Intravenous methylprednisolone induces rapid improvement in non-infectious uveitis: a multicentre study of 112 patients

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Abstract

Objective

Rapid control of intraocular inflammation in non-infectious uveitis (NIU) is mandatory to avoid irreversible structural and functional damage. In this study, we assessed the efficacy and safety of intravenous methylprednisolone (IVMP) pulses in the treatment of NIU.

Methods

A retrospective case series of 112 patients who received IVMP for the treatment of NIU, either isolated or associated with different underlying diseases, was studied. Intraocular inflammation (anterior chamber cells and vitritis) was the primary outcome measure. Secondary outcome measures were macular thickness and best corrected visual acuity (BCVA). Patients were assessed at baseline visit, and at days 2-5, 7, 15 and 30 after initiation of IVMP pulse therapy.

Results

A total of 112 patients (mean age 42±14.5 yrs) were assessed. An underlying immune-mediated disease was diagnosed in 73 patients. Inflammatory ocular patterns were panuveitis (n=68), posterior uveitis (n=30), anterior uveitis (AU) (n=12), and intermediate uveitis (n=2). Additionally, patients presented cystoid macular oedema (CME) (n=50), retinal vasculitis (n=37), and exudative retinal detachment (n=31). Therapies used before IVMP included intraocular glucocorticoids (n=4), high-dose oral systemic glucocorticoids (n=77), and conventional (n=107) or biologic (n=40) immunosuppressive drugs. IVMP dose ranged from 80 to 1,000 mg/day for 3-5 consecutive days. Improvement was observed in AU, vitritis, BCVA, CME, and retinal vasculitis. At first month evaluation, total remission was achieved in 19 patients. Side effects of IVMP were respiratory infections (n=3), uncontrolled hyperglycaemia (n=1), herpes zoster (n=1), and oral candidiasis (n=1).

Conclusion

IVMP pulse therapy was effective and safe, and achieved rapid control of NIU.

Key words

non-infectious uveitis, intravenous methylprednisolone, best corrected visual acuity, anterior chamber cells, vitritis

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Competing interests: page 148.

Introduction

Non-infectious uveitis (NIU) is one of the leading causes of preventable blindness (1). A strong correlation between delayed control of ocular inflammation and the likelihood of poor visual outcomes has been described. Therefore, the goals of NIU therapy are to provide rapid control of inflammation and to achieve complete remission, thereby mitigating or avoiding permanent cumulative damage and vision loss (2). Thus, rapid and effective remission-inducing therapy is mandatory to avoid irreversible structural and functional damage.

High-dose systemic glucocorticoids are critical to achieving prompt control of inflammation in most immune-mediated diseases, including NIU. In the treatment of NIU, glucocorticoids may be administered topically or systemically, or by regional injection. In general, anterior uveitis (AU) is treated with topical glucocorticoids; intermediate uveitis, with regional glucocorticoids injections (periocular or intravitreal) or systemic glucocorticoids; and posterior and panuveitis, with systemic glucocorticoids (1, 3, 4). In addition, conventional and/or biologic immunosuppressive drugs can be used in many cases to reach remission of ocular inflammation. The dose, type and way of administration of glucocorticoids define the efficacy, speed of improvement, and side effects. These may be related to glucocorticoid receptor saturation and to the occurrence of additional non-genomic effects at higher doses (5). The European League Against Rheumatism (EULAR) defines glucocorticoid dosage and duration according to prednisone equivalent dose per day, as follows (5): low if ≤7.5 mg; medium if >7.5 mg, but ≤30 mg; high if >30 mg, but ≤100 mg; very high if >100 mg; and pulse dose if ≥250 mg for 1 or more days. Similarly, definitions of short-term or long-term therapy also vary depending on the time of use: short-term if <3 months and long-term if >6 months (5).

Intravenous methylprednisolone (IVMP) pulses have been proven effective in treating different immune-mediated diseases, such as giant cell arteritis (6, 7), membranoproliferative glomerulonephritis (8, 9), autoimmune pancreatitis (10), and idiopathic inflammatory myopathies (11). Wakefield *et al*. published the first study on the effectiveness of IVMP in severe AU in 1985 (3). In the last twenty years, IVMP has been administered successfully in different patterns of NIU (4, 12-21). However, most studies on IVMP treatment of uveitis are small, include selected patients and/or diseases, and do not assess all ocular outcomes (3, 12, 13, 15, 16, 20, 21).

Although high-dose systemic glucocorticoids have a powerful anti-inflammatory effect, side effects often limit their use. Glucocorticoid-associated side effects may involve most major organ systems: musculoskeletal, gastrointestinal, cardiovascular, endocrine, neuropsychiatric, dermatologic, ocular, and immunologic (22-26). However, the risk/benefit ratio of glucocorticoid therapy can be improved by careful monitoring and use of appropriate preventive strategies (22).

After careful consideration of the above-mentioned data, the present study was conducted to assess the efficacy of IVMP in a large series of patients with severe NIU.

Materials and methods

Design and enrolment criteria

This study is a retrospective multicentre case series of 112 patients with severe NIU conducted in Uveitis Units of 11 Spanish referral centres. These patients were refractory to systemic therapy (oral glucocorticoids and conventional or biologic immunosuppressive drugs) and treated with IVMP and followed up over a 30-day period. The decision to start IVMP therapy was made solely on the presence of ocular inflammation.

The study was approved by the Clinical Research Ethics Committee (EPA2019022). Afterwards, written informed consent was requested and obtained from all the patients included in the study.

IVMP was always administered in hospital, and the dose ranged from 80 mg to 1,000 mg every 24 hours for a period from 2 to 5 consecutive days. The dose was adjusted to patients' comorbidities

and weight. For example, diabetics are known to be at increased risk for adverse effects of high-dose IVMP. We defined "pulse therapy" as the administration of ≥250 mg prednisone equivalent in a standard one-hour infusion of IVMP. Doses <250 mg were administered in less than 30 minutes. However, the repeated infusion of 80 mg MTP was considered as a "pulse therapy" according to its classical definition (27): a bolus/pulse of medication is the enteral or parenteral a drug at a rapid but controlled rate. The aim of pulse therapy is to achieve a faster response and stronger efficacy and to decrease the need for long-term use of systemic corticosteroids. In the present study the most frequent dose was 1000 mg (administered in 52 patients), followed by 500 mg (49 patients) and 250 mg (8 patients), only in three cases the dose was of 80 mg, 125 mg and 750 mg respectively.

Malignancy or systemic infectious diseases, including hepatitis B or hepatitis C infections, were excluded prior to IVMP administration (28-38). As indicated in the Spanish National Guidelines, all patients were tested for latent tuberculosis by tuberculin purified protein derivative skin test and/or an interferon-γ assay (QuantiFeron) and a chest radiograph. If positive results were obtained, active tuberculosis was ruled out.

Outcome measures

The main outcomes considered were efficacy and safety of IVMP during the first month of treatment. Intraocular inflammation, macular thickness and visual acuity were assessed to determine efficacy of IVMP. These outcome variables were recorded at baseline, and at days 2–5, 7 and 15 and at month 1 after initiation of IVMP administration. Slight improvement observed as early as days 2–5 after the first IVPM dose was a predictor of good treatment response. No further improvement was expected after 1 month of IVMP administration.

The degree of intraocular inflammation was assessed according to the Standardization of Uveitis Nomenclature (SUN) Working Group criteria (39). Inactive AU was defined as the presence of less than 1 cell per field on standard slit-lamp examination (grade 0). Following SUN recommendations, improvement of AU activity was defined as either a two-step decrease in the level of inflammation or a decrease to grade 0 (grading scale: 4, 3, 2, 1, 0.5 and 0) (40). Improvement in vitreous haze was similarly defined. Vitritis was assessed using the Nussenblatt scale (41).

Fluorescein angiography (FA) was performed to detect the presence of vasculitis, papillitis and CME. Retinal vasculitis was defined as a retinal leakage, staining and/or occlusion on FA. Choroiditis and retinitis were considered active or inactive depending on the presence or absence of activity data on ophthalmoscopic examination and/or FA.

Central macular thickness was measured by high-definition optical coherence tomography (HD-OCT). All HD-OCT scans were performed using Cirrus HD-OCT (Carl Zeiss, Oberkochen, Germany). Scans were obtained using the 512x128 scan pattern. Macular thickening was defined as macular thickness of >250 μm, whereas CME was considered present if macular thickness was >300 μm.

Visual acuity was assessed by Best-Corrected Visual Acuity (BCVA) estimated using the Snellen chart (41). According to this test, 20/20 vision (or 20/20 visual acuity) is considered normal vision (the subject can read a letter that most individuals can read at a distance of 20 feet). For the purpose of the present study, 20/20 vision (normal vision) was expressed as 1.0, and 0/20 vision was expressed as 0.0 (40).

Statistical analysis

Statistical analysis was performed using Statistica software (StatSoft, Tulsa, Oklahoma). Results were expressed as the mean ± standard deviation (SD) or median (interquartile range [IQR]), as appropriate. Wilcoxon's signed rank test was used to compare continuous variables prior to and after IVMP therapy. Results were reported considering the number of patients.

Results

Baseline demographic and clinical features

A total of 112 patients (66 women/46 men) with severe and refractory NIU were enrolled in the study (Table I). Mean age was 42±14.5 years. The course of NIU was acute in 80 patients and recurrent in 32.

Underlying diseases were idiopathic (n=29), Vogt Koyanagi Harada (VKH) (n=28), Behçet's disease (n=19), sarcoidosis (n=6), axial spondyloarthritis (n=6), rheumatoid arthritis (n=2), psoriatic arthritis (n=2), Sjögren's syndrome (n=2), multiple sclerosis (n=2), juvenile idiopathic arthritis (n=1), Eales's disease (n=1), aortitis (n=1), Cogan's syndrome (n=1), Crohn's disease (n=1), and reactive arthritis (n=1).Other conditions not associated with systemic diseases were multifocal choroidopathy (n=4), sympathetic ophthalmia (n=3), Birdshot chorioretinopathy (n=2), and acute posterior multifocal placoid pigment epitheliopathy (n=1).

Inflammatory ocular patterns were panuveitis (n=68), posterior uveitis (PU) (n=30), AU (n=12), and intermediate uveitis (IU) (n=2).

In addition, specific severe complications included exudative retinal detachment (n=31), ocular synechia (n=27), CME (n=50), retinitis (n=49), choroiditis (n=33), and retinal vasculitis (n=37).

Although IVMP pulse therapy is not the initial treatment of choice for AU, this study included data from 12 patients with AU who received IVMP because they experienced complications despite oral glucocorticoid and immunosuppressive drug treatments (3 patients had AU with CME; 2 patients had severe recurrent episodes of VKH with granulomatous AU; 2 patients had severe recurrent bilateral idiopathic AU; 2 patients had sudden severe uveitis with ocular synechias, and 1 patient had severe uveitis by sympathetic ophthalmia). Moreover, IVMP pulses were given to 2 patients with severe uveitis despite topical and oral glucocorticoid therapy in the setting of active spondyloarthritis.

At the time of diagnosis of uveitis, the following positive laboratory data were observed: antinuclear antibodies (ANA) (n=11), HLA-B27 (n=12), HLA-B51 (n=31), HLA-B29 (n=1), anti-neutrophil cytoplasmic antibodies (ANCA) (n=2), anti-saccharomyces

Table I. Baseline main general features of the 112 patients with non-infectious uveitis.

Age, mean ±SD, years	42 ± 14.5
Sex, female/male, n (%)	66/46 (58.9/41.1)
Associated diseases, n (%)	
Idiopathic	29 (25.9)
Associated systemic inflammatory diseases	
Vogt Koyanagi Harada	28 (25)
Behçet disease	19 (16.9)
Sarcoidosis	6 (5.3)
Axial spondyoarthritis	6 (5.3)
Rheumatoid arthritis	2 (1.8)
Psoriatic arthritis	2 (1.8)
Sjögren's syndrome	2 (1.8)
Multiple sclerosis	2 (1.8)
Cogan's syndrome	1 (0.9)
Juvenile idiopathic arthritis	1 (0.9)
Eales disease	1 (0.9)
Aortitis	1 (0.9)
Crohn's disease	1 (0.9)
Reactive arthritis	1 (0.9)
Non associated with systemic inflammatory diseases	
Multifocal choroidopathy	4 (3.6)
Sympathetic ophthalmia	3 (2.7)
Birdshot chorioretinopathy	2 (1.8)
Acute posterior multifocal placoid pigment epitheliopathy	1 (0.9)
Pattern of uveitis, n	
Panuveitis	68 (60.7)
Posterior uveitis	30 (26.8)
Intermediate uveitis	2 (1.8)
Anterior uveitis	12 (10.7)

SD: standard deviation; n: number of patients in each group; %: percentages.

Table II. Systemic immunosuppressive treatment before and after intravenous methylprednisolone (IVMP) therapy in non-infectious uveitis.

Treatment before IVMP		**Treatment after IVMP**	
Conventional immunosuppressive drugs		Conventional immunosuppressive drugs	
Methotrexate	30	Methotrexate	45
Cyclosporine A	38	Cyclosporine A	46
Azathioprine	26	Azathioprine	35
Mycophenolate	6	-	
Sulfasalazine	4	Sulfasalazine	4
Leflunomide	1	Mycophenolate	1
Cyclophosphamide	1	-	
Tacrolimus	1	-	
Biologic agents		Biologic agents	
Adalimumab	19	Adalimumab	34
Infliximab	12	Infliximab	17
Golimumab	4	Golimumab	1
Tocilizumab	3	Tocilizumab	3
Rituximab	1	Certolizumab	1
Daclizumab	1	-	

IVMP: intravenous methylprednisolone.

cerevisiae antibodies (ASCA) (n=1), rheumatoid factor (n=2), anti-Ro antibodies (n=1), and elevated angiotensin converting enzyme (ACE) (n=4).

Thirty-five of 112 (31%) patients had high erythrocyte sedimentation rate (ESR) prior to IVMP treatment. In most cases, apart from NIU, there was no active systemic disease that could explain ESR elevation.

Previous treatment before IVMP

Prior to IVMP pulse therapy, topical (n=20), intraocular (n=4) and oral (n=77) glucocorticoids were used (mean dose 30 mg/day). Treatment with oral glucocorticoids was rapidly switched to intravenous administration after underlying infection was ruled out. Some patients were on treatment with conventional immunosuppressive drugs or biologic agents due to underlying disease.

Conventional immunosuppressive drugs used prior to IVMP therapy (Table II) were as follows: methotrexate (MTX) 15–25 mg/m^2/week (n=30); cyclosporine A (CsA) 2–5 mg/kg/day (n=38); azathioprine (AZA) 1–4 mg/kg/day (n=26); leflunomide (LFN) adult dose of 100 mg/day for 3 days, and then 10-20 mg/day (n=1); mycophenolate mofetil (MMF) 2–3 g/day (n=6); sulfasalazine (SSZ) 2–3 g/day (n=4); cyclophosphamide (CFX) 1–2 mg/kg/day administered orally (n=1); tacrolimus 0.06 mg/kg/day (n=1).

Some patients had also received biologic agents prior to IVMP therapy: adalimumab (ADA) 40 mg subcutaneously (sc) administered every 1 or 2 weeks (n=19); infliximab (IFX) 3–5 mg/kg intravenous (iv) at weeks 0, 2, and 6, followed by a maintenance dose every 4, 6, or 8 weeks (n=12); golimumab (GLM) 50 mg/sc/month (n=4); tocilizumab (TCZ) 4 mg/kg or 8 mg/kg iv every 4 weeks (n=3); rituximab (RTX) in a single course of 2 doses of 1 g iv 2 weeks apart (n=1); and daclizumab 1-2 mg/kg iv every 2 or 4 weeks (n=1).

Treatment after IVMP

After IVMP, the following systemic therapies were used: oral glucocorticoids (n=110), conventional (n=91) and biologic (n=24) immunosuppressive drugs. In some cases, systemic therapies were maintained or changed due to acute uveitis flare. Oral glucocorticoid dose was progressively reduced.

Conventional immunosuppressive drugs used after IVMP therapy (Table II) were as follows: MTX 15–25 mg/m^2/week (n=45); CsA 2–5 mg/kg/day (n=46); AZA 1-4 mg/kg/day (n=35); SSZ 2–3 g/day (n=4); and MMF 2–3 g/day (n=1). Biologic immunosuppressive drugs used after IVMP were as follows: ADA 40 mg sc every 1 or 2 weeks (n=34); IFX 3–5 mg/kg iv at weeks 0, 2, and 6, followed by a maintenance dose every 4, 6, or 8 weeks (n=17); GLM 50

mg sc/month (n=3); certolizumab 400 mg sc at weeks 0, 2 and 4, followed by a maintenance dose of 200 mg sc every 2 weeks or 400 mg sc every 4 weeks (n=1); and TCZ 4 mg/kg or 8 mg/kg iv every 4 weeks (n=3).

Outcome variables after IVMP

Compared to baseline, rapid statistically significant improvement was observed in BCVA after one month from the first IVMP pulse (mean basal BCVA 0.46±0.27 *vs*. 0.74±0.24; $p<0.05$) (Fig. 1). This was also the case for macular thickness (409.7±168.3 *vs*. 275±87.6; $p<0.05$) (Fig. 2), and anterior chamber cells (mean basal Tyndall 1.17±1.19 *vs*. 0.05±0.24; $p<0.05$) and vitritis (mean basal Tyndall 0.87±1.05 *vs*. 0.08±0.26; $p<0.05$) according to SUN Working Group criteria (Fig. 3).

Following IVMP pulses administration, reduction of anterior chamber cells was observed in all patients, while vitritis was maintained in only 5% of patients (Fig. 3). Assessed using the Nussenblatt scale, 11 patients presented with grade 4 vitritis at baseline, while most patients presented with grade 2 or 3 vitritis. After IVMP therapy, grade 2 was the highest grade of vitritis observed, and it was present in only 3 patients. Synechiae were resolved in 6 out of the 27 (24%) patients affected at baseline, and CME was resolved in 38 out of 50 (44%) patients.

Resolution of specific severe complications occurred in a considerable number of patients after 1 month of IVMP pulse therapy. In this regard, patients who presented choroiditis (n=33), retinitis (n=49), and retinal vasculitis (n=37) at baseline experienced statistically significant improvement (69.9%, 69.3%, and 75.6% respectively; $p<0.05$ in all cases). Complete remission of ocular inflammation with IVMP was achieved in 19 (17%) patients at one month of IVMP treatment. No significant differences were found comparing patients with idiopathic NIU (n=29) and those with NIU associated with systemic inflammatory diseases (n=73) (data not shown due to heterogeneity of the sample).

After a 1-month follow-up, the only systemic relevant side effects observed were respiratory infections (n=3), uncontrolled hyperglycaemia (n=1), herpes zoster (n=1), and oral candidiasis (n=1). Other typical, though non-severe side effects were weight gain (n=1), reactive leukocytosis (n=1), and Cushingoid features (n=1).

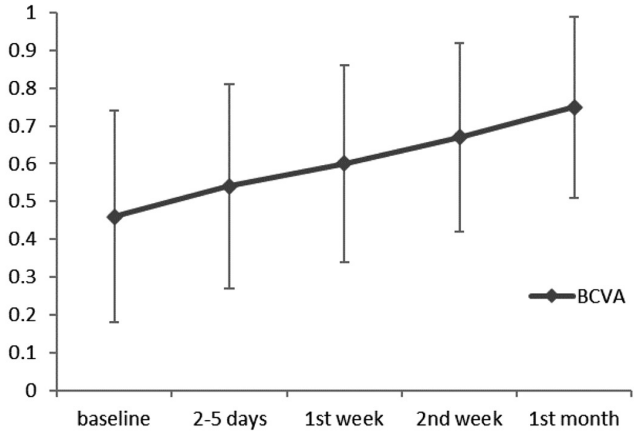

Fig. 1. Rapid improvement of best-corrected visual acuity following the onset of intravenous methylprednisolone.
BCVA: Best-Corrected Visual Acuity.
Data are expressed as mean values compared with baseline results ($p<0.05$).

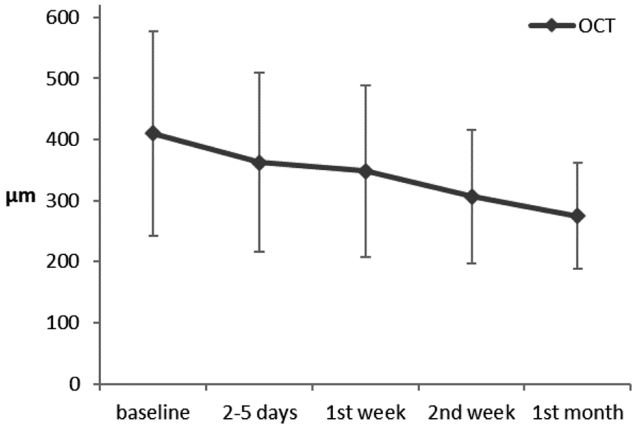

Fig. 2. Rapid improvement of mean macular thickness by optical coherence tomography following the onset of intravenous methylprednisolone.
OCT: optical coherence tomography.
Data are expressed as mean values compared with baseline results ($p<0.05$).

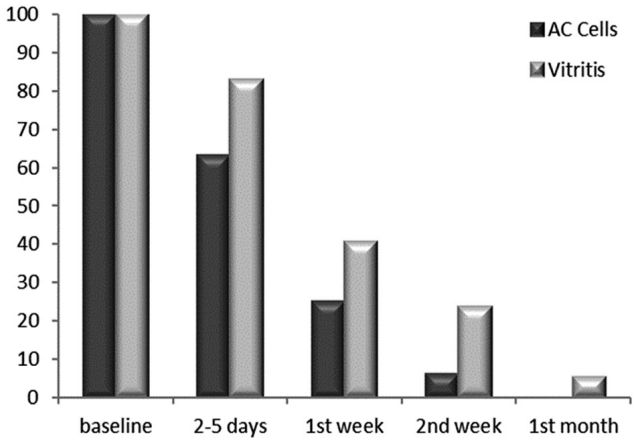

Fig. 3. Percentage of cases with reduction on anterior chamber cells and vitritis according to the SUN criteria following the onset of intravenous methylprednisolone.
AC Cells: anterior chamber cells;
SUN: Standardization of Uveitis Nomenclature Working Group criteria.
Data are expressed as mean values compared with baseline results ($p<0.05$).

Discussion

We studied 112 patients with severe and in most cases refractory NIU who showed rapid improvement following IVMP pulse therapy. To the best of our knowledge, this is the largest case series study published to date. Although patients presented with a wide spectrum of underlying inflammatory diseases, improvement was observed in all ocular outcomes at month 1 of IVMP treatment, and complete remission of ocular inflammation was achieved in 19 (17%) patients.

Glucocorticoid use has emerged as a major breakthrough in the management of inflammatory ocular disorders (42).

High-dose systemic glucocorticoid therapy, especially IVMP, is used in severe flares of most immune-mediated diseases, such as neuro-immune-mediated diseases (demyelinating diseases, myasthenia gravis, transverse myelitis, and non-infectious encephalitis), systemic autoimmune diseases (systemic lupus erythematosus [SLE], rheumatoid arthritis, systemic vasculitis, mixed connective tissue diseases, and systemic sclerosis), and hematological (autoimmune haemolytic anaemia and immune thrombocytopenia), renal, and other diseases (gastrointestinal, cutaneous, and respiratory) (43, 44).

Glucocorticoids are defined as pleiotropic hormones that at pharmacologic doses prevent or suppress inflammation and other immunologically mediated processes (45). At the molecular level, glucocorticoids form complexes with specific receptors, and these complexes migrate to the nucleus, where they interact with selective regulatory sites within DNA. This results in positive and negative modulation of several genes involved in inflammatory and immune responses (45). Nongenomic mechanisms are thought to explain the efficacy of pulse-dose glucocorticoid therapy, because pulse doses are generally higher than the saturation level of the glucocorticoid receptor (7). Oral glucocorticoids are well absorbed after administration and show variable degrees of binding to glucocorticoid-binding globulin and albumin (7). Only free, unbound drug can interact with the glucocorticoid receptor (7), which translocates to the nucleus and targets gene transcription (7). At the cellular level, glucocorticoids inhibit the access of leukocytes to inflammatory sites; interfere with the functions of leukocytes, endothelial cells, and fibroblasts; and suppress the production and the effects of humoral factors involved in the inflammatory response (45).

Treatment of severe NIU includes glucocorticoids and other immunomodulatory drugs. Glucocorticoids are the cornerstone of anti-inflammatory therapy, and dose increase is proportional to the clinical activity and severity of the disease (43). Indicators of severe inflammation in uveitis include impairment of visual function, bilateral disease, vitreous haze, macular or optic nerve disease, retinal vascular inflammation, macular edema, exudative detachment and ocular structural complications, all of which may threaten visual function (46). The presence of an associated systemic disease may influence the treatment approach in patients with NIU (46). For example, in the treatment of sarcoidosis, rheumatic diseases, and Crohn's disease, the use of glucocorticoids is beneficial for both NIU and extraocular manifestations.

Several reports support the benefits of systemic glucocorticoids in patients with NIU (1, 2, 4, 14, 42, 44-47). In this regard, Wakefield *et al*. (4) emphasised that IVMP therapy given on an intermittent basis may be effective in the treatment of various severe ocular inflammatory diseases, and given on a long-term basis can achieve complete disease remission (32).

Pulse glucocorticoid therapy has beneficial effects on severe retinal detachment in patients with VKH by improvement of the permeability of capillaries and the blood-retinal barrier rather than by anti-inflammatory or immunosuppressive action (16, 21). IVMP pulses are also effective in severe vision-threatening Behçet's uveitis attacks. In these cases, IVMP improves VA function in a short period of time and minimises flares during the first 6 months of treatment (15, 17, 20).

Humoral and cellular immune mechanisms are involved in the production of AU (3). Patients with HLA-B27+ AU have iris serum autoantibodies and T-cell lymphopenia during active acute attacks of AU, while HLA-B27- AU patients have an increased prevalence of serum autoantibodies to smooth muscle and raised serum IgE levels, as well as decreased T-cell-mediated immune mechanisms (3). Systemic glucocorticoids are not generally used in patients with AU. However, their efficacy in severe situations is widely accepted.

Guidelines for the systemic treatment of NIU were updated by a committee of ophthalmologists and rheumatologists in 2018 (46). According to them, glucocorticoids are proposed only as a first step, while the characterisation of the type of NIU is performed. Due to the side effects of glucocorticoids, immunosuppressive drugs have been incorporated to the management of NIU in an attempt to achieve a glucocorticoid-sparing effect (46).

The main problem with glucocorticoids is that side effects may occur at a wide range of doses and vary depending on the route of administration. Information on the relationship between glucocorticoid-related adverse events and glucocorticoid dose in patients with NIU is scarce. However, chronic use of moderate-to-high doses of glucocorticoids has been reported to cause ocular side effects (glaucoma, cataracts) and a wide range of systemic adverse events, including impaired glucose tolerance, hypertension, osteoporosis, ischaemic necrosis of bone conditions, and infections. Information retrieved from the databases of the VISUAL-1 and VISUAL-2 studies indicates that the most common glucocorticoid-related adverse events are cutaneous and subcutaneous tissue and muscular complications, laboratory abnormalities/weight change, infections, injection site reactions, ocular disturbances, and psychiatric disorders (48). The MUST Trial and Follow-up Study (46) evaluated the safety of systemic glucocorticoid therapy for uveitis. In this study, patients with non-infectious, intermediate, posterior and panuveitis were randomised to receive treatment with fluocinolone acetonide implants or systemic therapy with oral glucocorticoids and immunosuppression. Throughout 7 years of follow-up, no increased risk of global side effects was observed in the systemic therapy group although higher use of antibiotics was required due to infections. There was little and not significant difference in weight gain between the 2 groups. These data suggest that oral glucocorticoids and immunosuppression can be administered relatively safely.

On the one hand, the strengths of this study are the large number of patients recruited and the diversity of underlying inflammatory diseases associated with NIU. In general, patients showed improvement in all outcome variables in a short period of time. Moreover, the use of IVMP pulses shortens oral

glucocorticoid treatment time and reduces overall side effects. On the other hand, the weaknesses of the study are the small number of patients recruited for each underlying inflammatory disease, the short follow-up period and the previous systemic treatments received, which may influence outcome variable results.

Conclusion

In conclusion, IVMP pulse therapy seems to be an effective and safe therapeutic alternative for rapid control of inflammation in acute severe and refractory NIU, regardless of the underlying autoimmune disease associated with NIU. Further large prospective studies with long-term follow-up are required to assess the potential role of IVMP in the treatment of NIU.

Competing interests

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