Deep intramuscular methylprednisolone for the treatment of cystoid macular oedema in uveitis

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Abstract

Purpose To study the use of intramuscular methylprednisolone in the treatment of cystoid macular oedema in patients with uveitis.

Methods A total of 32 patients with various types of uveitis with unilateral cystoid macular oedema were recruited. Patients received 160 mg of intramuscular methylprednisolone into the thigh and were reassessed 6–8 weeks later. In 17 patients in whom there had been no significant improvement, a further injection of methylprednisolone was given; a total of 49 injections.

Results After a first injection a significant improvement in vision (an increase of ≥ 2 Snellen lines) was seen in 15 of 32 eyes (47%), and 17 of 32 eyes (53%) showed no significant change. After the second injection 7 of 17 eyes (41%) showed a significant improvement but there was no change in 9 of 17 eyes (53%). Only one eye deteriorated more than 2 lines of Snellen acuity. There were minimal ocular or systemic side effects associated with this form of treatment.

Conclusions Despite limited success, deep intramuscular methylprednisolone may have a role as an alternative mode of treatment in uveitis patients with unilateral cystoid macular oedema, thus avoiding the potential hazards of periocular injections. In comparison with orally administered systemic corticosteroids, an injection ensures patient compliance and is associated with fewer side effects.

Key words Cystoid macular oedema, Intramuscular, Methylprednisolone, Uveitis

Cystoid macular oedema (CMO) has been reported as the most important cause of reduced vision in patients with uveitis.¹ Previous treatments for CMO have included non-steroidal anti-inflammatory drugs, periocular (posterior sub-Tenon's^{2,3} or orbital

floor⁴) steroid injection and systemic corticosteroids, other immunosuppressive agents,^{5–7} acetazolamide,⁸ hyperbaric oxygen,⁹ pars plana vitrectomy¹⁰ and macular grid photocoagulation,¹¹ all with partial success and associated complications.

The most accepted first line treatment of CMO in uveitis is usually systemic steroids, with their well recognised side effects. Unilateral disease can be treated with periocular depot steroid but the results are often unpredictable, may be associated with a rise in intraocular pressure (IOP)^{12,13} and there are potential risks to the globe.

As an alternative to this route, we wished to evaluate the benefit of deep intramuscular (i.m.) injections of methylprednisolone in treatment of CMO in patients with uveitis. Intramuscular steroids have long been used in the treatment of rheumatological conditions^{14–16} and have been shown to be more effective than oral steroids, particularly during induction of chrysotherapy,¹⁶ but to our knowledge never for CMO.

Materials and methods

A total of 32 patients with various types of uveitis and unilateral CMO were recruited from the uveitis clinics of the Birmingham and Midland Eye Centre. There were 16 men and 16 women with an age range of 18–78 years (mean 44 years). Five patients had anterior uveitis, 5 intermediate uveitis and 22 panuveitis. All but one (VA 6/9) had reduction of best corrected Snellen visual acuity to 6/12 or worse in the affected eye before entering the study.

Of those patients with anterior uveitis, 1 had ankylosing spondylitis, 1 had psoriasis and ankylosing spondylitis and 1 psoriasis alone. Of those with panuveitis, 3 definitely had and 2 were strongly suspected of having sarcoidosis, and 1 patient had Behçet's syndrome. No underlying association was identified for any of the other patients.

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Following full ophthalmological examination, which included measurement of best corrected Snellen acuity, IOP and dilated funduscopy, all patients were assessed by one of the authors (P.I.M.) and the presence of clinically significant CMO confirmed. This procedure was repeated 6–8 weeks later at their next follow-up visit with the observer (P.I.M.) masked to the pre- and post-injection acuities. In cases where assessment of the macula was difficult because of media opacities, fundus fluorescein angiography was performed.

Concurrent systemic treatment for uveitis or associated systemic disease, which was not increased during the study, included oral prednisolone alone (8), oral prednisolone and cyclosporin A (CsA) (2), oral prednisolone and azathioprine (1) and CsA alone (3). Four patients had orbital floor injections of depot steroids at ≥ 2 months prior to the i.m. methylprednisolone and 1 patient with Behçet's syndrome had been started on CsA and had three pulses of intravenous methylprednisolone 3 months before our treatment. Despite these treatments all 5 patients showed no resolution of their CMO and were therefore included in the study.

Six patients were pseudophakic. One patient had Duane's syndrome in the eye with CMO; this patient had panuveitis of unknown aetiology. Three patients were known to have secondary glaucoma and were on topical anti-glaucoma treatment or had undergone trabeculectomy in the past.

All patients received 160 mg of deep i.m. methylprednisolone into the thigh given by nursing staff in the outpatients' department and were reassessed 6–8 weeks later. Blood pressure (BP), weight and urinalysis were recorded before and after treatment. Patients were also questioned at their following visit regarding any specific problems noticed following the injection. If a patient demonstrated partial or no improvement in visual acuity, or still had clinically significant CMO after the first injection, a second injection (160 mg) was given. An improvement was defined as ≥ 2 lines increase in Snellen visual acuity, and no change as < 2 lines change in Snellen visual acuity. In 17 patients a further injection was given; a total of 49 injections. For purposes of graphic representation Snellen visual acuities were converted to LogMAR values.

Results

After the first injection, 15 of 32 eyes (47%) showed a significant improvement and 17 of 32 eyes (53%) showed no significant change in visual acuity (Fig. 1). Following a second injection, 7 of 17 eyes (41%) showed a significant improvement, 9 of 17 eyes (53%) no change, but 1 eye (6%) deteriorated more than 2 lines of Snellen acuity (Fig. 2). The patient whose vision deteriorated had intermediate uveitis and had improved from 6/24 to 6/9 after the first injection but regressed to 6/24 following a second injection for residual macular oedema.

Only 3 patients developed a rise in IOP. In the first patient the IOP rose from 20 to 25 mmHg in the eye not affected with CMO. The second patient had a rise in IOP

Fig. 1. LogMAR visual acuities before and after the first i.m. injection of methylprednisolone.

from 20 to 23 mmHg in the affected eye. Both settled spontaneously without additional medication. The third patient had previously demonstrated an intermittent rise in IOP associated with the use of topical steroids. The IOPs were 18 mmHg in both eyes before the injection and after the first i.m. injection the IOP in the affected eye rose to 24 mmHg and was 17 mmHg in the unaffected eye. The patient was also using topical dexamethasone 0.1% to the affected eye. As this patient's CMO had reduced but persisted, he therefore received a second injection and the topical treatment was changed to clobetasone 0.1%. At the next post-injection review, the patient's CMO had decreased greatly; however, the IOP was 45 mmHg in the affected eye and 12 mmHg in the unaffected eye. The IOP settled on one topical anti-glaucoma medication and oral acetazolamide and the latter was discontinued after 2 days. Another episode of raised IOP to 46 mmHg, only in the affected eye, was noted 4 months later when the eye was quiet. In view of this we did not attribute the post-injection rise in IOP to

Fig. 2. LogMAR visual acuities before and after the second i.m. injection of methylprednisolone.

the i.m. methylprednisolone. None of the patients with pre-existing secondary glaucoma developed IOPs > 21 mmHg.

One patient gave a history of amblyopia in the affected eye. She had sarcoidosis-associated panuveitis and her vision did not improve significantly after two injections.

In general, treatment was well tolerated. None of the patients developed complications associated with systemic administration of steroids, specifically weight gain, BP rise or development of glycosuria. One patient complained of pain and tingling in the leg in which he had the injection, which lasted less than a week. Another noted a degree of subcutaneous fat atrophy at the site of injection and one patient complained of night sweats for 1 month following the injection.

Of the 22 patients in whom the i.m. injection resulted in significant improvement of vision, 8 maintained the same acuity for more than a year without any increase in systemic treatment. Nevertheless, 3 months following the injection the CMO recurred in the other patients.

Discussion

This is the first prospective study of i.m. steroids for the treatment of uveitic CMO. We wished to use this route because of the serious and potentially life-threatening side effects associated with the use of oral steroids and the limited success and potential hazards of periocular steroid injections. Varying degrees of visual improvement have been reported with posterior sub-Tenon's injections of triamcinolone acetate. Helm and Holland¹³ reported an improvement of at least 2 lines of Snellen acuity in 67% of their 20 patients. Nevertheless, 30% of their patients experienced a rise in IOP and 2 developed blepharoptosis. More recently, Tanner *et al.*³ in a combination retrospective/prospective study on 28 injections of triamcinolone to the superotemporal posterior sub-Tenon's space found 43% of eyes achieved similar improvement in acuity. A rise in IOP to > 25 mmHg was noted in 4 of 25 patients and 2 patients developed ptosis. Both these studies found a mean time to improvement of 3 weeks.

Several authors have previously reported on the associated risk of IOP rise.^{12,13} This appears to be more likely with multiple injections and anterior as opposed to posterior injections.¹² This IOP rise may be steroid-induced or related to an increase in aqueous production following decreased levels of intraocular inflammation.

According to Freeman *et al.*¹⁷ superotemporal injection of steroids to the posterior sub-Tenon's space may allow more appropriate placement of treatment over the macular area, as demonstrated by ultrasound. This must be weighed against the potential risks of globe perforation and iatrogenic ptosis.

A retrospective study by Riordan-Eva and Lightman⁴ on 54 orbital floor injections to 33 eyes showed a 35% improvement of 2 Snellen lines of acuity. In their patients 7 of 33 eyes had visual acuities of 6/9 or 6/6 before treatment. They found the injections unpredictable. Our

patients showed a similar lack of predictability in that failure to achieve significant improvement after the first injection did not predict lack of response to subsequent injections.

It was disappointing that the effects of the injections failed to last more than 3 months in 14 of 22 (64%) patients. Nevertheless, this is a treatment that can be repeated many times without hazard or potential long-term complications, as seen in those patients who have multiple i.m. injections for exacerbations of rheumatoid arthritis.

Our results show that deep i.m. methylprednisolone has a role to play in the treatment of CMO in uveitis patients, although it is clearly not successful in all patients. It has the advantage of a 'one-off' treatment similar to periocular steroid injections but without the potential hazards to the globe and adnexae. It can be administered by paramedical staff and is easily repeatable. In comparison with orally administered steroids, an injection ensures patient compliance and has not been shown to cause any of the recognised systemic complications associated with steroids in any of our patients. On the basis of this preliminary study we recommend further assessment of efficacy and durability of improvement in CMO and visual acuity provided by this treatment using a randomised controlled trial.

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