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Original Article

A study of standardized regimens of steroid treatment in reactions in leprosy at a referral centre

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It is a well known fact that reactions and nerve function impairment (NFI) account for majority of disabilities and morbidities in leprosy. Steroids are the principal agents administered for treatment of reactions and NFI. In this study, we compared the efficacy of two regimens namely high dose (60 mg) regimen tapered over 28 weeks and low dose (40 mg) regimen tapered over 22 weeks in treatment of reactions and early NFI as regards to incidence of recurrence of reactions in 209 patients. Concerns about the side-effects of steroids were also addressed by following a strict pre-steroid investigation protocol. We observed that the low dose regimen was associated with a higher incidence of recurrence (48.3%) as compared to high dose regimen (16%) signifying the efficacy of longer duration of therapy with a higher starting dose. No patient developed side-effects which necessitated withdrawal of steroids. Early detection with prompt and adequate therapy with proper dose and duration is the key to reduce recurrence of reactions and to minimize deformities due to reactions and NFI in leprosy.

Key words: Nerve function impairment, Leprosy, Steroid treatment

Introduction

Reactions and nerve function impairment (NFI) are the foremost causes of disability and morbidity in leprosy patients. Their early detection and prompt optimal treatment can reduce the complications associated with these conditions significantly (Kahawita et al 2008). Along with timely detection, precise and adequate therapy with appropriate drug regimens also play a major role in reducing morbidity associated with nerve damage in leprosy. Steroids being the principal agents used for treatment of nerve damage (Lockwood 2000, Naafs et al 1979, Walker and Lockwood 2008), many steroid regimens have been tested (Richardus et al 2003ab, Smith et al 2004, Rao et al 2006, van Brakel et al 2003, WHO 1998) and practiced for the same. Steroids being inherently associated with adverse effects, the dosage and duration of a regimen assume great importance. We, therefore, decided to study the efficacy of two standardized steroid regimens in leprosy patients at the Main Referral Center of Bombay Leprosy Project in Mumbai. The regimens were compared with reference to the proportion of recurrence of reactions and correction of early nerve damage in leprosy patients.

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Materials and Methods

Study design

This was a retrospective single centre study where the data was analyzed to compare between two steroid regimens namely high dose (60 mg) and low dose (40 mg) regimen in leprosy patients with reactions and other evidence of early nerve damage like lagophthalmos, foot drop and hand deformities. The study was conducted at the Main Referral Centre and satellite clinics of Bombay Leprosy Project between May 2006 and October 2009. The centre carries out operational and clinical research alongside providing outpatient management of both referred and self reporting leprosy cases for reaction management.

Participants

The data of 209 patients were analyzed who attended on outpatient basis at the Main Referral Center and satellite clinics. Informed consent was taken from each patient. All selected patients were adults and were confirmed for leprosy on clinical criteria/smear positivity and/or histopathological examination. Patients were selected for the study after clinical confirmation of reactions, NFI in the form of neuritis, lagophthalmos, early mobile claw hand or foot drop. Contraindications for steroid use (namely diabetes, tuberculosis, gastritis etc.) were meticulously ruled out on history and followed wherever necessary by a strict pre-steroid investigation protocol which included blood pressure monitoring, chest radiographs, complete blood count with liver function tests, urinalysis (routine and microscopy), stool examination, serum glucose (fasting, post-prandial or random).

Assessment

Special forms for recording nerve function assessment were maintained for every patient to note the baseline features and later during follow-up to assess response to treatment. To monitor the steroid administration special charts were used indicating the current dose being administered, dates for further dosing and development of any adverse effects. Patients were also issued due date cards reminding about the dates of visit to enhance patient compliance. We also maintained the record with reference to administration of steroids and follow-up for every patient using a graph sheet indicating the completion of the regimen and incidence of recurrence during the follow-up period. The criteria used to assess the motor function was based on World Health Organization (WHO) simplified grading using voluntary muscle test (VMT) and to assess the sensory change was by using ball point testing method. These tests are routinely practiced in the Referral Clinic at our centre.

Definitions and criteria

The definitions and criteria used for assessment in the study are as follows:

Early NFI: Patients having NFI either sensory or motor of duration six months to one year.

Improved: Complete regression and/or disappearance of lesions including erythema and edema in the lesions if any.

Static: No significant change in the existing lesion with respect to the size, shape, number of lesions and erythema.

Worsened: Increase in the activity and severity of the lesion with respect to size, shape and erythema without any clinical improvement.

Recurrence/additional steroid requirement: Reappearance of inflamed lesions with or without new lesions after complete or partial regression of old lesions on completion of regimen.

Observation/Evaluation

The patients received one of the two steroid regimens with 60 patients in the group that were treated with the low dose (40 mg) regimen and 149 patients treated with high dose (60 mg) regimen. Patients were followed- up for a period

of three years with thorough regular clinical examinations by trained medical officers and were classified as 'Improved', 'Worsened' or 'Static' depending upon the clinical response.

Protocols

i. **60 mg Regimen:** The principle adopted for practicing high dose regimen being high dose of prednisolone administered initially for a short period followed by low dose given for a longer period (Garbino et al 2008). The dose, duration and the frequency of tapering is as shown in the Figure 1. The total duration of regimen was 28 weeks and the total steroid dose administered was 4.69 grams.

ii. **40 mg Regimen:** The principle being 40 mg dose of prednisolone administered initially for short period and the dose of 20 mg per day being maintained for a longer period of twelve weeks followed by tapering of steroids. The dose of 20 mg is considered as the threshold as recurrences are noticed once the dose is tapered below 20 mg dose (Naafs et al 1979). The dose, duration and the frequency of tapering is as shown in Figure 2. Total duration of the regimen was 22 weeks with the total steroid dose administered being 3.08 grams.

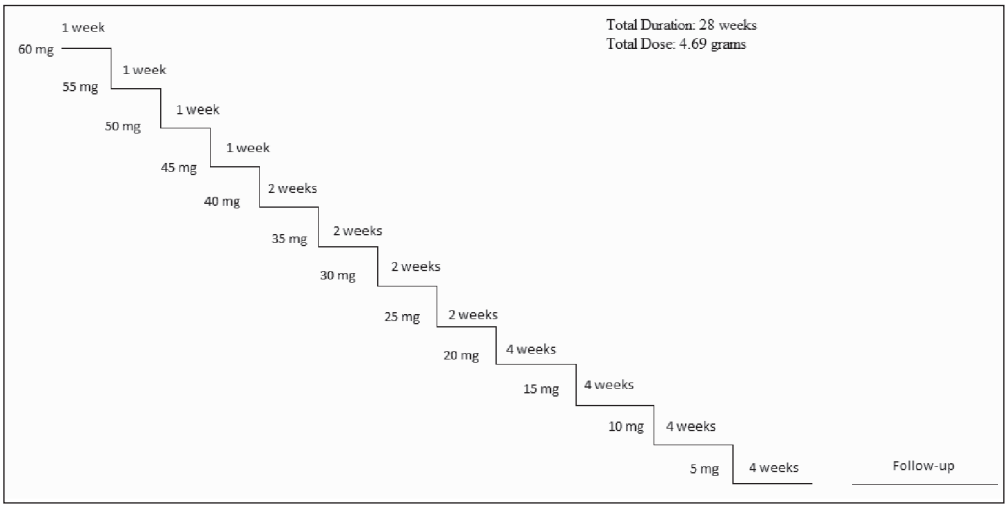

Fig 1: Proposed 60 mg regimen

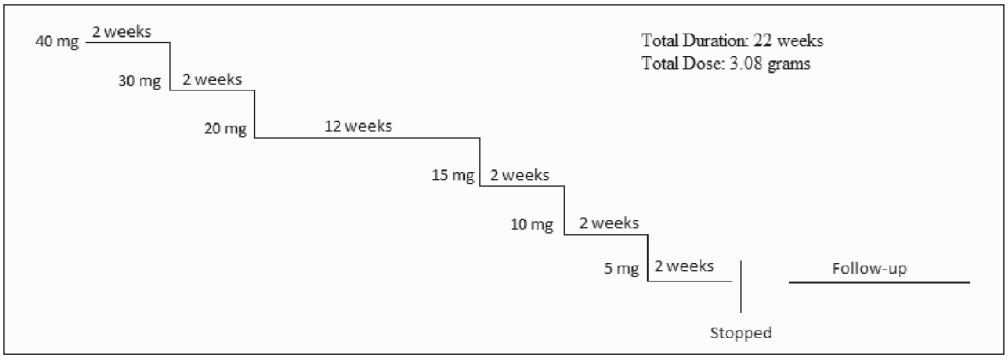

Fig 2 : Proposed 40 mg regimen

Results

Of the 149 patients in the high dose regimen, 144 patients were followed up and all 60 patients in the low dose regimen were followed-up. Five patients belonging to the high dose regimen were lost to follow-up while the rest were available for follow-up for three years. The results of the two regimens with respect to the number and proportion of patients who improved, worsened or remained static are shown in Figure 3 and Figure 4. Recurrence was noted in 24 (16%) patients and 29 (48.3%) patients in high dose (60 mg) and low dose (40 mg) regimen respectively. Figure 5 describes the comparison between the two regimens with regards to percentage of recurrence.

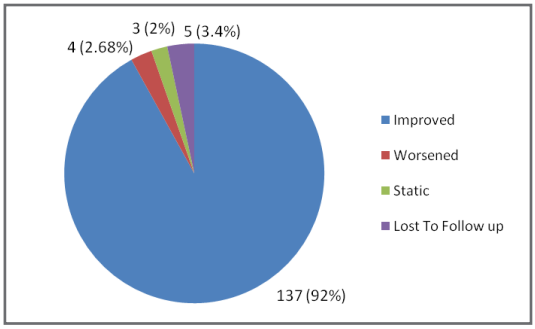

Fig 3: Outcome of high dose (60 mg) regimen

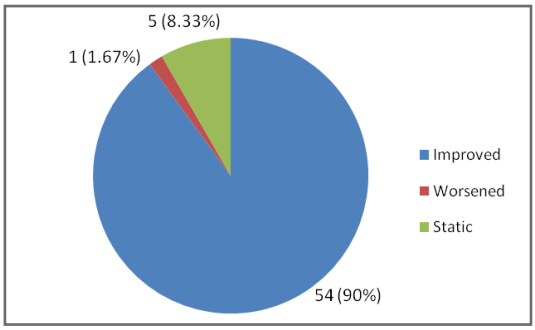

Fig 4 : Outcome of low dose (40 mg) regimen

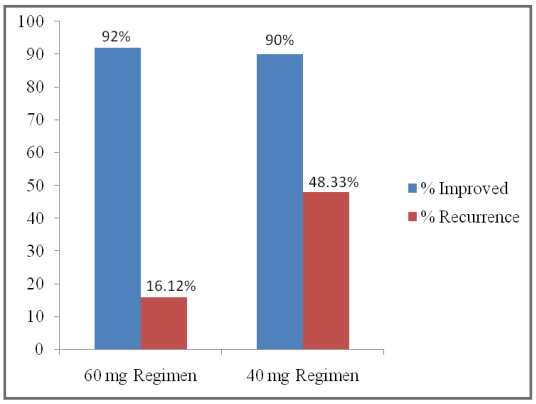

Fig 5: Comparison between the two regimens

Complications

In the 60 mg regimen, worsening of neuritis was seen in three patients whereas worsening of ulnar claw hand was seen in one patient. In the 40 mg regimen, new lesions were noted in five patients. No major adverse effects were observed in these patients treated with either of the regimens necessitating withdrawal of steroids. The known adverse effects with steroids seen in some patients were manageable.

Discussion

Steroids therefore remain an important part of treatment of reactions and NFI in leprosy (Naafs 1996, Sugumaran 1997). Various studies have been done demonstrating the efficacy of different steroid regimens in routine clinical practice (Naafs 2003, Rao et al 2006). The ideal duration and dose of steroids to be administered is still a matter of debate. The WHO regimen lasting for 3 months has been deliberated upon (Naafs 2006) in view of high recurrences and longer regimens have been warranted not only for effective treatment of reactions and nerve function impairment after stopping treatment but also to control the recurrence of reactions (Naafs et al 1979, Naafs 2003).

While some studies done previously challenge the long term efficacy of steroids in treating longstanding NFI (Richardus et al 2003b, Smith et al 2004, van Brakel et al 2003), our study demonstrates that steroids are very effective in the treatment of short term NFI of six months to one year. It has already been demonstrated that prognosis of NFI depends on the severity at the beginning of steroid therapy and earlier the treatment is started, better is the outcome (van Brakel and Khawas 1996).

The percentage of patients requiring additional steroids in various studies employing different regimens is highlighted in Table 1. These studies include the TRIPOD studies (2003, 2004), study done by Rao et al (2006) and Shetty et al (2010); the last study employing the WHO semi-standardized regimen. In our study, we observed that the high dose regimen (60 mg) has a lowest recurrence/additional steroid requirement at the end of three years of 16% which is lower than previously reported studies. Although the total dose is high as compared to the other regimens, the low recurrence rate is noteworthy.

The efficacy of a longer duration of steroid therapy has been established by Rao et al (2006) wherein they demonstrated better response rates and lesser additional steroid requirements in longer regimens (5 months) than shorter one (3 months). They have advocated that reversal reactions in multibacillary (MB) leprosy persist over many months and that duration of steroid treatment matters more than dose. While their study mentioned no significant difference between the efficacy of high (60 mg) and low (30 mg) dose long regimens whereas our study highlights that a high dose regimen for a longer duration reduces the rates of recurrence and additional steroid requirements even further.

Another interesting observation was that in the low dose regimen, of the 29 patients who had recurrence, 14 (48.3%) had it immediately within a period of six months after completion of the regimen whereas only 6 patients (25%) had recurrence within six months out of the 24 patients in the high dose regimen indicating that recurrences may occur earlier in low dose regimen.

Apprehensions about adverse effects of steroid therapy have been highlighted previously and are of a particular concern in a developing country like India (Richardus et al 2003a). But, no patient

Table 1 : Comparison of various steroid regimens used in different studies

	Total steroid given (g)	Duration (months)	Patients requiring additional steroids (%)
TRIPOD 1	1.96	4	17
TRIPOD 2	2.52	4	27
TRIPOD 3	2.52	4	-
Rao et al High	3.50	5	24
Rao et al Low	2.31	5	31
Rao et al Short	2.94	3	46
Shetty et al WHO semi-standardized regimen	1.68	3	27
BLP regimen high	4.69	7	16
BLP regimen low	3.08	5	48

in our study developed any major adverse effects necessitating withdrawal of steroids. The known adverse effects with steroids seen in some patients were manageable with routine measures. This demonstrates that even though the total dose of the 60 mg regimen being higher, the safety of the patient is not compromised.

For successful treatment it is imperative that the patients follow-up regularly according to the regimen and do not default. Even if patient is unable to maintain follow-up, the regimen can be practiced effectively even at field level by paramedical workers to ensure that the regimen is adhered to (Croft et al 1997). It is also important to note that in our study the patients with early onset nerve function impairment of motor origin which included abduction deformity, mobile claw hand, foot drop and lagophthalmos recovered with the high dose regimen coupled with physiotherapy measures like splints, strengthening exercises, muscle stimulation and wax therapy signifying the need for concurrent physiotherapy in treatment of early nerve damage.

Conclusion

Early detection of nerve damage in leprosy and its prompt treatment is of paramount importance in reducing deformities and disability. The high dose (60 mg) regimen provides sufficient coverage both in terms of dosage and duration to adequately treat reactions and early nerve damage in leprosy and minimize recurrence. In view of the reduced recurrence with this regimen, the need for additional steroid requirement or repeat therapy is minimized and so, several patients were free from reaction. However, contraindications to steroid therapy should be strictly ruled out before treatment is initiated.

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