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Original Article

A study of steroid-induced diabetes mellitus in leprosy

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Steroids, while still the most powerful drugs to manage leprosy reactions, predispose some patients to other morbidities such as diabetes, glaucoma, hypertension etc. A prospective cohort study was done in Kolkata, India among leprosy patients in reaction to determine the extent of steroid induced diabetes mellitus (SID). All leprosy patients with type 1 or type 2 reactions or neuritis admitted in 2006 to the Leprosy Mission Hospital in Kolkata, who had no past or current history and whose blood sugars on fasting were <126 mg/dl or post-prandial <200 mg/dl were monitored fortnightly while on steroid therapy, estimating blood glucose by a glucometer using standard strips. Of 81 patients, 19 (23.5%) manifested steroid-induced diabetes mellitus. Compared to those who didn't, there were significantly more LL/BL patients with positive BI among SID whose cumulative prednisolone dosage was nearly 9000 mg as compared to half the amount among others. Steroid induced diabetes is a serious complication among leprosy patients treated with prednisolone for reactions requiring careful monitoring for detection and appropriate clinical management.

Key words : SID, NSID, Leprosy

Introduction

The crux of the problem in leprosy is the occurrence of disability, an outcome of reactions leading to permanent damage of peripheral nerves (Roche et al 1988, WHO 1998). Steroids continue to remain the mainstay for treatment in the management of type 1 (reversal) and type 2 (erythema nodosum leprosum - ENL) reactions and neuritis in leprosy (Croft et al 2000, Richardus et al 2003, Rao et al 2006, Girdhar et al 2007). However, the prolonged use of systemic steroids may predispose one to other conditions like diabetes, hypertension, osteoporosis, psychosis, glaucoma and dermatological problems (Sugumaran 1998, van Brakel et al 2005, Bjelakovic et al 2007). Further, steroids may suppress immune response and thereby encourages bacillary multiplication (Britton 1998). Patients with recurrent ENLs require higher/ immunosuppressive dose of steroids for extended period which will result in systemic side effects increasing the likelihood of developing steroid dependency (Lockwood 1996).

Prevalence of diabetes in the Indian subcontinent is extremely high comparing Asian counterparts (Ramachandran et al 2001, Mohan et al 2006). The risk factors could be several including excessive use of drugs such as corticosteroids (Powers 2005, Mohan et al 2009, van der Linder et al 2009). Hence, early detection and adequate

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intervention would reduce morbidity significantly (Pai et al 2002).

A prospective cohort study was, therefore, undertaken at a leprosy referral hospital in Kolkata, West Bengal, India during 2006 on leprosy patients with recurrent reactional episodes, to determine steroid induced diabetes mellitus (SID) among those with no past or current history of diabetes with normal fasting and post-prandial blood sugars prior to initiation of steroids and with blood sugars that reverts back to normal on withdrawal of steroids. This paper describes the findings and discusses the implications.

Materials and Methods

This study was done during 2006, at the Leprosy Mission Premananda Memorial Hospital, a 78 - bedded leprosy referral hospital situated in the heart of Kolkata, serving the middle and lower classes residing mostly in urban metropolitan city. Leprosy patients having type 1 or type 2 reactions and/or neuritis requiring prednisolone were eligible to be enrolled into the study. Known cases of diabetes mellitus and those having past history of diabetes were excluded. These patients were further subjected to a baseline investigation consisting of complete haemogram and fasting and post-prandial blood sugars. Only those patients with fasting blood sugar less than 126 mg/dl and postprandial or random blood sugars less than 200 mg/dl were also included into the study. Those having preexisting diabetes detected at this stage were excluded. After enrollment, patients having irregular follow-up, irregularity in consuming steroids or discontinuation of steroids were excluded. Patients with other medical conditions such as severe peptic ulcer, systemic infection / ulcers or wound infection, glaucoma etc were also excluded.

The minimum starting dose of prednisolone has been fixed as 30 mg daily, hence, mild cases requiring lesser doses were excluded. Cases with severe lepra-reactions / recurrent reactions requiring adjuvant therapy of either thalidomide or azathorpine were excluded from the study. An informed consent was obtained from the study subjects, soliciting cooperation for regular follow-up.

Baseline data were collected for each patient which included age and sex, leprosy profile describing type of leprosy, lepra-reactions, smear status, deformity and treatment details. During follow-up, the patients were regularly monitored, estimating fasting blood sugars and postprandial/ random blood sugars every week, due to pragmatic reasons in this outpatient study instead of the ideal method of using 75 mg plasma glucose and measuring two hour later. Those manifesting a fasting blood sugar more than 126 mg/dl or postprandial/random blood sugar more than 200 mg/dl were closely followed-up to identify steroid induced hyperglycaemia or steroid induced diabetes mellitus (SID).

The method adopted for estimation of blood glucose is by a glucometer using standard strips (Accuchek, Glucotide) instead of the laboratory assessment due to practical considerations. The blood sugars were again checked during the course of steroid therapy at 2 weekly intervals for 3 months to detect any elevation. Patients were assessed after their steroid therapy to confirm that the patients had steroid induced diabetes (SID). Relevant data were noted in a special performa and transferred into excel spread sheet for analysis using SPSS software.

Results

A total of 81 patients satisfying the inclusion and exclusion criteria for the cohort study were followed up. Of these, 19 (23.5%) had manifested steroid-induced diabetes mellitus(SID). The characteristics of these patients were compared with those not manifesting any symptoms of steroid induced diabetes mellitus (NSID) and presented in Table 1.

The mean (SD) age was 39.2(14.6) years in the SID patients and 35.1(12.3) years in the non-SID group, the difference not statistically significant. Relative risk for SID was not significantly elevated

Table 1: Comparative profile of patients classified as SID and not SID

Characteristic	SID (19) No. (%)	Not SID (62) No (%)
Age (years)		
10 - 29	4 (21.1)	18 (29.0)
30 – 49	10 (52.6)	38 (61.3)
50 – 79	5 (26.3)	6 (9.7)
Sex		
Male	14 (73.7)	47 (75.8)
Female	5 (26.3)	15 (24.7)
Classification		
MB	19 (100.0)	60 (96.8)
PB	-	2 (2.5)
Ridley- Jopling cl.		
LL	9 (47.4)	7 (11.3)
BL	3 (15.8)	18 (29.0)
BB	-	3 (4.8)
BT	7 (36.8)	33 (53.2)
TT	-	-
PN	-	1 (1.6)
Bacterial index (BI)		
Positive	12 (63.2)	20 (32.3)
Negative	7 (36.8)	42 (67.7)
Lepra-reaction		
Type I (RR)	2 (10.5)	18 (29.0)
Type 2 (ENL)	10 (52.6)	8 (12.9)
Neuritis	15 (78.9)	54 (87.1)

by sex. However, MB patients, especially those in the LL and BL spectrum with positive slit-skin smear showed statistically highly significant association with SID ($P< 0.01$). The mean (SD) of prednisolone dosage was 8844 (6975) mg for SID as compared to 4591 (2644) mg among NSID, the difference statistically significant, even allowing for high variability ($p<0.05$). The Fasting blood sugar levels (mg/dl) in the SID and non-SID groups at entry to the study are given in Table 2. The distributions in the two groups are similar. The association between fasting blood sugar levels and the PPBS in the two groups are presented in Table 3. The increase in the PPBS in the SID group is significant. The mean (SD) of post-prandial blood sugars in the SID patients was 299.2 (77.7) as compared to 113.7 (25.8) in the NSID patients, the difference being statistically significant ($p<0.05$).

Discussion

The widespread use of corticosteroids in clinical practice emphasizes the need for a thorough understanding of their metabolic effects (Swartz and Dluhy 1978, Dendukuri et al 2002). Complications resulting from prolonged use of corticosteroids include development of glaucoma, reactivation of latent infections such as tuberculosis, sodium retention and/or elevation of mean arterial blood pressure (Quiram et al 2006, van Raalte et al 2009).

Corticosteroids continue to be the drug of choice for managing leprosy reactions and neuritis (Rao et al 2006) but their adverse effects especially diabetes have not been reported except for cases of diabetic ketoacidosis (Edward 1995, Agarwal et al 2002). The high prevalence of diabetes in India is triggered possibly by environmental, nutritional and specific drugs irrationally used and there is a need to explore the effect of

Table 2 : Fasting blood sugar (mg/dl) in the two groups at entry to study

Fasting blood sugar (mg/dl)	Group	
	SID	Non-SID
40-49	1(5.2%)	-
50-59	-	-
60-69	1(5.2%)	6(9.7%)
70-79	1(5.2%)	16(25.8%)
80-89	9(47.5%)	27(43.5%)
90-99	6(31.7%)	6(9.7%)
100-109	1(5.2%)	6(9.7%)
110-119	-	1(1.6%)
Total	**19(100.%)**	**62(100.0%)**

Table 3 : Correlation between FBS and PPBS during steroid therapy

Group and PPBS (mg/dl) Total	Fasting blood sugar(mg/dl)		
	40 -79	80 – 99	100- 112
SID			
200-249 7	1	6	-
250-299 4	2	2	-
300-349 2	-	2	-
350-399 4	-	3	1
400-489 2	-	2	-
All SID 19	**3**	**15**	**1**
Non-SID			
70 – 99 17	11	6	-
100-119 24	7	15	2
120-159 16	1	11	4
160-199 5	3	1	1
All non-SID 62	**22**	**33**	**7**

excessive steroids which are commonly used to manage leprosy reactions. Apart from steroid dependency, it is a necessary to identify steroid induced complications such as glaucoma or other ocular changes and diabetes and look for alternate or second line drugs such as thalidomide or azathioprine are necessary (Agarwal et al 2002, Lockwood and Bryceson 2003, Mahajan et al 2003, Athreya 2007, Walker et al 2007).

Diabetes is a metabolic disorder with increasing incidence even in developing countries with a high morbidity and mortality rates (Powers 2005, Zargar et al 2009). In a nested case-control study done in Netherlands, topical corticosteroids use was associated with an 1.24-fold increased risk of diabetes (van der Linden et al 2009). The present research has established the occurrence of diabetes in leprosy patients treated with prednisolone at standard dosages. Whether this occurred as a result of chronic,recurrent reactions in certain groups of leprosy patients or is the outcome of steroids used for their management is debatable (Pai et al 2002).

In this research, pragmatic measures were used to diagnose diabetes. Further research using the ideal and perhaps more correct diagnostic measure will be useful as also the test carried out using standard methods in the laboratory. Nonetheless, the findings from this study have cautioned that careful monitoring of blood sugars is essential in treatment of reactions requiring astute clinical management to prevent serious morbidity and mortality. Further studies may be needed to document additional risk factors for SID as well as to advocate more rational therapies in control of reactional episodes in leprosy especially in the management of type 2 reactions (ENL) which have shown a resurgence in MB cases with shortened duration of MDT or among defaulters (van Veen et al 2008).

Conclusions

Steroid induced diabetes mellitus (SID) is a serious complication which occurs in leprosy patients treated for reactions and requires careful clinical management.

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