Steroids in leptospiral uveitis: Does the route of administration matter?

Sir,

Leptospirosis, an emergent urban disease,\(^1\) can cause significant morbidity even following successful systemic treatment. In up to 90\%\(^2\) of patients, the causative leptospiral spirochete can persist in the anterior chamber of the eye\(^3\) resulting in uveitis.

Treatment of leptospiral uveitis primarily consists of steroid therapy\(^4\) - ocular as topical preparations, or posterior sub tenon (PST) steroid injections, and systemic steroid supplementation. We looked at the records of patients with leptospiral uveitis with a view to correlate the modality of steroid administration with clinical treatment outcomes, namely an improvement in visual acuity and decrease of inflammatory reaction in the affected eyes.

This study was conducted as an observational retrospective case series at Aravind Eye Hospital and Postgraduate Institute of Ophthalmology in Madurai, South India. Records of 75 consecutive patients confirmed serologically to have leptospirosis (107 affected eyes) who had presented to the Uvea Department from January 2005 to December 2008 with clinical signs characteristic of leptospiral uveitis,\(^5\) were studied. Vision had been recorded with Snellen’s chart at each visit. Each grade of Snellen visual acuity was assigned a score based on the level of vision to enable the analysis. Better vision was assigned higher scores. Visual acuity was then categorized into ‘good’ for scores of 11 (corresponding to 6/24) and above and ‘poor’ for those with less than 11. Anterior chamber (AC) inflammatory reaction was graded from 0 to 4.

Treatment regimen was designated R1 to R3. Those with mild anterior disease had been prescribed 1% prednisolone acetate suspension and homatropine bromide 2% (R1), while those with more severe anterior uveitis, intermediate or limited posterior uveitis had been treated with PST injection 0.5 ml triamcinolone acetonide (R2) and tablet prednisolone 1 mg/kg body weight (R3) tapered over a few weeks. The usual treatment pattern started at R1. If treatment response wasn’t adequate, the higher regimen was added to the current regimen. For example, if topical steroids alone (R1) were insufficient, periocular steroid was administered (R2) and so the therapy was now designated R1+R2. Patients who responded poorly despite maximum
steroid therapy were started on an immunosuppressive (Tab. methotrexate 2.5 to 10 mg per week) and the eyes of these patients were excluded from final analysis. Data was entered into Microsoft excel spread sheets and summary statistics done using SPSS (Statistical Package for the Social Science) version 16.0. The study was approved by the institutional review committee.

A total of 75 clinical records included 107 eyes of confirmed leptospiral uveitis. Fifty five (73.3%) were male patients, and the rest, female (26.6%). The mean age (SD) of presentation was 35.4 (12.2) years. The average period of follow-up (SD) was for a duration of 7.18 (6.81) months. Treatment duration ranged between 1 and 34 months. The intensity of the anterior chamber reaction recorded at first visit is shown in Table 1. There was no statistically significant difference in the improvement of visual acuity among the four groups. The various routes of administration of steroids with corresponding visual outcome are given in Table 2.

Eight percent of the patients (6 of 75) were also treated with tablet methotrexate (2.5 to 10 mg per week) for severe inflammation and these 12 eyes were excluded from statistical analysis. At the time of initial presentation to the clinic, 71 eyes had good vision scores (74.73%) which had improved to 91.57% (87 eyes) by final follow-up after treatment. Only 8 (8.42%) eyes showed poor final visual scores at final follow-up.

In our study, a decrease in inflammatory reaction was seen in all cases after treatment confirming that steroid therapy was indeed effective in controlling the inflammatory reaction. The visual scores of most eyes (91.57%) were in the ‘good’ category at the end of therapy. Our observations thus emphasize that, in general, visual outcome was good in leptospiral uveitis, as also affirmed by previous studies,[1,5] and that it responded well to steroid therapy. However, no single route of administration or combination of routes seems to have an advantage over the other routes.

While we studied the records of 75 leptospira seropositive patients with approximately 6 months of follow-up, it is a retrospective case series, and hence, one is unable to compare which of the modalities of steroid therapy was more effective in terms of rapidity of inflammation control which would require an interventional double blinded study with large cohort. We are also unable to comment on the mean duration of steroid usage in each modality required to control intraocular inflammation as this would have required more subjects in each group for proper analysis. In conclusion, it may be stated that steroid therapy seems effective in controlling intraocular inflammation associated with leptospiral uveitis and securing a good visual outcome in these affected eyes regardless of the route of administration of the steroid.

### Table 1: Anterior chamber reaction seen at first visit with corresponding visual outcome at final visit in the 95 eyes

| Grade of anterior chamber/vitreous reaction** | Total number (%) | Number of eyes with visual improvement |
|---------------------------------------------|------------------|---------------------------------------|
| +1                                          | 26 (27.36)       | 26                                    |
| +2                                          | 40 (42.10)       | 35                                    |
| +3                                          | 18 (18.94)       | 17                                    |
| +4                                          | 11 (11.57)       | 9                                     |

*The eyes of 6 patients (12 eyes) who exhibited AC reaction who had received systemic immunosuppressant therapy were excluded. **19 of the 107 eyes showed predominant vitreous reaction at presentation due to posterior uveitis.

### Table 2: Visual outcome in the 95 eyes with leptospiral uveitis which received different routes of steroid therapy

| Treatment modality | Number of patients with no decrease in final vision | Number of patients with decrease in final vision |
|--------------------|-----------------------------------------------------|-----------------------------------------------|
| Topical (R1)       | 19                                                  | 3                                             |
| PST(R2)            | 1                                                   | 0                                             |
| Oral (R3)          | 5                                                   | 0                                             |
| R1+R2              | 16                                                  | 1                                             |
| R1+R3              | 22                                                  | 1                                             |
| R2+R3              | 7                                                   | 1                                             |
| R1+R2+R3           | 17                                                  | 2                                             |
| Total              | 87                                                  | 8                                             |

*Actual number of eyes was 29. Six patients (12 eyes) who had in addition been given systemic immunosuppressant therapy were excluded. **PST-posterior sub tenon steroid injections

** REFERENCES**

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Sir,

Depression is one of the major mental disorders affecting hundreds of millions of people all over the world. There is a constant need to identify newer antidepressants from plants. *Benincasa hispida* (*Cucurbitaceae*) fruits were selected for evaluating its antidepressant potential in mice. There is only one study showing the antidepressant-like effect of the methanolic extract (0.6 and 1 g/kg administered three times and only once, respectively) of *B. hispida* fruits in mouse forced swim test (FST).

The study showed the antidepressant-like effect of the methanolic extract in FST only and the mechanisms responsible for this activity have not been studied. The fresh fruits of *B. hispida* were purchased from the local market of Hisar (Haryana, India) and authenticated as *B. hispida* (Thunb.) Cogn. (*Cucurbitaceae*) by Raw Materials Herbarium and Museum, NISCAIR, New Delhi, India (reference numbers NISCAIR/RHMD/Consult/-2010-11/1446/44 and 1448/46).

After removing the outer skin and the seeds, the fruit pulp (1 kg) of *B. hispida* was mashed using an electric juicer to afford a soft mass. The pulp was macerated with methanol (1:4) for 7 days at room temperature with occasional stirring daily. On the day 8, the pulp was filtered and the filtrate was heated (below 55°C) and evaporated using a water bath till a dark brownish liquid was obtained. The yield of the extract was 5.5% w/w. The extract obtained was stored at 2–4°C in a refrigerator and dissolved in distilled water prior to the administration to the animals.

Swiss male albino mice, weighing around 20–25 g, were purchased from Disease Free Small Animal House, Lala Lajpat Rai University of Veterinary and Animal Sciences (Hisar). Animals were housed under standard laboratory conditions with an alternating light and dark cycle of 12 h each. They had free access to food and water. The animals were acclimatized for at least 5 days before behavioral experiments. The study was carried out between 09:00 am and 5:00 pm. The experimental protocol was approved by IAEC and animal care was taken as per the guidelines of CPCSEA, Govt. of India.

Prazosin hydrochloride, (±)sulpiride, DL parachlorophenyl -alanine (p-CPA), baclofen (all from Sigma-Aldrich, St. Louis, MO, USA), imipramine hydrochloride, fluoxetine hydrochloride, and phenelzine (all from Ranbaxy Laboratories, Gurgaon, Haryana, India) were used in the present study. p-CPA was dissolved as reported earlier.

All other drugs were separately dissolved in normal saline. The mice were distributed into 25 groups and each group comprised a minimum of 6–10 mice. Methanolic extract (50, 100, and 200 mg/kg), imipramine (15 mg/kg), fluoxetine (20 mg/kg), and phenelzine (20 mg/kg) were administered orally for 14 successive days to separate groups.

### Table 1: Effect of the methanolic extract of *Benincasa hispida* on the immobility period of mice using the tail suspension test and forced swim test

| Treatment for 14 days (p.o.) | Dose (per kg) | Immobility period in TST (s) | Immobility period in FST (s) |
|----------------------------|-------------|-----------------------------|-----------------------------|
| Vehicle (distilled water)  | 10 ml       | 166.1 ± 6.26                | 161 ± 7.58                  |
| Imipramine 15 mg           | 114.4 ± 6.63*| 105.3 ± 5.53*              |
| Fluoxetine 20 mg           | 93.9 ± 8.69*| 89.6 ± 4.33*               |
| Phenelzine 20 mg           | 117.2 ± 3.84*| 106 ± 4.7*                |
| Methanolic extract 50 mg   | 148 ± 8.09 | 157.4 ± 3.75                |
| Methanolic extract 100 mg  | 106.7 ± 3.57*| 81.6 ± 4.12*              |
| Methanolic extract 200 mg  | 141 ± 4.06*| 147.3 ± 5.38               |

N = 10 in each group except the 50 mg/kg methanolic extract group where n = 9. Separate groups of animals were employed for recording immobility periods in TST and FST. Values are in mean ± SEM. Data were analyzed by one-way ANOVA followed by Dunnett’s t-test. F (6, 62) = 17.48; *P* < 0.0001 (for data of TST).

F (6, 62) = 40.07; *P* < 0.0001 (for data of FST). *P* < 0.05 when compared with the vehicle-treated group. FST - Forced swim test. TST - Tail suspension test.