Macedo CR, Elkis H, De Oleveira IR. Meta-analysis about efficacy of antiresorptive drugs in postmenopausal osteoporosis. J Clin Pharm Ther 1998; 23(5) : 345-52.

5. Blank RD, Bockman RS. A review of clinical trials of therapies for osteoporosis using fracture as an end point. J Clin Densitom 1999; 2(4) : 435-52.

6. Deluca HF. 1,25-Dihydroxyvitamin D_3 in the pathogenesis and treatment of osteoporosis. Osteoporosis Int 1997; 7 (Suppl. 3) : S24-9.

7. Nakamura T. Vitamin D for the treatment of osteoporosis. Osteoporosis Int 1997; 7 (Suppl. 3) : S155-8.

8. Orimo M, Shiraki H, Hoshino T Onaya T, Miyajaki S, Kurosawa H, Nakamura T, Ogawa N. Effect of 1a hydroxyvitamin D_3 on lumber bone mineral density and vertebral fractures in patients with postmenopausal osteoporosis. Calcif Tissue Int 1994; 54 : 370-6.

9. Aloia JF, Vaswani A, Yeh JK. Calcitriol in the treatment of postmenopausal osteoporosis. Am J Med 1987; 84 : 401-8

10. Gallagher JC, Goldgar D. Treatment of postmenopausal osteoporosis with doses of synthetic calcitriol. Ann Intern Med 1990; 13 : 649-55.

11. Christiansen C, Christiansen MS, McNair P. Prevention of early postmenopausal bone loss : controlled 2-year study in 315 normal females. Eur J Clin Invest 1980; 10 : 273-9.

12. Ott MS, Chesnut CH. Calcitriol is not effective in postmenopausal osteoporosis. Ann Intern Med 1989; 110 : 267 : 74.

13. Kanis JA, McCloskey EV, deTakats D. Treatment of osteoporosis with vitamin D. Osteoporosis Int 1997; 7 (Suppl. 3) : S141-6.

HUNTER SYNDROME (TYPE-B) - A CASE REPORT

M ISMAIL PATWARY[1], M NAZRUL ISIAM[2], FAISAL AIMED[2], M MATIUR RAHMAN[1]

Summary

The mucopolysaccharidoses (MPS) represent a broad spectrum of disorders due to deficiency of one of a group of enzymes that degrade three classes of mucopolysacharides: heperan sulfate, dermatan sulfate, and keratan sulfate. MPS are usually the disease of the early decades of genetic inheritance with variable morbidity and mortality. Presentation varies, though many of the clinical features are common. Identification of the type of MPS excreted in the urine, together with detailed clinical and radiological evaluation help to narrow the diagnosis but assay of specific enzymes may require. So far we know this is the first case report in Bangladesh. The only limitation of this case report is, failure of the demonstration of MPS type excreted in the urine due to lack of facility.

Case note :

15 years old boy was admitted in MAG Osmani Medical College Hospital with the complaints of short stature and umbilical swelling. His growth was normal up to the age of 5 years and retardation thereafter. School performance was good up to the class V and then discontinuation of study due to physical incapability. The umbilical swelling used to increase in size on coughing. His bowel and bladder habit was normal. One year back he had been hospitalized for generalized swelling of whole body, and was diagnosed as a case of chronic liver disease (CLD) of no detectable cause. His birth history was normal, since then he had no major ailment other then failure to growth. Other family members were of normal health and height. Mother didn't suffer any major illness and no history of taking teratogenic drugs during his intrauterine life. Parents had no consanguineous relation and there was no such abnormality in his maternal side. He is from low socio-economic class.

On examination, patient had a grotesque appearance with flat profile and large dolichocephalic head with prominent frontal sinuses. The patient was not anemic or edematous. Height - 112 cm (vertex to pubis 52 cm and pubis to heel 60 cm), Arm span110 cm, weight 25 kg. He had a hoarse and croaky voice. Corneas were normal. Abdominal wall was lax and bowel loops were visible. He had got a large reducible umbilical hernia (Fig. 1) and hepatomegaly of 6 cm without splenomegaly. Genitalia were infantile. Locomotor system examination revealed proportional limbs to his trunk. Joints were neither tender nor swollen, but stiff on extension.

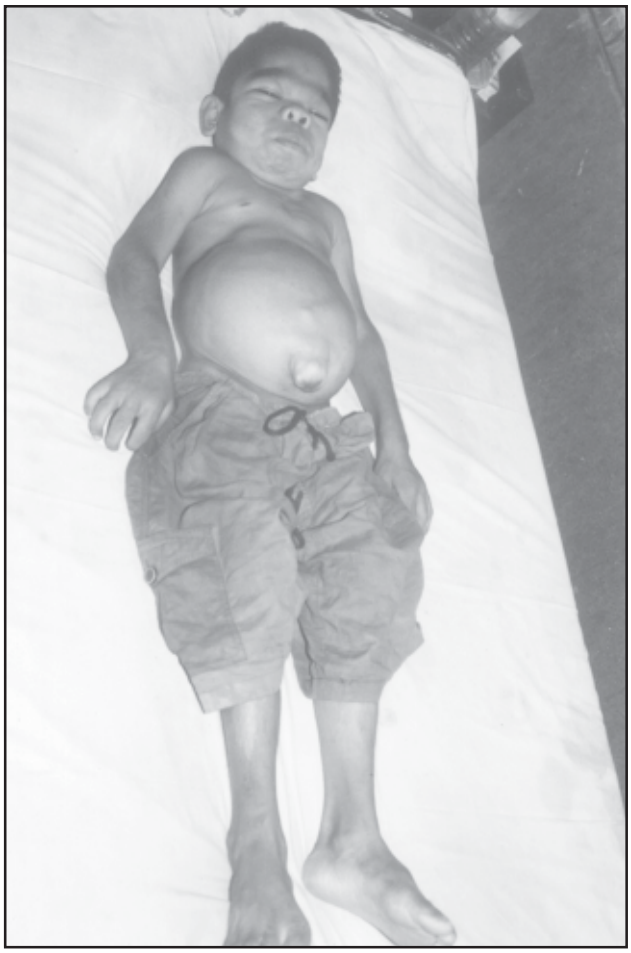

Fig.-1 : *Patient with short stature with umbilical hernia*

Routine investigation of urine, full blood count, X-ray chest were normal. Peripheral blood film was normal without any vacuolated lymphocytes. Ultrasonography revealed, hepatomegaly with coarse echo pattern. His thyroid function tests were normal. Follicle stimulating hormone (FSH), and Leuteniging hormone (LH) was normal but Testosterone was low-2ngm/ml (4.7- 17.2 ngm/ml). Skeletal survey revealed typical findings of mucopolysacchandoses (Fig: 2, 3 & 4). Histopathology of the liver biopsy revealed ballooning dilatation of hepatocytes with central

1. Dept. of Medicine and Neuromedicine, MAG Osmani Medical College, Sylhet
2. Dept. of Medicine BSMMU, Shahbag, Dhaka.

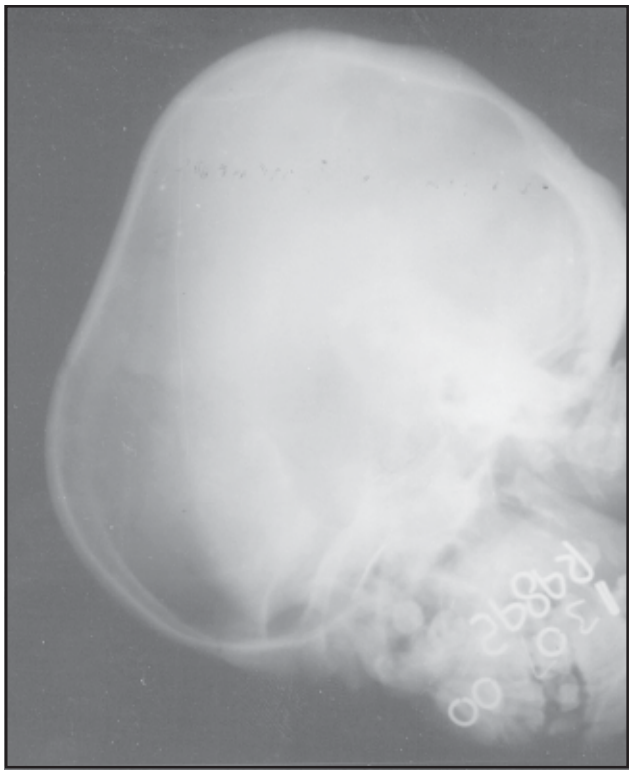

Fig.-2 : *Skull X-ray showing hyperostosis, large boot shaped sella turcica.*

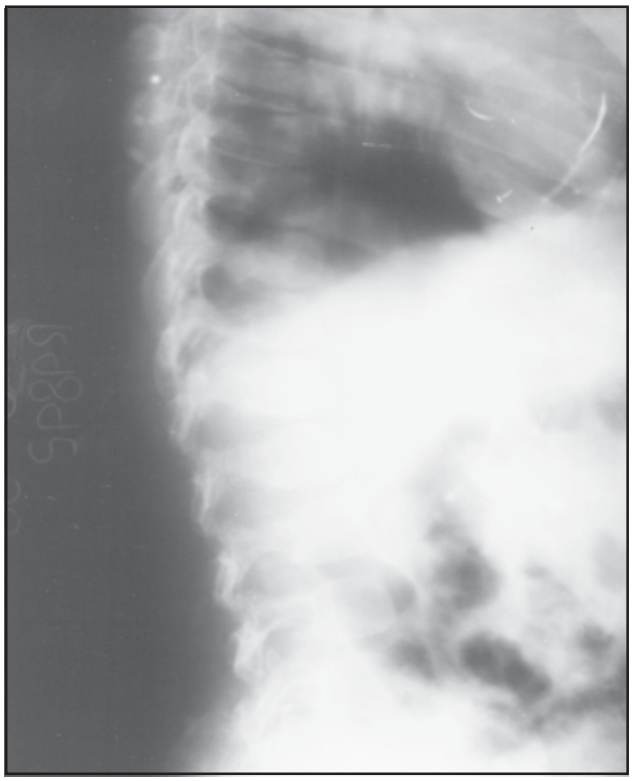

Fig.-3 : *Vertebral X-ray showing upper border hypoplastic and lower border peak shaped anteroinferiorly.*

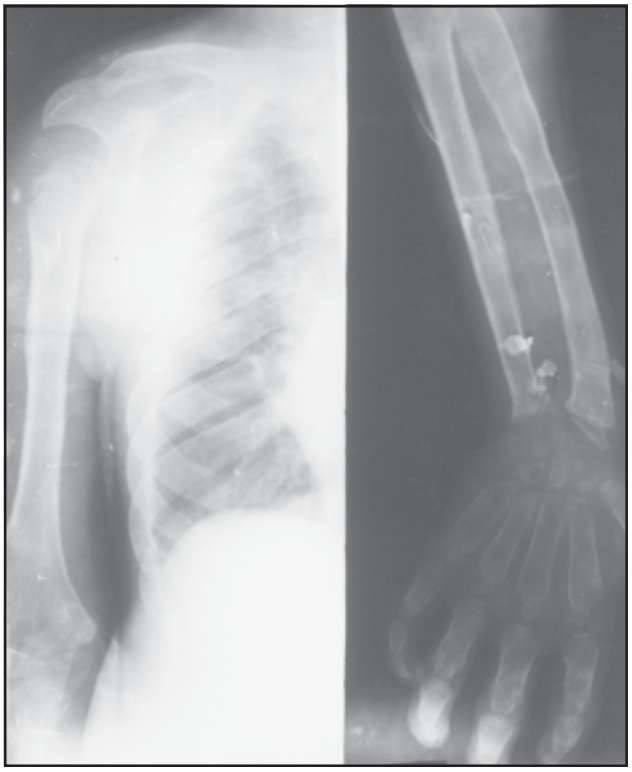

Fig.-4 : *X-ray of the forearm & hand showing articular surface of the radius and ulna forming a V shape with each other. Distal end of the metacarpals are widened with tapered proximal end & pointed terminal phalanges. Medial end of the clavicle is thickened & ribs are spatulated.*

nuclei and accumulation of the storage substance. There were early cirrhotic changes & the findings were consistent with storage disease.

Discussion :

The mucopolysaccharidoses are a group of inherited disorder caused by incomplete degradation & storage of acid mucopolysacharides (glycosaminoglycans) and specific degradative lysosomal enzyme deficiencies have been identified.[1] Mucopolysacharides are major component of the intracellular substance of connective tissue, bony changes are characteristics & the skeletal deformities seen in the roentgenograms are referred to as dystosis multiplex. The Central Nervous System (CNS) may also be affected leading to progressive mental retardation. In addition, the cardiovascular system, liver, spleen, tendon, joints & skins may be involved. The degree of disability & overall prognosis in each of the mucoplysaccharidoses are determined by the extent of the physical & mental involvement.[2-3] Mucopolysaccharidoses type II (Hunter syndrome) is the only X- linked disorder among the mucopolysaccharidosis. It is a rare lysosomal disease caused by deficiency of the enzyme

iduronate-2-sulfatase (IDS).[3,4] It is milder than Hunter syndrome with respect to the skeletal & mental defects. Affected patients show a wide spectrum of clinical phenotypes from severe to mild[5] but there is no biochemical or enzymatic difference between the severe form of the disease designated type A & the mild disease type B. Mutational analysis of this disease resulted in the identification of more than 200 alternation.[4-7] The IDS gene (xq 28) has been completely sequenced. The absence of obvious correlation between transcript content and size, IDS protein amount &IDS activity suggests that it is IDS protein processing that may be regulated rather than IDS gene transcription.[6-8] Classic form of the hunter syndrome (type - A) is characterized by skeletal abnormalities, hepatosplenomegaly & neurological dysfunction as in our case with coarse facial features, short stature, joint stiffness, hepatomegaly & umbilical hernia. Severe mental retardation and corneal clouding is feature in type A but not in type B, like in our case. Progression of the disease process is slower and the dystosis multiplex is milder than in hunter syndrome. Airway obstruction due to accumulation of mucopolysaccharides in the trachea & bronchi is a complicating feature of type B. In our case there was croaky voice probably due to this. In type B, patients have a longer life expectancy as in our case: The physical features, dystosis multiplex, dermatan & heparan sulphaturia suggests either Hurler or Hunter syndrome but X - linked inheritance is specific for Hunter but we failed to elicit this. Studies show iduronosulfate sulfatase deficiency in serum, WBC & cultured fibroblasts. Bone marrow transplantation (BMT) is specific & unique for each disorder treated to replace the defective enzymes in the various mucopolysaccharidoses.[3.5.8] Patients with Hurler disease benefit the most. Treatment is directed to prevent or ameliorate the inexorable neurological deterioration that is a major patho-physiological event in all these inherited metabolic storage disease. Skeletal changes don't improve. However when the transplant is done early in life, skeletal deterioration may be minimal. Differences in improvement depend upon how old the patient was when onset occurred & the rate of progression of the disease. Hunter syndrome patients don't seem to be benefited intellectually from BMT. Prenatal diagnosis and carrier detection are available for all the mucopolysaccharidosis. Lysosomal storages diseases are rare but significant cause of non-immunehydrops fetalis. In view of the poor prognosis, the use of fetal blood for early and all biochemical diagnosis is a valuable supplement in the diagnostic work-up and the management. Ten various forms of gene therapy have been evaluated, [3,11] and found to be promising in future treatment but accurate quantification of gene transfer is a universal challenge in thus field. Peripheral blood lymphocytes PBL (MPS) transductants exhibited a proviral IDS enzyme level approximately threefold higher than in normal PBLs. The Hollofibre biorector could be used to culture and transduce human PBLs.[10] In developing a clinical trial of lymphocyte gene therapy for Hunter syndrome, method using southern blot and automated DNA sequencing technology was employed but we found to be laborious and subject to considerable variation. As an alternative approach, a real time kinetic PCR assay appropriate to new instrumentation was evaluated and the results are encouraging.

References

1. Metalon RK. Disorders of mucopolysaccharide metabolism, In: Behrman RE, Kliegman RM, Arvin AM, editors. Nelson textbook of pediatrics, 15th ed. 1996; 398404
2. Barone R, Wigro F, Triulzi F, Musumeci S, Fiumara A, Pavone L. Clinical and neurological follow up in mucopolysacchandosis type 111 (Sanfiloppo Syndrome). Neuropediatrics 1999; 30: 270-74
3. Hartung SD, Reddy RAG, Whitley CB, Melvor RS. Enzymatic correction and crosscorrection of mucopolysaccharidosis type 1 fibroblast by adeno associated virus mediated transduction of alpha -L- Iduronidase gene. Human gene Ther 1999; 10: 2163-72
4. Cudry S, Froissart R, Bowton O, Mairel, Bozon D. The 2.1-, 5.4- and 5.7- Kb transcript of the IDS gene are generated by different polyadenylation signals. Biochim Biophys Acta 1999; 1447: 35-42
5. Coppa GV, Cabriellio, Gordiali R, Villam GR, Di Natal P. Bone marrow transplantation in a Hunter patient with P266 H mutation. Int J Mol Med 1999; 4: 433-36
6. Gert L, Chaban A, Coll M J. A new polymorphism in the iduronate-2-sulphatase gene. Implication for the diagnosis of Hunter syndrome. J Inherit Metab Dis 1999; 22: 844
7. Karsten S, Voskoboeva E, Kragnopolskaja X, Bondeson ML. Nobel type of genetic rearrangement in iduronate-2-sulphatase (IDS) gene involving deletion duplications and inversions. Human mutat 1999; 14: 471-6
8. Krivit W, Aurbourg P, Shapiro E, Peters C. Bone marrow transplantation for global cell leucodystrophy, adrenoleucodystrophy, metachromative leucodystrophy and Hurler syndrome. Current Opin Hematol 1999; 6: 377-82
9. Becker K, Pan D, Whitely CB. Real time quantitative polymerase chain reaction to assess gene therapy. Human Gene Therapy 1999; 10: 2559-66
10. Groener JE, de Graaf FL, Foorthuis BJ, Kanhai HH. Prenatal diagnosis of lysosomal storage diseases using fetal blood. Prenat Diagno 1999; 19: 930-33
11. Pan D, Shankar R, Stroncek DF, Whitley CB. Combined ultrafiltration in a hollow fibre bioreactor facilitates into peripheral blood lymphocytes from patients with mucopolysaccharidosis type 11. Human Gene Ther 1999; 10: 27&9-2810

CASE REPORTS

ACUTE SUPERINFECTION OF HEPATITIS DELTA VIRUS (HDV) IN A PATIENT WITH DECOMPENSATED CIRRHOSIS OF LIVER DUE TO HEPATITIS – B VIRAL INFECTION (HBV)

PK ROY, SK SAHA, MAR MIAH, MMR KHAN, MT RAHMAN

Summary

We report a case of acute superinfection of Hepatitis Delta Virus (HDV) in a patient with decompensated Cirrhosis of liver due to Hepatitis-B viral infection (HBV) with Diabetes mellitus. Tests done for liver function and viral markers revealed serum bilirubin- 306 mmol/L ALT-130 u/L, Prothrombin time- control- 12 secs & patient- 22.4 secs, Total Protein- 74 g/L, Serum Albumin-21g/L. HbsAg (Elisa)- Positive, Anti HBc IgM - Negative, Anti HBc (total) - Positive, HBeAg-Negative, Anti HDV Ig M- Positive, Anti HCV (Elisa) -Negative, Anti HEV IgM - Negative. Upper GI Endoscopy showed grade III oesophageal varices with portal hypertensive gastropathy. The patient underwent conservative treatment with dierutics, fresh frozen plasma, vitamins and discharged on improvement.

Introduction

Acute HDV infection can occur in a patient with established HBV infection (Superinfection) or concurrently with acute HBV infection (Coinfection)[1]. Superinfection with HDV of individuals with established HBV infection results in chronic progressive liver disease in more than 90% of patients.[2] Fulminant hepatitis may result from HDV superinfection and is characterized by the presence of HDV markers and the absence of anti HBcIgM in serum.[1] We report a case of acute superinfection of Hepatitis Delta Virus (HDV) in a patient with decompensated cirrhosis of liver due to Hepatitis-B viral infection (HBV). This is the first case of acute Hepatitis Delta viral infection in Bangladesh.

Case Note

A 32 years old man was admitted into the Gastrointestinal, Liver and Pancreatic Diseases Unit-2 of BSMMU with the complaints of upper abdominal pain, fever, anorexia and weight loss for 6 months; jaundice, ascites and bilateral ankle oedema for one week. Pain was episodic, persisted for 4-6 days and occurred at an interval of few weeks. Fever was intermittent and was associated with the episode of abdominal pain. Fever remitted with the relief of abdominal pain. Patient developed jaundice, ascites and bilateral ankle oedema for the last one week. Jaundice was progressively deepening. Patient had a history of jaundice 8 years back.

Physical examination revealed that patient was anxious, ill looking. Patient had moderate jaundice and mild bilateral ankle oedema.

Investigations revealed- Hb%-13.2 g/dl, ESR-45 mm in 1st hour, total count of WBC-12,000/cm, differential count of WBC-Neutrophil-84%, Lymphocyte-10%, Eosinophil-4%, Monocyte-2%. Blood glucose 2 hr after breakfast-13.1 mmol/L, urine sugar-green reduction. Liver Function test : Serum bilirubin-306 micro mol/L, Serum ALT-130 U/L, Alkaline Phosphatase-250U/L, Prothrombin time- control-12secs, patient-22.4 secs. Total Protein-74g/L, Serum Albumin-21g/L. Kidney function test; urea-30mg/dl, creatinine-l.lmg/dl. Viral markers: HBsAg-positive, HBeAg-Negative, Anti HBc IgM-Negative, Anti HBc(total)-Positive, Anti HCV-Negative, Anti HEV IgM-Negative, Anti HDV IgM-Positive. Ultrasonogram of abdomen showed liver normal in size and coarse echotexture. No focal lesion is seen. X-ray chest P/A view- NAD. Upper Gastrointestinal Endoscopy showed Grade iii oesophageal varices with portal hypertensive gastropathy. Ascitic Fluid study- Protien-0.9 gm/dl, no malignant cell was seen. Cells were mostly lymphocytic and few reactive mesothelial cells were seen.

Discussion

Chronic Hepatitis B is a common disease with an estimated global prevalence of more than 300 million carriers or approximately 5% of the world's population. Approximately 1 to l.25 million persons in the United

Dept. of Gastrointestinal, Liver & Pancreatic Diseases, Bangabandhu Sheikh Mujib Medical University, Dhaka

States have chronic HBV infection as indicated by HBsAg positivity[3]. The prevalence of HBV infection varies widely in different parts of the world. In the Far East (e.g. South East Asia, China, the Philipines, Indonesia), the middle east, Africa and Parts of South America, the prevalence is high, with HBsAg positivity ranging from 8% to 15%[4]. In Bangladesh, the prevalence of HBsAg positivity varies from 7.5 to 6-10%[5,6].

Hepatitis Delta viral infection is not a common disease in the world as well as in Bangladesh. It occurs as a superinfection or coinfection with the infection of Hepatitis B virus. In the north, the prevalence of Hepatitis Delta virus infection ranks among the highest in the world. In the south, the problem appears negligible, although it is increasing within high risk urban communities. HDV superinfection has been the cause of large outbreaks of fulminant hepatitis[7].

In this case, HDV superinfection causes acceleration of the hepatic damage in a preexisting liver disease due to Hepatitis B viral infection. This patient was in a compensated state but HDV superinfection caused decompensation of the state of the liver. As a result patient had developed moderate ascites, deep jaundice and prolongation of the prothombin time. So, a patient with deep jaundice and ascites, all hepatotropic viral markers should be sought for the confirmation of the diagnosis.

References

1. Terrault NA, Wright TL, Viral hepatitis A throughs G. In : Sleisenger & Fordtrans Gastrointestinal and Liver Disease. Feldman M, Scharschmidt BF, Sleisenger MH. editors. 6th edition, vol-2, WB Saunders Company, Philadelphia, 1998. P. 1123-1170.
2. Rosino F and Cozzolongo R, Interferon for HDV infection. Antiviral Res 1994; 24 : 165.
3. Alter M and Mast E. The epidemiology of viral hepatitis in the United Status. Gastroenterol Clin North Am 1994; 23 : 437.
4. Margolis H, Alter M and Hodler S. Hepatitis B : Evidence epidemiology and implications for control. Semin Liver Dis 1991; 11 : 84.
5. Khan M, Ahmad N, Seroepidemiology of HBV and HEV in Bangladesh. International Hepatology Communications 1996; 5 : 27-29.
6. Chen CJ, Wang LY, YUMW. Epidemiology of hepatitis B Virus infection in the Asia Pacific region. Journal of Gastrointestinology and Hepatology 2000;15 (suppl) : E3-E6.
7. Saracco G, Macogno S, Rosina Fetal. Serological makers with fulminant hepatitis in persons positive for hepatitis B surface antigen. A world wide epidemiologic and clinical surgery. Ann Intern Med 1988; 106 : 380-383.

VISCERAL LEISHMANIASIS AMONG THE SUSPECTED FEBRILE PATIENTS

NILUFAR BEGUM[1], MA MASUM[1], AB AL MAMOON[1], AFROZA BEGUM[3]

Summary

Direct agglutination test (DAT) for Kala-azar was performed in 9111 blood samples from febrile cases after being referred to IEDCR during 1996-98. Out of 9111 blood samples, 4095 (44.9%) were found seropositive for kala-azar cases were found in 39 districts of Bangladesh. The highest prevalence of positive cases were seen in the district of Mymensingh (42.07%) followed by that of Tangail (13.60%), Gazipur (8.62%), Dhaka (6.64%), Sirajgonj (6.17%) and Manikgonj (4.05%). The data shows that the number of referred cases are more or less static with a slight increase in the year 1997. There were two peak incidence of age group, one within range of 0-10 years and another within the age range of 26-30 years. The sex ratio is more or less equal in children within 0-10 years age group but from age 11 years and above, a decrease of seropositivity is noticed visibly among females in comparison to males and this pattern stands valid for all 3 years data

Introduction

Visceral leishmaniasis (VL), commonly known as Kala-azar is a chronic febrile disease caused by the protozoan parasite, Leishmania donovani and its sub-species.[1]

The disease agent is transmitted from the reservoir host to the susceptible host by a tiny insect usually known as sandfly. Kala-azar is characterized by chronic fever, hepatosplenormegaly, emaciation and anemia. Its mortality is very high among the untreated patients[2,3]. Worldwide there are estimated to be approximately 500.000 cases of Visceral leishmaniasis per year and many of them are associated with epidemics particularly in Indian sub-continent and Sudan[4]. In Bangladesh Visceral leishmaniasis or Kala-azar is one of the major public health problem with a gradual increase in indence and prevalence. It is a notifiable disease since 1987. In the late; 1970s Kala-agar re-emerged in Bangladesh sporadically. Since then Kala-azar cases have gradually increased, and from 8 thanas reporting Kala-azar during the 1981-1985 period; the number has grown to 62 THCs in 1991 and 91 THCs in 1996. During the last few years the Kala-azar situation has assumed epidemic proportion with number of reported cases increasing from a total of 3978 in 1993 to 6813 in 1996.[5] The disease pattern is extremely focal with most cases from rural areas exhibiting a familial and contiguous household clustering pattern among the lowest socio-economic group. An increased vector population following cessation of widespread DDT spraying together with an available human reservoir of infection in the form Post-Kala-azar Dermal Leishmaniasis (PKDL) and active VL cases led to rise in number of cases in early 1970s.[6] In many studies it has been found that the disease is more common among male than the female and children are more susceptible than adults[7].

Materials and Methods

Nine thousand one hundred and eleven blood samples (9111) from kala-azar (KA) suspects were examined after referral to IEDCR during the period from 1996-98. These febrile patients with suspected VL were from 39 districts of Bangladesh. Direct Agglutination Test (DAT) was done in the department of Parasitology of IEDCR (Harith et al., 1998) for serodiagnosis of VL. A titre of $\geq$ 1:3200 was regarded as diagnostic.

Result

Out of 9111 fever cases studied, 5458 were males and 3653 females (Table-I). The highest prevalence of positive cases was seen in the district of Mymensingh followed by that of Tangail, Gazipur, Dhaka, Sirajgonj and Manikgonj in that order.

Out of 9111 blood samples tested 44.9% were found seropositive for VL. Of the 5458 males and 3658 females tested, 2638 males (48.3%) and 1459 (39.9%) females were positive for DAT respectively. Table-I shows the age and sex-wise proportion of DAT positive cases among the total cases studied.

From 1.1.1996 to 31.12.1996 a total of 2801 blood samples were examined of which 1290(46%) were

1. Department of Parasitology, IEDCR, Dhaka
2. Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Dhaka

found seropositive for VI,. Out of 1290 seropositive cases 829 (48.4%) were males and 461 (42.3%) females. Table-2 shows the age and sex-wise proportion of those DAT positive cases among the febrile cases in 1996.

Table-III shows the proportion of DAT positive suspected to be cases of VL in 1997. Out of 3512 cases 1507 (42.9%) were DAT positive. Of the seropositive cases 994 (48.1%) were males and 513 (34.8%) were females.

In the year 1998, a total of 2798 samples were examined where 815 (48.5%) males were DAT positive and 483 (43.2%) females were seropositive for VL. The age and sex-wise DAT results have been shown in Table-IV. Table-V shows the district-wise distribution of positive cases.

Table-I

Age and sex-wise DAT result of the total blood samples-taken from febrile cases suspected to be suffering from YL from 1996-98.

Age group	Male		Female		Total	
No.	No. Exam	DAT +ve cases (%)	No. Exam	No. DAT +ve cases (%)	No. Exam	No. DAT +ve cases (%)
0-5	724	46 (38.4)	151	76 (50.3)	401	172 (42.9)
6-10	946	167 (55.1)	222	123 (55.4)	525	290 (55.2)
11-15	648	125 (62.8)	128	60 (46.9)	327	185 (56.6)
16-20	631	118 (54.4)	127	55 (43.3)	344	173 (50.3)
21-25	539	88 (50.3)	106	44 (41.5)	281	132 (47)
26-30	571	70 (43.7)	120	43 (35.8)	280	113 (40.3)
30 +	1399	165 (40.4)	235	60 (25.5)	643	225 (35)
Total	5458	2638 (48.3)	4089	461 (42.3)	2801	1290 (46)

Table-II

Age and sex-wise DAT result of the total blood samples taken from febrile cases suspected to be suffering from VL in 1998.

Are group	Male		Female		Total	
	No. EXam	No. DAT +ve cases (%)	No. Exam	No. DAT +ve cases (%)	No. Exam	No. DAT +ve cases (%)
0-5	250	46 38.4	151	76 (50.3)	401	172 (42.9)
6-10	303	167 55.1	222	123 (55.4)	525	290 (55.2)
11-15	199	125 62.8	128	60 (46.9)	327	185 (56.6)
16-20	217	118 54.4	127	55 (43.3)	344	173 (50.3)
21-25	175	88 50.3	106	44 (41.5)	281	132 (47)
26-30	160	70 43.7	120	43 (35.8)	280	113 (40.3)
30 +	408	165 40.4	235	60 (25.5)	643	225 (35)
Total	1712	829 48.4	4089	461 (42.3)	2801	1290 (46)

Table-III

Age and sex-wise DAT results of the total blood sample from the febrile cases suspected to be VL for 1997

Age group	Male		Female		Total	
	No. Exam	No. DAT +ve cases (%)	No. Exam	No. DAT +ve cases (%)	No. Exam	No. DAT +ve cases (%)
0-5	269	124 (46.1)	192	106 (55.2)	461	230 (49.9)
6-10	372	210 (56.4)	260	136 (47.4)	632	346 (54.7)
11-15	250	1.36 (54.4)	137	50 (36.5)	387	186 (48.1)
16-20	239	119 (49.8)	255	57(22.3)	494	176 (35.6)
21-25	213	97 (45.5)	159	57 (35.8)	372	154 (41.4)
26-30	211	102 (48.3)	164	52 (31.7)	375	154 (41.1)
30 +	511	206 (40.2)	280	55 (19.6)	791	261 (33)
Total	2065	99 (48.1)	1447	513 (34.8)	3512	1507 (42.9)

Table-IV

Age and sex-wise DAT results of the total blood sample from the febrile cases suspected to be VL in 1998

Age group	Male		Female		Total	
	No. Exam	No. DAT + ve cases (%)	No. Exam	No. DAT + ve cases (%)	No. Exam	No. DAT + ve cases (%)
0-5	205	100 (48.8)	127	71 (55.9)	332	171 (51.5)
6-10	271	152 (56.1)	188	120 (63.80)	459	272 (59.2)
1 I -15	199	115 (57.8)	124	63 (50.8)	323	178 (55)
16-20	175	76 (43.4)	149	70 (47)	324	146 (45)
21-25	151	75 (47.7)	140	55 (39.3)	291	134 (44.7)
26-30	200	10 (4.52)	132	40 (30.3)	332	144 (43.4)
30 +	480	193 (40.2)	257	64 (24.9)	737	257 (34.9)
Total	1681	815 (48.5)	1117	483 (43.2)	2798	1298 (46.4)

Table-V

Year-wise distribution of DAT +ve cases.

Age group	% of DAT +ve cases.								
In years	1996			1997			1998		
	M	F	Total	M	F	Total	M	F	Total
0-5	38.4	50.3	42.9	46.1	55.2	49.9	48.8	55.9	51.1
6-10	55.1	55.4	55.2	56.4	47.4	54.7	56.1	63.8	59.2 1
11-15	62.8	46.9	56.6	54.4	36.5	48.1	57.8	50.8	55
16-20	54.4	43.3	50.3	49.8	22.3	35.6	43.4	47	45
21-25	50.3	41.5	47	45.5	35.8	41.4	47.7	39.3	44.7
26-30	43.7	35.8	40.3	48.3	31.7	41.1	52	36.3	43.4
30 +	40.4	25.5	35	40.2	19.6	33	40.2	24.9	34.9

Table-VI

Distribution of DAT positive kala-azar cases according to their resident district.

SL. No.	DISTRICT	DAT + V E CASES
1	Mymensingh	1723
2	Tangail	557
3	Gazipur	353
4	Dhaka	272
5	Manikganj	166
6	Narayngani	83
7	Thakurgaon	75
8	Gaibandha	68
9	Jamalpur	59
10	Comilla	59
11	Rajbari	52
12	Munshiganj	37
13	Potuakhali	30
14	Brahammanbaria	28
15	Dinajpur	27
16	Norshingdhi	27
17	Kustia	26
18	Natore	25
19	Sherpur	22
20	Chandpur	21
21	Rajshahi	18
22	Bogra	13
23	Pabna	10
24	Jessore	09
25	Rangpur	09
26	Faridpur	08
27	Netrokona	08
28	Barisal	07
29	Panchagarh	07
30	Shariatpur	07
31	Noakhali	07
32	Kishoreganj	05
33	Magura	05
34	Laxmipur	04
35	Gopalganj	02
36	Norail	01
37	Chapainawabganj	01
38	Chittagong	01

Discussion

In this study we found that the proportion of Kala-azar among the chronic febrile patients was very high and caused considerable morbidity.

The incidence of Kala-azar has been increasing since 1987 and 90% of all Kala-azar cases occur in Bangadesh, Brazil, India, Nepal and Sudan.[8] There was a serious outbreak in Bihar state in 1970-71 and the disease was reported in epidemic form from two districts of West Bengal state of India in 1980.[9] West Bengal and Bihar state of India are adjacent and close to Bangladesh.

There was an outbreak of Kala-azar at Shahazadpur thana, in the district of Sirajgonj (under greater Pabna district) during 1980-81 and out of 218 serum samples from suspected cases, 134 were diagnosed as Kala-azar on the basis of Aldehyde test.[10] Subsequently parasitological and serological investigation were conducted and reported.[11] Reports from. district health authorities and clinical units indicate that

>15,000 new cases can be expected annually in Bangladesh (Masum et, al. 1995).[12]

In the present investigation a total of 9111 Kala-azar suspects from 39 endemic areas of the country were examined and 44.9(%) cases were seropositive for Kala-azar. These results revealed that Kala-azar cases reported so far are a small fraction of the total cases in the community. Zijlotra et. al reported 51 % Kala-azar among 132 suspected cases and this was slightly higher than our overall rate.[13] The occurrence of Kala-azar among the febrile cases during outbreak investigation in Bangladesh ranged from 58-78%.[14,15,16]

The results in the present study show that Kala-azar is widespread in many areas of Bangladesh. The VL cases diagnosed in the Parasitology Dept of IEDCR is a very small proportion of the total cases in the country. DAT has been decentralized in five VL endemic districts of the country and Kala-azar cases detected in these district laboratories are not included in this report.

The DAT is a simple, highly sensitive and specific test for diagnosis of VL. Feasible facilities may be arranged in the endemic areas to collect blood samples from chronic fever cases, not responding to anti-malarial drugs and antibiotic for serodiagnosis using DAT in the nearest laboratories.

Above facts and findings reveals that Kala-azar cases are there in the endemic rural village in high percentage where diagnostic facilities are very limited or absent. So the undiagnosed Kala-azar cases are being treated using available all types of antibiotics, anti-malarial and sometimes anti-tuberculosis drugs and steroids causing huge economic losses and death of many cases due to maltreatment. In the circumstances diagnostic facilities like simple Direct Agglutination test (DAT), which is simple, highly sensitive and specific should be made available in the Kala-azar endemic areas for early diagnosis and proper treatment to mitigate this hidden health problem.

References :

1. WHO Technical. Report Series. No. 701,1984. The Leishmaniasis. Report of Expert Committee.
2. Marinkelle C.J. The control of Leishmaniasis. Bulletin of the World Health Organisation, 1980 58:807.
3. Chatterjee K.D. Parasitology(Protozoology and Helminthology).12th edition, 1980.
4. T.K. Jha, Shayam Sundar, Thakur, Bachmann Peter, Juntra kabwang, Chris Fisher, Andreas Voss et. al. Miltefosine, an oral agent for the treatment of Indian Visceral Leishmaniasis. The New England Journal of Medicine. 1999; 341 (24):1 7995-99.
5. Kala-azar Control Programme-Plan of Action 1997-98.
6. Thakur, C.P. Epidemiological, clinical and therapeutic features of Bihar Kala-azar (including PKDL). Transmission of Royal Society of Tropical Medicine and Hygiene. 1984;78:391-98.
7. M.A. Masum, M.S.Chowdhury, Rafiquddin Ahmed and MAH Mia Journal of Preventive & Social Medicine. 1990;4(9):38-41.
8. Desjenx, P. Human Leishmaniasis: Epidemiology and Public Aspects. World Health Statistics Quartile, 45 (2/3): 167-275. 1992.
9. Addy, M. and Nandy. A. Ten years of Kala-axar in West Bengal. Part 1. Did post-kala-azar dermal leishmaniasis initiate the outbreak in 24 Parganas? Bulletin of the World Health organisation, 70(3): 341-346. 1992.
10. Ahmed, T.U. and Ahmed, R.U. An entomological investigation of a Kala-azar focus in Bangladesh. Journal of Preventive and Social Medicine. 2(2):31-36.1983.
11. Khan, N .I. and Desowitz, R. S. A Comparison of counterimimunoelectr olphoresis and indirect heamagglutination test for the immuno-epidemiological investigation of kala-azar. South East Asian Journal of Tropical Medicine and Pubic Health, 17 : 3 77-3 80. 19 85 .
12. Masum, M. A.; and Evans, D. A. Minter, D. M. and Harith, A. E. Visceral leishmaniasis in Bangladesh: The Value of DAT as a diagnostic test. Transactions of the Royal Society of Tropical Medicine and Hygiene, 89; 185—186, 1995.
13. Zijlotra, E E.; Ali, M. S.; El - Hassan, A. M.; El-Toum, LA.; Satti, M.S. Ghalib, H.W.; Sondor, E. and Winkler, A. Kala-azar in displaced people from Southern. Sudan: epidemiological, clinical and therapeutic findings. Transactions of the Royal Society of Tropical Medicine and Hygiene, 85 365.369. 1991.
14. Masum M A.; Chowdhury, M.S.; Ahmed, R. U. and Mia, M. A. H . Outbreak of visceral leishmaniasis in Thakurgaon, Bangladesh. Journal of Preventive and Social Medicine, 4-9(2): 38-41. 1990a.
15. Masum MA, Alam, B and Ahmed, R.U. Kala-azar outbreak in Dinajpur District of Bangladesh, The Hygeia, 4-(2): 122-124.199ob.
16. Masum MA, Alam, B and Ahmed, R.U. An epidemiological investigation of a Kala-azar outbreak at Kalahati Upazila of Tangail district, Bangladesh. Journal of Preventive and Social Medicine, 4-9(I): 13-1 ,5. I 990c.

CLINICAL PROFILE & OUTCOME OF DENGUE PATIENTS DURING THE FIRST OUTBREAK IN DHAKA – A HOSPITAL BASED STUDY

AINUN AFROZE[1], MAJ CHOWDHURY[2], G. KIBRIA[3], RK SAHA[4], MA JALIL[5], MA KHAN[6]

Abstract

Dhaka has witnessed an outbreak of dengue fever in the new millennium. Effort is going on to identify the virus. During the peak period of the outbreak from July to October 2000, 15 patients in pediatric ward and 38 patients in Medical ward of Bangabandhu Sheikh Mujib Medical University were admitted for the clinical suspicion of Dengue fever.

Clinical profiles of 11 children and 20 adult Antidengue antibody positive cases were documented and analyzed in order to understand the nature of the disease in an urban situation during the first outbreak.

Introduction

Dengue fever (DF) has been known for more than a century in the tropical areas of the South East Asia and Western Pacific regions.[1] Epidemics of Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS) were first recognized in the Philippines in 1956 where Dengue virus types 2,3,4 were isolated.[2] In India, the first epidemic of DHF was reported in Calcutta (DEN-2) in 1963.[3] Delhi witnessed dengue epidemics in 1967 (DEN-2), 1970 (DEN-1 &3), 1982 (DEN- 1&2), 1988 (DEN- 2) and in 1991.[4-6] Dengue remains a public health problem in Thailand and Singapore as well[7].

The first documented outbreak of DF in Bangladesh was in 1965 when it was called Dhaka fever[8]. Another epidemic fever with features closely mimicking that of DHF occurred again in 1968 in areas of Bangladesh bordering Myanmar.[9] Subsequently in 1977 and in 1982 some cases were documented in clandestine surveys.[10] The first formal sero-epedemiological study for the presence of dengue in Bangladesh was done in 1996 through 1997 at Chittagong Medical College Hospital, where 13.75% of fever cases were found to be sero-positive for dengue infection.[11] Later on in 1998 and 1999 sporadic cases of dengue were coming up in the media, especially from Dhaka city.[12] In the beginning of the new millennium Dhaka witnessed the outbreak of the so long unfamiliar disease, dengue. Increased number of Dengue suspected cases started getting admitted in the urban hospitals. In this paper, the clinical profiles and outcome of the hospitalized dengue cases admitted in a tertiary care hospital during the year 2000 outbreak are described.

Material & Methods

This is a cross-sectional observational study carried out during outbreak of Dengue in Bangladesh in 2000. During the period from July to October 2000, 38 adult and 15 pediatric patients suspected to be dengue were admitted in medical and pediatric units of Bangabandhu Sheikh Mujib Medical University (BSMMU) hospital, Dhaka. In all patients, detailed history was taken and clinical examination was performed on admission; and subsequently during the stay in the hospital they were under close observation. The criteria used for the diagnosis of DHF included : acute febrile illness of less than 10 days duration with bleeding manifestations and thrombocytopenia or raised haematocrit. When there was evidence of circulatory failure, it was termed as DSS. In the present study the term "Dengue Syndrome" (DS) is used to encompass all the entities of dengue viral infection. Platelet count and PCV, complete blood count were done in all the cases and repeated. Chest x-ray and ultrasonography of the abdomen were also done routinely. Liver and renal function tests were done when deemed essential. IgM and IgG antibodies against dengue virus were

1. Nutrition and Paediatric Gastroenterology, BSMMU, Dhaka
2. Internal Medicine, BSMMU, Dhaka
3. Internal Medicine, DMC, Dhaka
4. Dept. of Paediatrics, BSMMU, Dhaka
5. Diabetes Care, Aventis Pharmaceuticals
6. Medical Affairs Associate, Aventis Pharmaceuticals

Bangladesh J Medicine 2002; 13 : 16-20

done on 5th day of the fever. Intravenous fluids, platelet riched plasma (PRP), fresh whole blood were infused as and when considered necessary. In patient with mild dehydration, normal saline or 5% dextrose-saline were used. Paracetamol was used as antipyretic in the hospital, though some patients had used clofenac suppositories before reporting to the hospital. Corticosteroid was used in some cases (Table-VI).

Results

There were 15 pediatric and 38 adult dengue patients admitted in BSMMU Hospital during the period from July to October 2000. Antidengue antibody either IGM or IgG or both was present in 11 (73.3%) pediatric patients and in 20 (52.6%) adult patients which have been evaluated for presentation.

Out of 11 paediatric patients 7 were male and 4 were female with mean age of 8.9 years (range 4-15 years). Among the adult patients 10 were male and 10 were female with mean age of 29.6 (range 16-57) years. Fever was present in all the paediatric and adult patients. In the paediatric group mean temperature during admission was 103.7° F (range 102-105° F) and in adult group it was 103.9° F (range 102-106° F). In the paediatric patients vomiting, body ache, abdominal pain, retro-orbital pain was present in 27.3%, 54%, 63.4%, and 27.3% cases respectively. In the adult group 55%, 90%, 30%, & 42% of the cases had vomiting, body ache, abdominal pain and retro-orbital pain respectively (Table-I). 15 (75%) adult patients had sweating and became restless during the treatment in the hospital. In the paediatric subjects only 4(36%) had sweating and became restless.

Table-I

Symptoms in dengue syndrome cases

Symptoms	Pediatric (n-11)	Adult (n-20)
Vomiting	3	11
Body ache	6	18
Abdominal pain	7	6
Retro-orbital pain	3	16

Bleeding manifestations were evaluated by observing epistaxis, gum bleeding, haematemesis, malena, skin rash, visible purpura, echymoses and petechae. 4 (36.4%), 1 (9%), 1 (9%) 3(27.2%) paediatric cases had epistaxis, gum bleeding, haematemesis and malena respectively. On the other hand 1(5%), 4(20%), 2(10%), 3(15%) adult patients had epistaxis, gum bleeding, haemetemesis and melena respectively. 7 (63.4%), 5(45.5%), 4(36.3%) paediatric dengue cases had skin rash, visible purpura, and petechae respectively, where as 10 (50%), 4(20%), 1(5%), and 2(10%) adult cases had skin rash, purpura, echymoses and petechae respectively (Table-II & III). Liver was palpable only in two adults and one child.

Table-II

Bleeding manifestations in dengue cases

Bleeding manifestations	Pediatric patients (n-11)	Adult patients (n-20)
Epistaxis	4	1
Gum bleeding	1	4
Haematemesis	1	2
Malena	3	3

Table-III

Rashes in dengue syndrome cases

Rashes	Pediatric patients (n-11)	Adult patients (n-20)
Skin rash	7	10
Visible pupura	5	4
Echymoses	0	1
Petechae	4	2

In paediatric group 4 (36.6%) patients had pleural effusion and 5 (45.5%) had ascites, whereas 4 patients had both pleural effusion and ascites. In the adult group 5(25%) had pleural effusion and 6 (15%) had ascites, where as in 4 (20%) had both effusion and ascites. It was observed that platelet count started to rise as the fever and other manifestations of dengue began to subside more or less within a week (Table-IV&V).

Table-IV

Platelet count in Pediatric dengue cases (n-11)

Day	<100,000	<150,000	>150,000
2	4	4	3
3	3	2	6
4	1	1	9
5	-	-	11

Table-V

Platelet count in adult dengue cases (n-20)

Day	< 100,000	< 150,000	> 150,000
1	9	5	6
2	6	4	10
3	5	3	12
4	6	2	12
5	4	3	13
6	2	1	17
7	1	-	19
8	-	1	19

Of the 11 antibody positive paediatric cases both the IgG and IgM were positive in 7 cases and only IgG was present in 4 cases. Among the 20 adult antibody positive cases both antibodies were positive in 7 cases, only IgM in 8 and only IgG in 5 cases (Table-VII).In the pediatric unit 7 were diagnosed as DHF and 4 as classical DF, In Medicine ward 12 were labeled as DHF and 8 as classic dengue. During the course of illness 8 patients from each of the pediatric and adult group had platelet count below 100,000/ cumm. Increase in mean haematocrit value from 38.9% to 46.5% was observed as platelet count decreases. All the dengue cases survived.

Table-VI

Treatment received in the hospital

Medication	Paeditric patients (n-11)	Adult patients (n-20)
IV fluid	7	12
Platelet riched plasma	5	1
Blood transfusion	1	-
Antibiotic	5	1
Corticosteroid	1	

Table-VII

Antidengue antibody in dengue syndrome cases

Antibody positivity	Pediatric cases (n-11)	Adult cases (n-20)
Both IgM or IgG	7	7
Only IgM	0	8
Only IgG	4	5

Disscussion

This presentation of dengue is based mainly on clinical manifestations recorded by the attending physicians and pediatricians in their respective wards. The purpose of this paper is to highlight the clinical presentation of the dengue cases encountered in the recent outbreak of the disease. The outbreak of dengue was unexpected at this time in our country.

The syndrome of dengue comprises of undifferentiated fever (UF), Dengue fever (DF), Dengue Hemorrhagic Fever (DHF), and Dengue Shock Syndrome (DSS). All entities initially present in a similar fashion indistinguishable from one another. One cannot differentiate DHF and DF at the very beginning. So for simplicity we have used the tenn "dengue syndrome" to denote any of the entities of dengue viral illness.

The disease, especially the severe form, has a predilection for the pediatric age group. Some of the epidemiological studies show that 90% of hospitalized dengue patients were children less than 15 years of age.[13] Disease trend of dengue in many countries reveal that initially it affects people of all ages, but gradually the children become the most susceptible group.[13] Over half of the reported cases of dengue infection and 13% of related deaths in a recent epidemic in Delhi were seen in children less than 12 years of age.[14] Epidemiological study done by Ahasan et al, reveals that a quarter of the case were less than 10 years of age, about 69% less than 60 years and about 82% were less than 30 years of age.[15]

Dengue hemorrhagic fever (DHF) occurs where multiple types of dengue viruses are simultaneously or sequentially transmitted, as seen in hyper-endemic regions. The severe illness seen in DHF is thought to be due to a secondary dengue infection with heterogenous serotype. The first infection probably sensitizes the patients, while the second appears to produce an immunological catastrophe.[16] DHF can occur during primary dengue infection in infants whose mothers are immune and probable carriers of nonneutralizing antibodies against dengue.[17] In many outbreaks such as one seen in Cuba in 1981, DSS was documented exclusively in children less than 14 years of age. All such patients had a secondary rise of antibodies against dengue, indicating a previous infection with a closely related virus or another strain of dengue virus.[18] Non immune (unsensitized) subjects exposed to dengue virus even during outbreaks of DHF may present with the milder classical dengue fever.[19] Studies from Thailand indicate that mortality from DHF occurs as a result of hypovolemic shock which in turn, result from increased capillary permeability leading to raised haematocrit. Therefore WHO has included raised haematocrit as one of the important criteria for the diagnosis of DHF. Ideally, serial estimation of haematocrit should be done in patients with suspected

DHF. However, in the study group haematocrit was not estimated in all patients because of tremendous workload on the laboratories. On the other hand haematocrit value in our context may not give the exact picture of dengue because of chronic anemia and use of intravenous fluid previously. Reports from Philippines and Kualalampur showed significant haemoconcentration in only 39.5% and 22% of DHF respectively.[20,21]

In the present study bleeding manifestations were observed in 9 out of 11 children and 10 out of 20 adult patients. Various kinds of rashes were observed in all the 11 pediatric and 17 out of 20 adult cases. Sharma et al during Delhi outbreak observed bleeding from various sites in 70 out of the 98 adult cases.[22] Although thrombocytopenia was a constant finding, there was a poor correlation between thrombocytopenia and bleeding diathesis indicating that the abnormal platelet aggregation rather than reduction in absolute numbers was the cause of bleeding diathesis. Hepatomegaly was observed in only one child and in two adult cases. Hepatomegaly was observed in 22.2% patients in Calcutta[3] and in 13.5% in Philippines.[20] Splenomegaly was found in one child but none of the adults. Splenomegaly was found in 8.2% in Delhi[22] and 9.3% cases in Calcutta.[3]

In our series skin rash has been found in 7 out of 11 pediatric cases and 10 out of 20 adult dengue cases whereas various skin rashes were observed in 36.7% in Delhi and in 27.1 in Visakhapatnam.[23] Pleural effusion or ascites demonstrable by ultrasonography in DHF patients with no clinical evidence of theses findings has been reported earlier in pediatric patients with DHF.[24] Routine ultrasonography and X-ray chest would have revealed more cases of ascites and pleural effusions than found at present.

In the present study we have analyzed only anti-dengue antibody positive cases. So there is chance of exclusion of few cases of dengue that has not been seroconverted when the tests were done.[25] There is no mortality in our series. This may be due to the fact that in BSMMU there is no provision for emergency admission except in pediatric ward. Epidemiological and laboratory evidence suggests that virus strain and perhaps serotype may also be important as a risk factor for DHF.[26] Although not well understood, other risk factors for individual susceptibility to DHF have been suggested. Ironically, undernourished infants seem to have a lower risk of DHF than infants with good nutritional status.[27]

References

1. Viral haemorrhagic fevers. Diagnosis, Treatment and Control. World Health Organization 1986 : 1
2. Quintos FN, Lim LE, Julliano L, Reyes A, Laeson P. Haemorrhagic fever observed among children in the Phillipines. Phil J Pediatr 1954; 3 : 1-19.
3. Aikat BK, Konar NR, Banerjee G. Haemorrhagic fever in Calcutta area. Indian J Med Res 1964; 52 : 660-75.
4. World Health Organisation. Monograph on dengue and dengue hemorrhagic fever. Geneva 1993.
5. Kabra SK, Verma IC, Aorora NK, Jain Y, Kalra V. Dengue haemorrhagic fever in Delhi. Bull World Health Organization 1992; 70 : 105-8.
6. Mohan Rao CVR. Epidemics of dengue fever in India. Indian J Paediatr 1987; 54 : 1114
7. Viral hemorrhagic fevers. Report of a WHO Expert Committee. Technical Report Series 1985; 721 : 14.
8. Aziz MA, Gorham R & Gregg MB. Dhaka Fever. Pakistan Journal of Medical Research. 1967; 6 : 83-92.
9. Bang YH and Shah NK. Regional review of DHF situation and control of Aedes Egypti in South - East Asia. Dengue News letter 1986; 12 : 1-9.
10. Khan AM and Ahmed TU. Dengue status in Bangladesh. Dengue News letter 1986; 12 : 11.
11. Yunus EB. Dengue and dengue haemorrhagic fever : Bangladesh perspective. JCMCTA 1999; 10 : 1-8.
12. More Dengue cases. The daily Star, 1999; 32, p-1.
13. Dengue and Dengue hemorrhagic fever. In : WHO : Prevention and Control of dengue and dengue hemorrhagic fever. WHO/SEARO, publication No. 29. New Delhi 1999. p 3-9
14. Ramji S. Dengue strikes Delhi. Indian Pediatr 1996; 33 : 978.
15. Ahasan HAM, Rasul CH, Karim SR, Mamun AA, Baker MA, Gazi EA. Dengue - an epidemiological study. Bangladesh Medical Journal (Khulna) 2000; 33 : 48-50.
16. Simpson DIH. Togaviridae. In : Principles of Bacteriology, Virology, and Immunity. Vol 4. 7h edn. Brown F, Wilson G. editors. London. Edward Arnold. 1984 : p233-249.
17. Kiliks S, Nimmannity S, Nisalak N. Evidence that maternal dengue antibodies are important in development of dengue haemorrhagic fever in infants. Am J Trop Med Hyg 1988; 38 : 411-414.
18. Kouri GP, Guzman MG, Bravo JR, Triana Jr C. Dengue hemorrhagic fever/dengue shock syndrome : lesson from the Cuban epidemic. Bull WHO 1989; 67 : 375-380.

19. Halstead S. Arboviruses. In : Nelson's Text book of Pediatrics. Nelson WE, Behrman RR, Kliegman RM, Arvin AM, editors. Philadelphia : WB Saunders Co. 1996; p 920-926.

20. Hayes CG, Manaloto CR, Gonzales A, Ranoa CP. Dengue infection in the Philippines : clinical and virological findings in 517 hospitalised patients. Am J Trop Med Hyg 1988; 39 : 110-116.

21. Ibrahim NM, Cehong I. Adult Dengue hemorrhagic fever at Kuala Lumpur hospital : retrospective study of 102 cases. Br J Clin Pract 1995; 49 : 189-91.

22. Sharma S, Sharma SK, Mohan A, Wadhwa J, Dar L, Thulkar S & Pande JN. Clinical profile of Dengue haemorrhagic fever in Adults during 1996 - outbreak in Delhi, India. Dengue Bulletin 1998 : 22 : 20-27.

23. Krishnamurthy K, Kasturi TE, Chittipantulu G. Clinical and pathological studies of an outbreak of denguelike illness in Vishakapatnam. Indian J Med Res 1965; 53 : 800-12.

24. Pramuljo HS, Harun SR. Ultrsound findings in dengue haemorrhagic fever. Paediatr Radiol 1991; 21; 100-102.

25. Rigau-Perez JG, Clark GG, Gubler DJ, Sanders EJ, Vomdam AV. Dengue and dengue haemorrhagic fever. Lancet 1998; 352 : 971-77.

26. Gubler DJ, Suharyono W, Lubia I, Eram S, Gunans S. Epidemic dengue in central Java, associated with low viraemia in man. Am J Trop Med Hyg 1981; 30 : 1094-99.

27. Thiayakom U, Nimmanity S. Nutritional status of children with dengue hemorrhagic fever. Clin Infect Dis 1993; 16 : 295-97.

ASSOCIATION NEWS

13th National Convention & Scientific Session of the Association will be held in the first week of March 2002.

Registration is open for all doctors & post graduate students. Registration fee for each participant is taka 500/- and for the accompanying person is taka 300/- only. The last date for registration is 10th February 2002.

Participants willing to present paper in free paper session or poster session are requested to submit their abstracts typed in English by 10th February 2002. Registration of the presenting author will be considered as a pre requisite for acceptance of the paper.

Further information please contact :
Conference Secretariat
Room No.- 415
Department of Nephrology
Blcok - 'C' 3rd Floor
BSMMU, Shahbag, Dhaka