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Posterior sub-Tenon's steroid injections for the treatment of posterior ocular inflammation: indications, efficacy and side effects

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Abstract ● Purpose: Posterior sub-Tenon's steroid injections (PSTSI) are a standard drug delivery method used for the treatment of chronic uveitis of the posterior segment. The aim of this study was to analyse the indications, efficacy and complications of PSTSI in the treatment of chronic uveitis. ● Methods: During the period 1990–1994, 53 (9.5%) of 558 patients (58 eyes) followed up in the uveitis clinic received a total of 162 PSTSI of triamcinolone acetonide 40 mg in the superior quadrants. Indications for treatment were vision inferior or equal to 0.7 and/or intolerable visual disturbance. Only patients in whom PSTSI were the only treatment parameter changed were analysed. Among the main parameters analysed were visual acuity, aqueous laser flare photometry, intraocular pressure (IOP) and complications. ● Results: Anatomical location of uveitis was as follows: anterior HLA-B27-related uveitis with CME (1 patient/1 eye), intermediate uveitis (28/32), posterior uveitis (10/10) and panuveitis (14/15). Mean duration of follow-up was 448±57 days. Visual acuity improved significantly from 0.40±0.03 to 0.79±0.07, with 59.4% of eyes having a gain of 2–5 Snellen lines and 18.7% a gain of>5 lines. Mean aqueous flare photometry decreased significantly from 29.6±3.5 to 13.6±2.2 photons/ms. Mean IOP increased significantly from 13.6±0.5 to 18.5±0.8 mmHg with a rise of pressure >8 mmHg in 23 cases (36%), transient in 16 cases, but chronic in 6 cases, needing filtering surgery. Partial superior ptosis was seen in two cases and cataract progressed in seven cases. ● Conclusion: PSTSI are very effective in restoring visual acuity in chronic uveitis of the posterior segment, without systemic complications, but at the expense of intraocular hypertension, a complication that was found more frequently than expected.

Introduction

Steroids still represent the mainstay of antiinflammatory therapy in uveitis [3]. The goal is to reach a sufficient concentration at the site of inflammation. The ophthalmologist has the choice between topical, periocular or systemic administration and between preparations of different strengths [11]. Slow-release preparations have been developed to reach a prolonged therapeutic level of corticosteroids, particulary in chronic inflammation. Among the periocular administration routes, the most useful modalities are parabulbar injections of aqueous steroids in acute anterior uveitis resistant to topical steroids, and posterior sub-Tenon's injections of repository steroids in inflammation principally located in the posterior segment and/or for cystoid macular oedema (CME) [1, 5, 13].

The main advantage of posterior sub-Tenon's repository steroid injections (PSTSI) is a prolonged effect (one injection every 3–4 weeks) obtained through a maximal lo-

cal concentration of the drug that causes minimal systemic side effects [11].

As is the case for most indications for steroid use, PSTSI have been routinely used in common ophthalmological practice in an empirical way without proper placebo-controlled studies having been performed [7]. Systematic data from mostly retrospective open studies have only become available recently [4, 6, 13, 15]. Previously, information on PSTSI mainly relied on anecdotal evidence, one prevailing concept being that PSTSI only rarely produced intraocular hypertension [7, 10, 12].

The aim of our study was to gather more reliable data on the indications, efficacy and side effects of PSTSI in patients seen during a 4-year period, from January 1990 to January 1994.

Patients and methods

Patients

Since 1990, all patients seen at the uveitis clinic of Hôpital Ophtalmique Jules Gonin have been systematically recorded into a data base system. For this study, all patients treated by PSTSI from January 1990 to January 1994 were considered. Charts of these patients were reviewed retrospectively, recording in particular the type of uveitis, the indication for PSTSI, the number of injections and the evolution of the following clinical parameters: visual acuity (VA), intraocular pressure (IOP), slit-lamp examination, flare and cells, vitreous infiltration and fundus findings. Anterior chamber inflammatory activity was more precisely measured by laser flare photometry (LFP) [2, 9]. Complications were recorded, as were associated antiinflammatory and other therapies.

Each patient was examined at least 3 weeks after the first injection and parameters were evaluated at 2 months (short term), 4 months (mid-term) and at the end of follow-up (long term); >1 year).

By means of a questionnaire, we also recorded retrospectively the patient's subjective evaluation of their treatment, regarding efficacy, discomfort (pain during and after the injection or other complaints) and general appreciation.

Inclusion and exclusion criteria

For evaluation of the side effects, all patients treated by PSTSI during the indicated period were included. For evaluation of the efficacy, in order to analyse as much as possible the effect of PSTSI alone, only patients that had no change in associated systemic antiinflammatory therapy were considered. Consequently, patients that had a concomitant increase or introduction of systemic steroids were excluded from efficacy analysis, as were patients with insufficient follow-up.

Posterior sub-Tenon's repository steroids injections

Rules for the injection of posterior sub-Tenon's repository steroids in our clinic were the following: posterior segment inflamation with a visual acuity reduced to 0.7 or less due to the vitreous infiltration, CME or any visual disturbance due to vitritis intolerable for the patient.

The repository steroid used was a suspension of 40 mg of triamcinolone acetonide (Kenacort), a repository steroid whose vehicle is non-toxic in case of accidental intraocular injection [8]. Sub-Tenon's injection was performed according to the method described by Smith and Nozik [11]. Briefly, after topical anaesthesia of the conjunctiva by drops of tetracaine and with a cotton swab soaked with cocaine 4%, an injection of 1 ml of triamcinolone acetonide (40 mg/ml) was administered with a 25-G needle, in the superonasal or superotemporal sub-Tenon's space, using side-to-side movements in order to make sure that the needle was away from the sclera.

Associated treatments

Most patients were using topical steroids and/or topical nonsteroidal antiinflammatory drugs (NSAIDs). In the case of CME, standard management was performed as described elsewhere [1]. In brief, patients were treated with a combination of acetazolamide (Diamox), diclofenac sodium 0.1% (Voltaren Ophta) and prednisolone acetate 1% (Ultracortenol) for 3 weeks, and in the event of treatment failure (VA improvement of less than 2 Snellen lines), they received 3 PSTSI of triamcinalone acetonide 40 mg at 3-week intervals.

Statistical analysis

Student's *t*-test with the Bonferroni correction for multiple comparisons was used to compare the evolution of parameters during the follow-up.

Results

From January 1990 to January 1994, 558 new patients were examinated at the uveitis clinic of Hôpital Ophtalmique Jules Gonin. Fifty-three patients (9.5%; 58 eyes) received treatment with PSTSI. Their mean age was 42.0±16.6 years (range 9–75 years) with a male:female ratio of 2:3. After relapse of uveitis, four patients received a total of two treatment courses each and one patient had three treatment courses. These retreatments were each included as separate "eyes" as they occurred more than 18 months apart. A total of 64 eyes in 53 patients were treated by PSTSI. An average of 2.5±1.1 injections (range 1–5) per patient was performed. Three patients (three eyes) were not considered for efficacy analysis, because

Table 1 Distribution of patients according to the specific uveitis diagnosis

Diagnosis	Number of patients
Undefined	17
Intermediate uveitis	9
Panuveitis	5
Posterior uveitis	3
Pars planitis	16
Sarcoidosis	8
Acute retinal necrosis	5
Multifocal choroiditis	1
Lyme	1
HLA-B27	1
Eales	1
Behcet	1
Birdshot	1
Sjögren with uveitis	1

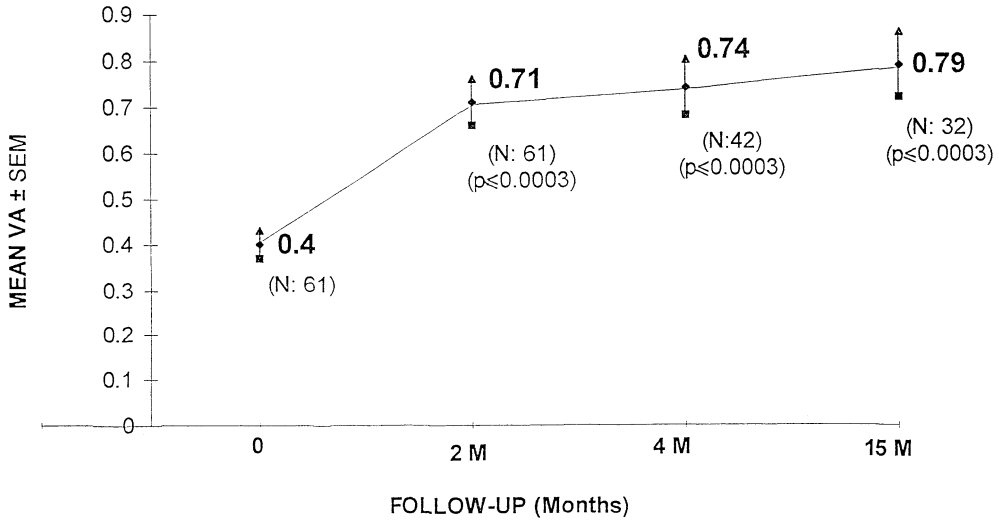

Fig. 1 Effect of PSTSI on visual acuity (*VA*; *n*: 61 eyes, 50 patients)

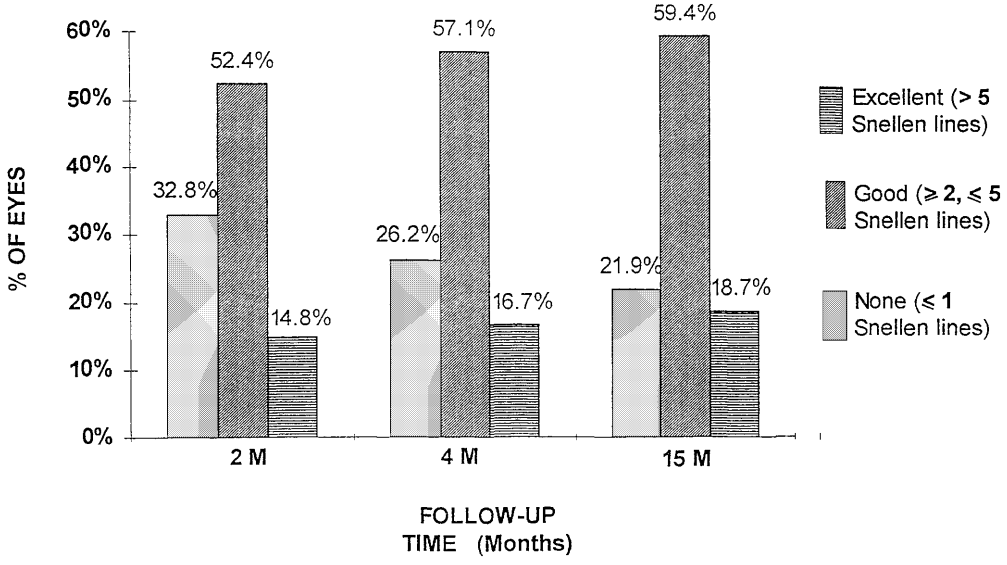

Fig. 2 Effect on visual acuity (*n*: 61 eyes, 50 patients) according to the number of Snellen lines improvement

they had a concomitant change or introduction of systemic steroid therapy.

Eyes rather than patients were reported, as results did not differ when only the first eye or episode was considered for statistical analysis.

Patients were classified according to the anatomical location of their uveitis and their specific diagnosis [14]. Anatomical location of uveitis was as follows: anterior HLA-B27-related uveitis with CME (1 patient/1 eye), intermediate uveitis (28/32), posterior uveitis (10/10) and panuveitis (14/15). (Table 1). Follow-up times were 55±3 days for short term, 131±5 days for mid-term and 448±57 days for long term follow-up.

Visual acuity

Visual acuity was assessed by analysing the evolution of mean VA and by classifying patients into groups according to the amount of visual improvement. There was a highly significant increase of VA from 0.40±0.03 (range 0.01–1.0, n=61) to 0.71±0.05 (range 0.03–1.5, n=61; $P<0.0003$) at short-term follow-up, to 0.74±0.06 (range 0.01–1.5, n=42; $P<0.0003$) at mid-term follow-up and to 0.79±0.07 (range 0.02–1.5, n=32; $P<0.0003$) at long-term follow-up (Fig. 1).

Patients were further subdivided into three groups according to the evolution of VA: no improvement of VA (<2 Snellen lines), good response (2–5 Snellen lines) and excellent response (>5 Snellen lines). The distribution of patients within these three groups is shown in Fig. 2. Roughly, 80% of patients showed good or excellent improvement in VA at long-term follow-up.

Table 2 Efficacy of PSTSI according to the specific uveitis diagnosis

	>5 Snellen lines	2–5 Snellen lines	<2 Snellen lines
Pars planitis (*n*=15)	4	7	4
Undefined intermediate uveitis (*n*=9)	4	4	1
Sarcoidosis (*n*=8)	2	5	1
Undefined panuveitis (*n*=5)	1	3	1
Undefined posterior uveitis (*n*=2)	0	2	0
ARN (*n*=5)	0	1	4
Sjögren (*n*=1)	1	0	0
Birdshot (*n*=1)	0	1	0
Lyme (*n*=1)	0	1	0
Behcet (*n*=1)	0	1	0
Eales (*n*=1)	0	0	1
Anterior uveitis HLA-B27+ (*n*=1)	0	0	

The efficacy of PSTSI by diagnosis is shown on Table 2. In summary, the best responders (VA improvement ≥2 Snellen lines) were patients with pars planitis (11/15), sarcoidosis (7/8), intermediate uveitis (8/9), posterior uveitis (2/2) or panuveitis of unknown origin (4/5). The nonresponders were those with acute retinal necrosis (4/5).

Flare values

The evolution of mean flare values (photons per millisecond), measured by laser flare photometry (LFP; FC-1000, Kowa Electronics, Tokyo, Japan) [5], is shown in Fig. 3. There was a highly significant decrease of flare following PSTSI injections. The pre-treatment value of 29.6±3.5 photons/ms (range: 5.6–125.7, *n*=53) diminished to 14.7±1.7 photons/ms (range 3.3–72.5, *n*=58; $P<0.0003$) at short-term follow-up, to 14.9±1.6 (range 4.1–42.6, *n*=31; $P<0.009$) at mid-term follow-up and to 13.6±2.2 (range 3.5–58.2, *n*=28; $P<0.009$) at long-term follow-up. A 50% decrease in mean flare values was seen already at short-term follow-up and persisted to the long term follow-up.

Intraocular pressure

The evolution of mean IOP is shown in Fig. 4. Intraocular pressure was analysed by calculating mean pre- and post-treatment pressures and by calculating the proportion of cases that developed ocular hypertension. Mean pre-treatment pressure was 13.6±0.5 mmHg (range 4–28, *n*=60), increasing significantly to 18.5±0.8 mmHg (range 6–30, *n*=62; $P<0.0003$) at short-term follow-up and to (19.0±1.2 mmHg, (range 7–44, *n*=40; $P<0.0003$) at mid-term follow-up. At long-term follow-up, pressures were still higher than before treatment (16.6±1.4 mmHg, range 5–42, *n*=34, $P<0.02$).

Intraocular hypertension

Because the notion prevails that PSTSI do not tend to significantly raise IOP [7], we analysed this point more carefully.

The proportion of eyes with intraocular hypertension (IOHT), defined as a pressure over 21 mmHg or a rise in pressure of 8 mmHg or more, was 36% (23/64; 21 patients) at any time post-injection. The mean pressure in these eyes was 27.9±1.0 mmHg (range 21–44).

The mean time from the first injection to the registration of IOHT was 79±14 days (range 21–240 days). Sixty-five per cent of eyes (15/23) developed IOHT by 2 months after the first injection, a further 22% (5/23) by 3 months and the remaining 13% (3/23) by 6 months or more.

At the time of IOHT, most patients (18/21) had no sign of an increase in inflammation. Six of 21 were taking systemic steroids. The three patients who developed IOHT 6 months or more after the beginning of PSTSI did not show any sign of increase in inflammation, but all of them were on chronic treatment with systemic steroids.

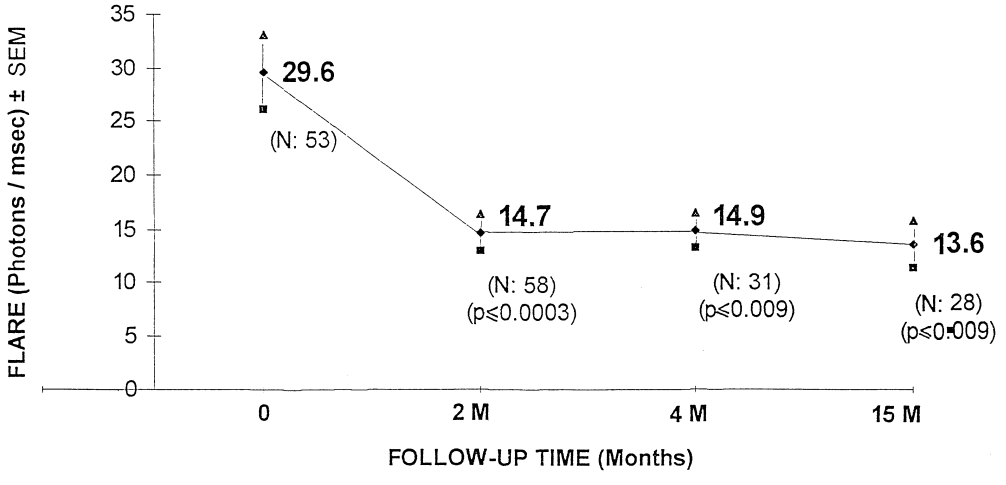

Fig. 3 Effect on aqueous flare (laser flare photometry; *n*: 61 eyes, 50 patients)

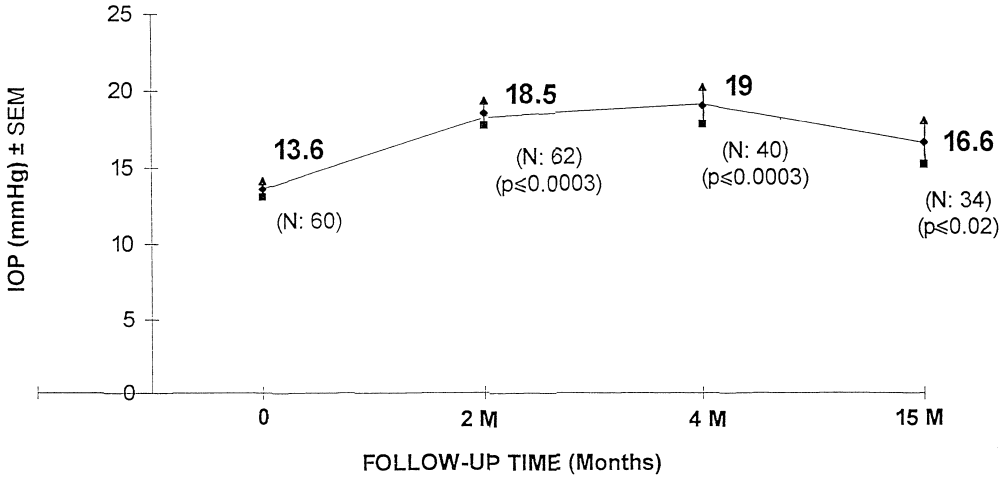

Fig. 4 Effect on intraocular pressure (*IOP*; *n*: 64 eyes, 53 patients)

Table 3 Patients with intraocular hypertension (*IOHP*)

Age, sex	Specific unveitis	Number of injections	Time to IOHP (days)[a]	Level of max. IOHP	Treatment	Inflammation rise	Systemic steroids
33-M	Lyme	3	42	8 (from 14 to 22 mmHg)	Medical	No	No
50-M	Pars planitis	3	58	10 (13–23)	Medical	No	No
44-M	Undefined posterior uveitis	1	43	10 (15–25)	Medical	No	Yes
29-M	Pars planitis	3	21	11 (10–21)	Medical	No	No
52-M	Undefined postermediate uveitis	3	83	11 (11–22)	Medical	No	No
66-F	Undefined panuveitis uveitis	4	180	11 (15–26)	Surgical	No	Yes
38-M	Undefined intermediate uveitis	1	26	12 (17–29)	Medical	No	No
33-M	Undefined panuveitis	3	49	13 (13–26)	Surgical	No	No
24-F	Pars planitis	5	93	13 (15–28)	Medical	Yes	No
28-M	Undefined panuveitis	3	183	14 (16–30)	Medical	No	Yes
		1	52	14 (14–28)	Medical	No	Yes
17-M	Pars planitis	1	26	14 (15–29)	Medical	No	No
31-F	Undefined intermediate uveitis	3	42	15 (14–29)	Surgical	No	No
62-F	Undefined posterior uveitis	5	61	15 (15–30)	Surgical	Yes	No
20-M	Pars planitis	3	36	15 (17–32)	Medical	No	Yes
29-F	Sarcoidosis	1	69	16 (10–26)	Medical	No	Yes
26-M	Undefined intermediate uveitis	3	43	16 (12–28)	Medical	No	No
		1	68	16 (14–30)	Medical	No	No
26-M	Pars planitis	4	84	16 (12-28)	Medical	Yes	No
09-M	Pars planitis	2	240	16 (12–28)	Surgical	No	Yes
29-M	Pars planitis	1	21	16 (14–30)	Surgical	No	No
53-F	Sarcoidosis	3	105	17 (10–27)	Medical	No	No
63-M	HLA-B27	3	90	18 (28–44)	Medical	No	No

[a] Time to develop IOHP after the first injection

Six of the 21 patients with IOHT were not controlled by a maximal medical treatment and had to be operated by filtering surgery. A detailed analysis of all patients with IOHT is given in Table 3.

It is of interest to note that mean ocular pressure also increased slightly, though not significantly, in the contralateral noninjected eyes (12.9±0.66 mmHg, vs 14.7±1.00 mmHg after PSTSI treatment; $P<0.137$).

Two of the patients with IOHT presented transitory IOHT in the contralateral noninjected eye, one after 21 days and the other one after 2 months, the latter also presenting an improvement of visual acuity of 3 Snellen lines. The pressure rise was attributed to the PSTSI treatment because associated treatments had not been modified.

Other complications

Other complications worth mentioning are occurrence or progression of lens opacities and blepharoptosis.

Patients treated with oral steroids (n=8 patients, 8 eyes) or pseudophakic patients (n=6 patients, 6 eyes) were excluded for evaluation of lens opacities. Forty eyes had a clear lens at the initial examination, and 7 (17.5%)

developed moderate *lens opacities*. Four eyes (4 patients) already had lens opacities before PSTSI that did not progress during the follow-up. *Blepharoptosis* of the upper eyelid occurred in two patients. It was minimal in one case and more pronounced (6 mm) in the second case.

Thirty-four patients (64%) responded to the questionnaire sent to them. Their subjective evaluation was as follows. The PSTSI procedure was well tolerated: 16 patients (47%) described no pain during the injection, 10 (29%) mild pain, 6 (18%) moderate pain and 2 (6%) severe pain. After the injection, 12 patients (35%) reported no pain, 13 (38%) pain for 1–2 h, 6 (18%) pain for 4–12 h and 2 (6%) pain for more than 24 h. Headaches, a burning sensation and periorbital swelling were also reported by a few patients (8/34). In conclusion, 76% of them were satisfied with PSTSI, 15% stated it was an unpleasant treatment and 9% gave no answer.

Discussion

Posterior sub-Tenon's repository steroid injections are fairly commonly used in uveitis. In our collective of 558 patients, nearly 10% were treated with this modality, including 52% of those with intermediate uveitis. Our study reports one of the largest collectives so far of patients treated by PSTSI and systematically followed up for a relatively long period.

This treatment appears especially useful in cases of unilateral involvement, as an adjunct to systemic antiinflammatory or immunosuppressive treatments or when systemic treatment is contraindicated.

Our data show that PSTSI is an effective therapy for inflamation of the posterior segment: nearly 80% of the treated eyes showed an improvement of at least 2 Snellen lines, and 20% of all eyes had an improvement of more than 5 Snellen lines at long-term follow-up. The mean level of associated anterior chamber inflammation, measured by LFP, was significantly reduced, by more than 50%, after PSTSI injection as early as 8 weeks after initiation of therapy and until the end of follow-up. This 50% decrease in anterior chamber flare was comparable to the effect of systemic steroid therapy obtained in the same time span after initiation of therapy in sarcoidosis and pars planitis [2]. The flare evolution was inversely proportional to the increase in VA during follow-up.

Similar good results were reported by Helm and Holland [4] in a series of 18 patients and by Yoshikawa et al. [15] in a series of 24 patients (improvement of at least 2 Snellen lines in 78% of cases in the former study vs 56.4% in the latter.

Unlike Helm and Holland, we did not find an association between good response to treatment and age.

As for any administration of steroids, PSTSI is not devoid of known side effects. In the original articles on PSTSI, little systematic information was given on side effects. As for any therapy offered to patients, it is crucial to have precise information not only on the benefit of the proposed treatment but also on the risks, in order to be able to properly inform the patient and get his/her informed consent for the procedure.

For this purpose, patients subjective impressions represent valuable information that should be passed on to potential injectees. Local transient discomfort was reported by about 53% of our patients, but about 75% of them stated that the treatment was very well tolerated.

In the published literature, the idea has prevailed that IOHT is a rare complication of PSTSI [6, 7, 10, 12]. Our data show this complication in 23 eyes (36%); in 6 eyes (9%), filtering surgery was needed to resolve the IOHT. These results are comparable to those of the recent study by Helm and Holland [4], who found IOHT in 6 (30%) of their patients [4], whereas IOHT did not seem to be a problem in the study of Yoshikawa et al. [15], as no information is given. The definition of IOHT was much more severe in our study than in that by Helm and Holland, indicating that this complication was even more pronounced in our collective.

The fact that Mueller et al. [6] did not find a significant pressure rise in their series can only partly be explained by preselection – only patients that had not shown a pressure rise after topical and/or systemic steroids were included.

Another factor speaking in favour of severity of IOHT was the proportion of cases needing surgery, which was also higher in our study. Given that all injections were performed by the same two clinicians (C.P.H. and Y.G.C.) using the usual method, avoiding anterior diffusion of injection, IOHT cannot be attributed to improper administration.

We found no significant risk association between IOHT and either the number of injections or the age of the patients. However, the natural evolution of uveitis is also associated in a small proportion of cases with secondary glaucoma.

The development of cataract secondary to steroid therapy was less frequent and less pronounced than could be expected. However, the follow-up time still has to be considered short for assessment of this gradually developing complication.

In conclusion, PSTSI seems effective in improving VA and in reducing inflammatory activity in the long term in uveitis of the posterior segment, at the expense of IOHT, a complication found more frequently than expected.

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