Diploma thesis

Periocular steroids in non-infectious uveitis: 6 month outcomes

submitted by

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Statutory Declaration

I declare that I have authored this thesis independently, that I have not used other than the declared sources / resources, and that I have explicitly marked all material which has been quoted either literally or by content from the used sources.

Graz, ……. *Matthias Maximilian Veitz eh*

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Abstract

Introduction:

Steroids are the mainstay short term treatment for non-infectious uveitis. The exposure of the globe makes the eye especially suited for local application of these drugs, thus avoiding or diminishing many of the systemic complications of steroids. For this purpose, steroids are used in the form of drops and intraocular or periocular injections. The latter offer high intraocular drug concentrations by a well-tolerated in office procedure leaving the globe intact, which virtually eliminates the intraocular injection's risk of severe complications such as endophthalmitis. Periocular steroids have been shown to be efficacious, but their risk benefit profile has been insufficiently characterized.

Methods:

In this retrospective analysis, we reviewed the charts of 100 eyes of 86 patients with the diagnosis of uveitis who had received a periocular corticosteroid injection at any time between 2006 and 2016 at the department of Ophthalmology at the Medical University of Graz. Basic demographic information as well as intraocular pressure and best visual acuity were collected and statistically analysed.

Results:

The results show that eyes treated with periocular steroids show a significant improvement in visual acuity one month ($p<0.001$) as well as the six months after treatment ($p<0.001$). Patients also showed a statistically significant rise in intraocular pressure from baseline at the one month ($p<0.001$) as well as at six months ($p<0.001$). However, only 11.11% showed an intraocular pressure increase of more than 10 mmHg.

Conclusion:

The treatment of uveitis patients with a periocular steroid injection shows an improvement of visual acuity within the first month after the injection, but also a significant rise of intraocular pressure.

Zusammenfassung

Einführung:

Steroide sind die Eckpfeiler der Kurzzeittherapie bei nichtinfektiöser Uveitis. Aufgrund der anatomischen Lage eignet sich das Auge hervorragend für lokale Applikationen dieser Medikamente. Auf diese Weise können viele der systemischen Komplikationen von Steroiden vermieden oder zumindest verringert werden. Zu diesem Zweck können Steroide in Form von Tropfen sowie als intra- oder periokulare Injektionen verwendet werden. Letzteres kann in einem ambulanten Setting durchgeführt werden, ohne das Auge zu eröffnen. Somit werden schwere Komplikationen wie zum Beispiel eine Endophthamitis weitestgehend vermieden und trotzdem können hohe intraokulare Konzentrationen des Medikaments erreicht werden. Periokulare Injektionen haben sich bereits als eine effektive Therapie erwiesen, das Risiko-Nutzen Profil ist jedoch bisher unzureichend aufgezeigt.

Methoden:

In dieser retrospektiven Analyse wurden Daten von 100 Augen von 86 Uveitis-Patientinnen und Patienten analysiert, welche in den Jahren von 2006 bis 2016 an der Medizinischen Universität Graz/Österreich eine periokulare Injektion mit Steroiden bekommen haben. Demographische Basisinformationen sowie Augeninnendruck Messwerte und Visusdaten wurden gesammelt und statistisch ausgewertet.

Ergebnisse:

Die Resultate dieser Studie zeigen eine statistisch signifikante Visus-Verbesserung zum Ausgangswert ein Monat ($p>0.001$) sowie sechs Monate nach der Injektion ($p>0.001$). Auch eine statistisch signifikante Erhöhung des Augeninnendrucks zum Ausgangswert konnte nach einem Monat ($p>0.001$) und nach sechs Monaten ($p>0.001$) festgestellt werden. Allerdings zeigten nur 11.11% aller Augen eine Erhöhung des Augeninnendrucks über 10 mmHg.

Schlussfolgerung:

Die Therapie von Uveitis-Patientinnen und Patienten mittels periokularer Steroidinjektionen zeigt eine deutliche Visus Verbesserung innerhalb eines Monats, jedoch gleichzeitig eine signifikante Erhöhung des Augeninnendrucks.

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1. Introduction

1.1. Uveitis

1.1.1. Definition

Uveitis is defined as an inflammation of the uveal tract, which includes the iris, the ciliary body, and the choroid. It refers to over 25 different diseases involving an inflammatory state of the interior of the eye such as iritis, pars planatis, vitritis, retinal vasculitis, choroiditis, and papillitis. (1,2)

1.1.2. Etiology

Uveitis can be caused by infectious and non-infectious factors. In immunocompetent patients, the most common infectious cause is toxoplasmosis, which is usually diagnosed through the presentation of a retinochoroidal inflammatory lesion. (3,4) In immunocompromised patients, the most frequent infectious cause of uveitis is cytomegalovirus which often occurs in AIDS patients or otherwise immunocompromised non-AIDS patients (e.g. systemic lupus erythematosus) with a low CD4 T-cell count. (5,6) Although, in the majority of non-infectious uveitis patients the disease remains idiopathic, there are several autoimmune diseases that may cause inflammation of specific parts of the eye. (3) In 40-50% of patients with non-infectious anterior uveitis, an association with the human leukocyte antigen HLA-B27 can be found. (7,8) However, the presence of the gene does not always cause an ocular inflammation and is therefore not an appropriate marker to determine the risk of ocular problems. (3) Other systemic disorders such as rheumatoid arthritis, ankylosing spondylitis, Reiter's syndrome, ulcerative colitis, regional enteritis, and Behcet's disease may be associated with uveitis. (9)

1.1.3. Epidemiology

Based on epidemiological studies the incidence of uveitis is estimated to be 17 - 52 cases per 100,000 and has a prevalence of about 38 - 714 per 100,000. (10–14) Although it is a relatively uncommon disease, (2) it accounts for 5-20% of legal blindness in Europe and the United States of America, and perhaps as much as 25% in the developing world. (4,9,15) According to de Smet et al *"racial, genetic, geographical, social and environmental factors can all affect the distribution on*

uveitis between different populations". (9,16,17) In most cases, females and males seem equally effected, although some aetiologies may have a different sex distribution. For example, HLA-B27 associated anterior uveitis is more common in males, whereas juvenile idiopathic arthritis associated uveitis is far more common in young girls. (18) Uveitis may develop in any age group. 70 – 90% of the patients are aged from 20 to 60 years, with a disease onset occurring in the 3rd or 4th decade of life in about half the patients. (4,9,11,13,19) This specific age distribution leads to a significant socioeconomic impact. (20) The incidence in children is approximately five times lower than that in adults at 4 per 100,000 per year in Northern Europe.(13)

1.1.4. Signs and Symptoms

The different signs presented by active uveitis are dependent upon the anatomic location of the inflammation in the eye, the rapidity of onset of the inflammation as well as the duration and course of the disease. (1)

Signs of ocular inflammation of the anterior segment include:

- anterior and posterior synechiae
- iris nodules
- iris atrophy
- keratic precipitates
- cells
- flare
- fibrin
- hypopyon

Signs of ocular inflammation of the intermediate segment include the following:

- vitreal cells
- "snowball" opacities in the vitreous
- exudates over the pars plana ("snowbanking")
- neovascularization of the pars plana

(1)

Signs of an inflammation of the posterior segment include:

- vascular sheathing
- retinal pigment epithelial hypertrophy or atrophy
- cystoid macular edema
- atrophy or swelling of the retina, choroid, or the optic nerve
- exudative, tractional, or rhegmatogenous retinal detachment
- retinal or choroidal neovascularization

The symptoms of uveitis are similarly dependent upon the location of in the eye. Anterior segment uveitis usually shows ocular injection, light sensitivity, pain, blurry vision and epiphora. Intermediate and posterior segment uveitis typically shows floaters, flashing lights, and blurry vision. (1)

1.1.5. Diagnostics of uveitis

Uveitis involves a multitude of different aetiologies and disease phenotypes. Therefore, a comprehensive evaluation of uveitis patients is mandatory. A structured clinical examination is the first step. (9) It should include the identification of the primary anatomical site of inflammation, the degree of inflammation, the presence of any other features or complications, and the presence of any systemic disease association. (9,21) Furthermore, information regarding general medical history, family and social status as well as recent travel history is of importance. (9)

1.1.5.1. Diagnostic testing

Traditional biomedical thinking in uveitis has led to an overemphasis on diagnostic testing. Indiscriminate laboratory tests have shown to be unhelpful in diagnosing uveitis. (9,22) Therefore, the testing strategy should rely on the evidence gained through the clinical examination and history. In order to detect specific systemic disease entities such as systemic lupus erythematosus or granulomatosis with polyangiitis (Wegener's disease), haematological and immunological testing for antinuclear antibodies and anti-neutrophil cytoplasm antibodies may be helpful. (9,21) HLA-typing is only useful when the clinical picture resembles birdshot chorioretinopathy (HLA-A29) or when there are any systemic and ocular features of

a disease associated with the HLA-B27 gene present. (9,23) The use of anterior chamber and vitreous needle biopsies is well established in diagnosing infective uveitis. Additionally, PCR techniques can be used for viral detection. (9)

1.1.6. Disease management

As mentioned in the previous chapters, uveitis is a disease of varying phenotypes which can make finding the right diagnosis and the appropriate treatment challenging. The inflammation may be mild, moderate or severe. (9) The sight-affecting or sight-threatening complications may or may not already be present at the presentation. Patients can be asymptomatic or may be very symptomatic, especially if there is severe anterior chamber involvement, macular oedema with visual loss or vitritis with numerous floaters present. (9) All these factors often drive clinical decision-making. However, not all patients with uveitis require treatment. For example, in patients with mild intermediate uveitis the risks of the treatment may outweigh the potential visual benefit. (9) It is important to mention that the treatment is not curative, but suppresses inflammation and needs to be continued until the disease goes into remission. Whenever there is a systemic disease associated with uveitis, the treatment for the systemic disease may or may not be enough to control the uveitis. (9) There are many different immunosuppressive agents used for the therapy. The most commonly used systemic therapy is predominately based on steroids. (see chapter 1.3.) About two thirds of patients with posterior uveitis can be controlled on steroids alone. (9,24) However, systemic steroids in higher doses than 10mg prednisolone equivalent are short term solutions due to their side effects profile and cases insufficiently controlled with adequately low steroid doses require a steroid-sparing strategy. For that purpose traditional medications and newer biological agents such as the anti-tumour necrosis factor-alpha (TNF-α) (e.g. infliximab, etanercept and adalimumab) are on the market. (see table 1) These agents may be useful in patients who are refractory to conventional therapy, albeit with the risk of potentially severe side effects. (9)

Category	Class	Subtypes	Examples
Corticosteroids	Corticosteroids	-	Prednisolone
			Methylprednisolone
			Iluvien
			Ozurdex
			Retisert
Second-line agents	T-cell inhibitors	Calcineurin inhibitor	Cyclosporine
			Tacrolismus
			Sirolismus
	Antimetabolites	Purin antagonist	Azathoprine
		DHFR inhibitor	Methotrexate
		IMPDH	Mycophenolate mofetil
	Alkylating agents	-	Chlorambucil
			Cyclophosphamide
Biologics	Anti-TNF	Anti-TNFα	Adalimumab
			Certolizumab
			Golimumab
			Infliximab
		Anti-TNFα and β	Etanercept
	Other biologic agents	Anti-CD20	Rituximab
		Anti-IL1 β	Anakinra
		Interferons	Interferon α/β
Other agents	Other	-	Intravenous Immunoglobulins

Table 1: List of most frequent therapeutic agents

(25)

1.1.7. Impact on quality of life

Quality of life can be significantly impaired for patients with eye diseases. This has been extensively shown for more common diseases such as age-related macular degeneration. The data regarding uveitis is more scarce.(26) Generally there is a close correlation between visual acuity in the worse eye and the general health-related quality of life. (9,27,28) Still the quality of life is affected by more than just visual impairment. Kempen et al. showed that *"patients with intermediate uveitis, posterior uveitis and panuveitis had a high burden of reduced visual acuity and overall quality of life was lower than expected based on visual acuity alone"*. (29) Other factors seem to be the presence of systemic diseases and their treatment with oral corticoids or immunosuppressive agents. (9)

1.2. The standardization of uveitis nomenclature project (SUN)

Uveitis patients are a highly heterogeneous group of patients with infectious and non-infectious intraocular inflammatory pathologies. Since 2000, many advances concerning microbiological diagnosis, introduction of biologic drugs, and electronic communication to facilitate research have provided uveitis specialists with unprecedented opportunities to establish evidence-based algorithms concerning uveitis treatment. (30) In the late 1990's a working group of uveitis specialists started to work on a project called "The standardization of uveitis nomenclature". Its intent was to develop an "international consensus for the use of terms to report on uveitis at academic meetings and in the literature". (31) Its aim was to establish a clear vocabulary to ensure a standardization of clinical studies and trials. Most importantly, this effort was supported by three major uveitis organizations: the "American Uveitis Society (AUS)", the "International Uveitis Study Group (IUSG)" and the "International Ocular Inflammation Society (IOIS)". (31) The first workshop organized by the SUN Working Group was held in Baltimore, Maryland in 2004. It was attended by 45 uveitis specialists from all over the world. This international meeting was held to achieve a consensus on the definition of several commonly used terms. (32) One year later in 2005 the results were published as "Standardization of Uveitis Nomenclature for Reporting Clinical Data: Results of the First International workshop". A consensus was made on nomenclature for presenting clinical data, including uveitis terminology, grading of inflammation and reporting outcome results. (30) (see table 4 and table 5)

In 2009, a second meeting took place in Miami, Florida. 59 uveitis experts from various regions of the world identified 193 terms and mapped them to 28 major uveitic disease entities. (31,33)

1.2.1. Main results of the SUN work-shop

1.2.1.1. Terminology

An agreement on a clear terminology was the first step of the SUN meetings. The classification of the anatomic location of the uveitis should serve as a framework for the work on diagnostic criteria for specific uveitic diagnoses. It should be based on

the site of the actual inflammation rather than on the presence of structural complications. (31)

The term “intermediate uveitis” should be used when the vitreous is the major site of the inflammation. The presence of macular oedema or peripheral vascular sheathing should not change this classification. The diagnostic term “pars planitis” should only be used for intermediate uveitis with the presence of snowball or snowbank formation occurring without an associated infection or systemic disease. When there is no predominant site of inflammation, but inflammation is present in the anterior chamber, the vitreous, as well as the retina and/or the choroid, it should be diagnosed as “panuveitis”. An inflammation in the anterior chamber and the vitreous, which is more vitritis than iridocyclitis and with more anterior chamber inflammation than in intermediate uveitis, should be referred to as “anterior and intermediate uveitis” and not as “panuveitis”. (9) The term “posterior uveitis” should be used for inflammation of the retina and/or choroid, including focal, multifocal, or diffuse choroiditis as well as chorioretinitis, retinochorioretinitis, retinitis, and neuroretinitis. (9,32) (see table 2)

The SUN Working Group Anatomic Classification of Uveitis

Type of uveitis	Primary site of inflammation	Includes
Anterior uveitis	Anterior Chamber	Iritis Iridocyclitis
Intermediate uveitis	Vitreous	Pars planitis Posterior cyclitis Hyalitis
Posterior uveitis	Retina or choroid	Focal, multifocal, or diffuse choroiditis Chorioretinitis Retinochoroiditis Retinitis Neuroretinitis
Panuveitis	Anterior Chamber, vitreous, and retina or choroid	

Table 2: The SUN Working Group Anatomic Classification of Uveitis (32)

(32)

According to the SUN working group, the terms “acute” and “chronic” have been used quite inconsistently and variably to refer to the onset, the duration of an attack or to the course of uveitis. Consensus was found that the use of these terms should be reserved for the description of the clinical course of the uveitis only. (32) Specific uveitic syndromes characterized by a sudden onset and a limited duration, such as HLA-B27 associated “acute anterior uveitis”, should be described with the term “acute”. (7,32) The term “recurrent” should be used to describe repeated episodes of uveitis, which are separated by periods of inactivity without treatment of at least 3 months in duration. Persistent uveitis characterized by a prompt relapse within less than 3 months after discontinuation of the therapy, should be described as “chronic”. (32) (see table 3)

The SUN Working Group Descriptors of Uveitis

Category	Descriptor	Comment
Onset	Sudden	
	Insidious	
Duration	Limited	≤ 3 months duration
	persistent	> 3 months duration
Course	Acute	Episode characterized by sudden onset and limited duration
	Recurrent	Repeated episodes separated by periods of inactivity without treatment
		≥ 3 months duration
	Chronic	Persisted uveitis with relapse in < 3months after discontinuing
		Treatment

Table 3: The SUN Working Group Descriptors of Uveitis (32)

(32)

1.2.1.2. Grading of inflammation

Consensus was achieved regarding standard anterior chamber cells (see table 5) and anterior chamber flare (see table 4) as well as how standardized photographs should be established in order to assist in grading of the anterior chamber flare. (32) The developed grading is an ordinal system, which levels represent a non-linear hierarchy of increasing magnitude, but do not have a numerical relationship to the amount of inflammation. (34) No consensus was made on a grading system for vitreous cells. (32)

The SUN Working Group Grading Scheme for Anterior Chamber Flare

Grade	Description
0	None
1+	Faint
2+	Moderate (iris and lens details clear)
3+	Marked (iris and lens details hazy)
4+	Intense (fibrin or plastic aqueous)

Table 4: The SUN Working Group Grading Scheme for Anterior Chamber Flare (32)

(32)

The SUN Working Group Grading Scheme for Anterior Chamber Cells

Grade	Number of Cells in Field [1]
0	less than 1 cell
0.5+	1 to 5 cells
1+	6 to 15 cells
2+	16 to 25 cells
3+	26 to 50 cells
4+	more than 50 cells

[1] Field size is a 1mm by 1mm slit beam

Table 5: The SUN Working Group Grading Scheme for Anterior Chamber Cells (32)

(32)

1.2.1.3. Documenting Complications

Depending on the complication the required level of evidence may vary. The presence of macula oedema can either be determined clinically or by further tests such as fluorescein angiography or optical coherence tomography. Subretinal neovascularization should only be reported when it is confirmed by fluorescein angiography, indocyanide green angiography and/or optical coherence tomography angiography. (32) The term “glaucoma” should not be used synonymously with

elevated intraocular pressure in a patient with uveitis. It should be reserved for situations with either glaucomatous disk damage or visual field loss. (32) At the same time the term “elevated intraocular pressure” should be used when the pressure is above a normal range (>21 mmHg) or when there is an increase of more than 10 mmHg from the baseline pressure during a study with longitudinal data. (32)

1.2.1.4. Outcomes and results reporting

The goal of treatment of patients with uveitis is always to suppress the inflammation completely. However, for short term evaluation it may be useful to determine whether the inflammation has improved or worsened. (32) Therefore, the terms “inactive”, “worsening activity”, “improved activity” and “remission” were introduced. (table 6) Improvement in the inflammation was defined as either a two-step decrease in the level of inflammation (table 4 and 5) or a decrease to “inactive” (Grade 0). Worsening of inflammation was defined as either a two-step increase or an increase to the maximum (Grade 4+). The term “remission” should be reserved for an inactive disease for at least 3 months after discontinuing all treatments for uveitis. (32)

The SUN Working Group Activity of Uveitis Terminology

Term	Definition
Inactive	Grade 0 cells (anterior chamber) [1]
Worsening activity	Two-step increase in level of inflammation (e.g. anterior chamber cells, vitreous haze) or increase from grade 3+ to 4+
Improved activity	Two-step decrease in level of inflammation (e.g. anterior chamber cells, vitreous haze) or decrease to grade 0
Remission	Inactive disease for ≥ 3 months after discontinuing all treatments for eye disease

[1] Applies to anterior chamber inflammation

Table 6 The SUN Working Group Activity of Uveitis Terminology

(32)

A popular outcome of uveitis studies is the visual acuity. The SUN work-group decided that in order to not introduce uncontrolled bias into the study, reporting a “final visual acuity” in patients with variable follow-ups is not useful. On the contrary,

rates of visual loss or gain, or else the rate of visual acuity change should be reported. (32,35,36)

1.3. Systemic Corticosteroids

Corticosteroids amongst others have become important agents for treating many inflammatory, immunologic, and hematologic diseases. There is a great variety of different modifications of steroids on the market. Each group of synthetic steroids has its own characteristics which are pharmacologically and therapeutically important. (table 7) In most cases corticosteroids are rapidly and completely absorbed when given orally. The actions of synthetic steroids are quite similar to those of cortisol. They bind to the specific intracellular receptor proteins and produce the same effects but have different ratios of glucocorticoid and mineralocorticoid potency. (37)

Agent	**Activity** (Potency relative to hydrocortisone)			Equivalent Oral Dose (ml)	Forms Available
	Anti-Inflammatory	Topical	Salt-Retaining		
Short- to medium acting glucocorticoids					
Hydrocortisone (cortisol)	1	1	1	20	Oral, injectable, topical
Cortisone	0.8	0	0.8	25	Oral
Prednisone	4	0	0.3	5	Oral
Prednisolone	5	4	0.3	5	Oral, injectable
Methylprednisolone	5	5	0.25	4	Oral, injectable
Meprednisone	5		0	4	Oral, injectable
Intermediate-acting glucocorticoids					
Triamcinolone	5	5 (-100)	0	4	Oral, injectable, topical
Paramethasone	10		0	2	Oral, injectable
Fluprednisolone	15	7	0	1.5	Oral
Long-acting glucocorticoids					
Bethamethasone	25-40	10	0	0.6	Oral, injectable, topical
Dexamethasone	30	10	0	0.75	Oral, injectable, topical
Mineralocorticoids					
Fludrocortisone	10	0	250	2	Oral
Desoxycorticosterone acetate	0.8	0	20		Injectable, pellets

Table 7: Some commonly used natural and synthetic corticosteroids for general use

(1)

1.3.1. Toxicity

The benefits obtained from corticosteroids may vary considerably. Therefore, every use of these drugs must be carefully weighed in each patient against their effects on every part of the organism. When synthetic steroids are used for only a short period of time (less than two weeks), it is uncommon to see side effects even with moderately large doses. (37)

1.3.2. Complications

Most Patients given a daily dose of 100 mg hydrocortisone or more (or the equivalent amount of synthetic steroid) for more than two weeks may undergo a variety of changes that have been termed iatrogenic Cushing's syndrome. Patients usually show facial fat disposition (moon facies), increased growth of fine hair over the face, thighs and trunk as well as steroid induced punctate acne, insomnia and increased appetite. Furthermore, fat tends to be redistributed from extremities to the trunk, back of the neck and the supraclavicular fossae. Large doses of steroids may be associated with hypomania and acute psychosis. Long-term usage of glucocorticoids may be a cause of depression, the development of posterior subcapsular cataracts, and an increase of intraocular pressure. Other serious adverse effects of glucocorticoids include peptic ulcers, and benign intracranial hypertension. (37)

1.3.2.1. Adrenal Suppression

When administered in high doses for more than two weeks, corticosteroids may cause adrenal suppression. Appropriate supplementary therapy should be considered if the treatment extends over weeks to months. The reduction process should be quite slow in order to ensure an acceptable function of the hypothalamic-pituitary-adrenal axis. If the dosage of glucocorticoids is reduced too rapidly, the symptoms of the previous pathology may reappear or even increase in intensity. Patients without an underlying disorder may develop symptoms including anorexia, nausea or vomiting, weight loss, lethargy, fever, headache, joint or muscle pain, and postural hypotension. (37)

1.3.3. Contraindications and Cautions

Patents treated with glucocorticoids should be monitored carefully for the development of hyperglycaemia, glycosuria, sodium retention with oedema or hypertension, hypokalaemia, peptic ulcer, osteoporosis, and hidden infections.

Even patients maintained on relatively low doses of corticoids may require supplementary therapy. Therefore, the steroid dosage should be kept as low as possible and intermittent administration should be used when satisfactory results are shown. (37)

1.4. Injectable ocular corticosteroids

1.4.1. Introduction

The treatment of ocular inflammation with corticosteroids can be tracked back to the 1950s. (38) Systemic steroids as well as local therapy with drops or injections have become quite common.

Systemic corticosteroid use can subject the patients to numerous side effects. (see section 1.3.) Periocular and intravitreal injections showed to be particularly useful in patients with unilateral disease that is not amenable to topical therapy alone. (39) Nevertheless, if frequently repeated injections are necessary or systemic manifestations of the disease exist, the use of a systemic-sparing immunosuppressive agent may be a better option. (39) The form of corticoid treatment in ophthalmology is also determined by the location of the inflammation. In cases where the inflammation is restricted to the anterior chamber, often the preferred method of treatment is locally applied prednisolone acetate. In cases of severe anterior inflammation not amendable to topical therapy, or when the posterior segment is involved, periocular or intraocular injections have proven effective. (39) Investigations of the side effect profiles of these drugs have focused on intravitreal drugs; not least because of the commercial interest in very efficient, but expensive intravitreal implants. The less invasive and cheaper alternative of periocular steroids has not been thoroughly investigated.

1.4.2. Types of corticoids

To this date, there is a great variety of different forms of corticosteroids on the market. A commonly used formulation for intra- and periocular injections is triamcinolone acetonide. It is a minimally water-soluble suspension. This leads to a longer half-life compared to more water-soluble forms such as dexamethasone. Additionally, triamcinolone acetonide acts as depot of sustained-released crystals when injected into the vitreous cavity. However, if a rise of the patient’s intraocular pressure is a significant concern, corticosteroids with a shorter half-life are sometimes used in order to decrease the risk of a prolonged intraocular pressure rise. (39) The dose of injected corticosteroid is not internationally standardized, but typically 4 mg are used albeit doses up to 25mg have been reported. (40)

1.4.3. Intravitreal Triamcinolone acetate in Uveitis

The first periocular injection of corticosteroids for the treatment of uveitis was originally described by Nozik in 1972 (41). The first documented administration of intravitreal triamcinolone acetonide was in 1979 during retinal detachment surgery to reduce cellular proliferation. (42) Today, it is widely used for a variety of ocular pathologies such as macular oedema, diabetic retinopathy, retinal vein occlusion and uveitis. (43–46) Although, intravitreal triamcinolone acetonide injections allow a rapid and effective resolution of active uveitis, they have a half-life of only several weeks to months which leads to a limitation of the duration of the therapeutic effect. (38,47,48) (see section 1.4.6.) In this case, repeated injections may be required which increases the risk of developing ocular side effects. (49)

1.4.4. Systemic distribution

Even when locally applied, drugs are to some degree being absorbed systemically. This holds true for steroids as drops, periocular injections and to a lesser degree as intraocular injections. However, there is only a very small number of studies targeting this topic. A study of 20 patients treated with a high dose intravitreal injection of 20-25 mg triamcinolone showed that in over 90% of the cases no triamcinolone acetonide was detectable in the patient's serum samples. Only two patients showed marginally detectable amounts of the substance, one five days, the other seven days after the injection. (38,39,50) Periocular injections of steroids however, may cause high serum spikes systemically, causing exacerbations of arterial hypertension or diabetes. (51)

1.4.5. Intravitreal distribution

Not only the systemic distribution, but also the intravitreal concentration of the applied corticosteroid is important for the anti-inflammatory effect of the treatment.

Therefore, studies comparing periocular and sub-tenon injections to intravitreal injections were performed. A study of 12 patients in 2005 showed higher intravitreal concentrations of TA in patients after intravitreal injection compared to patients after periocular injection. (39,52) However, another study of 25 patients in 2006 showed that in some cases intravitreal concentrations after sub-tenon injections were comparable to those after intravitreal injections. (39,53)

1.4.6. Duration of anti-inflammatory effect

The duration of the anti-inflammatory effect of intravitreal triamcinolone acetonide appears to depend on the dose of corticosteroid injected. With the typical dose of 4 mg used in the United States effect lasts for four to six months. Given a dosage of 20 mg a duration of effect of six to nine months has been reported. (39,52) However, the peak concentration as well as the half-life of triamcinolone acetonide showed a considerable variation among subjects. The range of measureable concentrations was 71-132 days. (38) This fact gives triamcinolone acetonide superiority over dexamethasone sodium phosphate, which has a half-life of approximately 5.5 hours in the human eye and is cleared from the vitreous within 72 hours. (54,55) Another factor seems to be whether patients have undergone a vitrectomy prior to the injection. After a single 4 mg injection, the mean elimination half-life was 18.6 days in patients without vitrectomy. In patients who had undergone vitrectomy, the mean elimination half-life was only 3.2 days. (38,39) Whenever the effect of the injection seems to have faded and clinical signs suggest a worsening of a condition, a reinjection should be considered. (39,56)

A rather new approach is slow-release corticosteroid delivering devices such as the dexamethasone-containing intravitreal implant Ozurdex® which is injected in to the vitreous where it slowly dissolves to provide a longer local disease control. Ozurdex® may provide an anti-inflammatory effect of up to three months. (57)

1.4.7. Effect mechanism

The exact effect mechanism of triamcinolone in intravitreal injections in not fully known. (39) "*Glucocorticoids appear to have a variety of actions, including inhabitation of expression of genes contributing to inflammation and this decreased production of cytokines, enzymes, receptors and adhesion molecules".* (39,58)

1.4.8. Risks and Side Effects

Including the various side effects of corticoid therapy (see chapter 1.3.), there is also a variety of ocular risks associated with intravitreal injections such as sterile inflammatory reaction, endophthalmitis, elevation of intraocular pressure as well as cataract progression. Therefore, patients should be aware that further intervention may be needed if any of these occur. (39)

1.4.8.1. Sterile inflammatory reaction

With the preserved formulation of triamcinolone acetonide sterile inflammatory reactions after intravitreal injections had been reported relatively frequently. This typically develops within the first 2 days following the injection. It is thought to be that the inflammatory process is not a reaction to the triamcinolone acetonide itself but to a chemical used in its formulation. (59) One retrospective study of 310 eyes showed that sterile inflammatory reactions may be more frequent in eyes underlying inflammatory predilection including uveitis. 4 out of 20 uveitic eyes developed this complication in comparison to only 2 of 290 eyes treated for non-inflammatory posterior segment disease. (39,60)

1.4.8.2. Endophthalmitis

Endophthalmitis is a rare, yet serious complication. After an intravitreal triamcinolone acetonide injection, the endophthalmitis can be infective as well as due to a non-infectious inflammation possibly caused by a toxic reaction against triamcinolone acetonide or its preservatives. (49,61) The incidence of infectious endophthalmitis following intravitreal triamcinolone acetonide injection ranges from 0% to 0,87%. (39,62) Typical symptoms such as pain, redness, blurry vision, and vitritis can develop at any time following the injection, but will typically appear by post-injection day five. (39,63)

1.4.8.3. Elevation of intraocular pressure

An increase of intra ocular pressure may occur with systemic, topical or periocular administration of corticosteroids, although it may be more common after local therapy. (41,64–66) While there may be cases where an elevation of intra ocular pressure is beneficial to the patient, it is typically an unwanted side effect. It can occur immediately or develop up to 7 months after the injection. (39,67) A baseline intra ocular pressure of greater than 16 mmHg as well as receiving a reinjection of triamcinolone acetonide showed to be risk factors for developing an intra ocular pressure elevation. (68)

1.4.8.4. Cataract progression

The use of corticosteroids is a well-known cause for cataract progression, in particular of a posterior subcapsular cataract. (69–72) Whereas increased visual acuity was often recorded relatively soon after intravitreal corticosteroid injection, visually significant cataracts may form as long as 2 years after. (39) The risk of developing visually significant cataracts following intravitreal triamcinolone acetonide injection can vary. Yet, one study from 2004 reported that 29% of eyes treated showed this condition after intravitreal triamcinolone acetonide injection compared to only 5% of eyes which received a placebo injection. (73) Repeated injections may also increase the risk of developing significant cataract. Up to 100% of patients require cataract extraction surgery by the fourth injection. (74)

1.4.9. Contraindications

In cases where an infectious uveitis has not yet been excluded or uveitis is secondary to toxoplasmosis reactivation, intravitreal triamcinolone acetonide injections must not be used. Ignoring this fact may lead to a fulminant chorioretinits. (75)

2. Methods

2.1. Study population

The cases reported in this study include all patients with non-infectious uveitis who had received at least one periocular corticosteroid injection at the department of ophthalmology at the Medical University of Graz/Austria between 2006 and 2016. All forms of periocular injections and all forms of corticosteroids were included, although the subconjunctival approach was typically used to administer triamcinolone acetate. Patients who received a periocular injection due to a chronic macular oedema were excluded from the study. In total, 100 eyes of 87 patients, 59 females and 28 males, were taken into account.

2.2. Literature research

All literature used for this diploma thesis was searched through the PubMed database. The main focus of the search was on periocular treatment outcomes, the "standardization of uveitis nomenclature project", as well as general steroid use in treating non-infectious uveitis.

2.3. Data collection and statistics

A retrospective review of the data stored at the Department of Ophthalmology was performed to identify suitable patients for this study using the documentation program 'iMed'. Basic demographic information as well as clinical assessment information including best visual acuity, intraocular pressure and ocular inflammation activity status was obtained from the initial visit, from a one month follow up visit and a six month follow up visit.

All collected data was documented in a Microsoft Excel® file and later transformed into a IBM SPSS® data file in order to perform further anonymised analysis and to build graphs.

Because of multiple testing we corrected the significance level of $p = 0.05$ via Bonferroni correction to a significance level of $p = 0.001$. In other words, a p-value smaller than 0.001 is considered statistically significant.

All study procedures were approved by the ethics review board of the Medical University of Graz and the study adhered to the Helsinki declaration.

2.4. Main outcome variables

The main outcome variables were the best visual acuity and the intra ocular pressure at one month and six months after the treatment.

2.4.1. Methods of Measurement

Individual eye examinations of each of the 100 eyes were performed by trained experts at the department of ophthalmology at the Medical University of Graz.

2.4.1.1. Optical coherence tomography (OCT)

Optical coherence tomography (OCT) is the investigation of choice for diagnosis of a cystoid macular oedema and for the follow up of such. It is used to obtain high-resolution images of the eye's anterior segment and retina. The characteristic feature of a cystoid macular oedema in the optical coherence tomography is thickening of the retina with hypo reflective lesions scattered through the retina (most often encompassing the nuclear layers of the retina). However, the changes in the retinal and choroidal microstructure in uveitis are multiform and a variety of changes can be appreciated on OCT. (76,77)

2.4.1.2. Visual acuity

Visual acuity was measured using a standard Snellen visual acuity chart at a six-meter distance. Normal vision was documented as 1.0 or higher (20/20 or 6/6). For further analyses, visual acuity data was converted from a decimal notation to a logarithmic notation (LogMAR).

2.4.1.3. Intraocular pressure

Intraocular pressure was measured using the Goldmann applanation tonometer. It measures the force necessary to flatten an area of cornea of 3.06 mm diameter. Therefore, a special disinfected prism is mounted on the tonometer head and then placed against the cornea. The intraocular pressure in mmHg equals the flattening force in grams multiplied by ten. (78)

2.4.1.4. Physical Examination

Cases of uveitis may present ocular symptoms such as eye redness, pain, sensitivity to light etc. (see section 1.1.4.) which are not very specific for the disease.

Inflammation or infection in other parts of the eye may produce similar symptoms. Therefore, it is important to distinguish a case of uveitis from diseases of other eye structures such as conjunctivitis or keratitis. A slit lamp was used to distinguish these entities. It is instrument using a high-intensity light source in conjunction with a microscope to examine the anterior and posterior segment of the eye. (79) Anterior chamber cells and flare, as well as vitreous haze were graded according to the SUN classification (see chapter 1.2).

3. Results

There were 100 eyes of 86 different patients included in this study. In ten cases both eyes of the patient were treated either at the same time or with an interval of at least six months. In three cases the same eye of one patient was injected with an interval of at least 18 months. Therefore, we chose to include these cases as separated treatments. 68.6% of the patients were female, 31.4% were male. The mean age was 45.91 years (female 45.24 years; male 47.74 years). Simultaneous bilateral injections were performed in three cases. In 19 cases the patients were receiving systemic corticoids and/or any other oral immunosuppressive medication. In 12 cases the patients were HLA B27 positive, one of which had been diagnosed with ankylosing spondylitis, one patient had been diagnosed with psoriatic arthritis, and one patient was ANA positive at the time of the first injection.

Among all injected eyes, there were 44 cases of acute iridocyclitis, 34 cases of panuveitis, 9 cases of uveitis intermedia, 6 cases of chronic iridocyclitis, 4 cases of retinal vasculitis, 2 cases of chorioretinitis, and 1 case of scleritis.

3.1. Intraocular pressure

A repeated measures ANOVA with a Greenhouse-Geisser correction determined that the mean intraocular pressure differed statistically between the baseline (12.7±4.2 mmHg), the one month (15.4±5.0 mmHg), and the six months follow examination (15.0±5.0 mmHg) (n=58, p=0.001). The comparison of the mean pre-injection intraocular pressure of 12.5±4.4 mmHg and one month post injection intraocular pressure of 15.1±4.8 mmHg (n=82, p<0.001, paired t-test) as well as the difference between pre-injection and the 6 months follow up intraocular pressure of 15.1±5.0 mmHg (n=63, p<0.001, paired t-test) showed a statistically significant increase. However, the difference between the mean one month post-injection intraocular pressure of 15.4±5.0 mmHg and six months post-injection ocular pressure of 15.0±5.0 mmHg was not statistically significant (n=58, p=0.578, paired t-test). (see figure 2 and table 9)

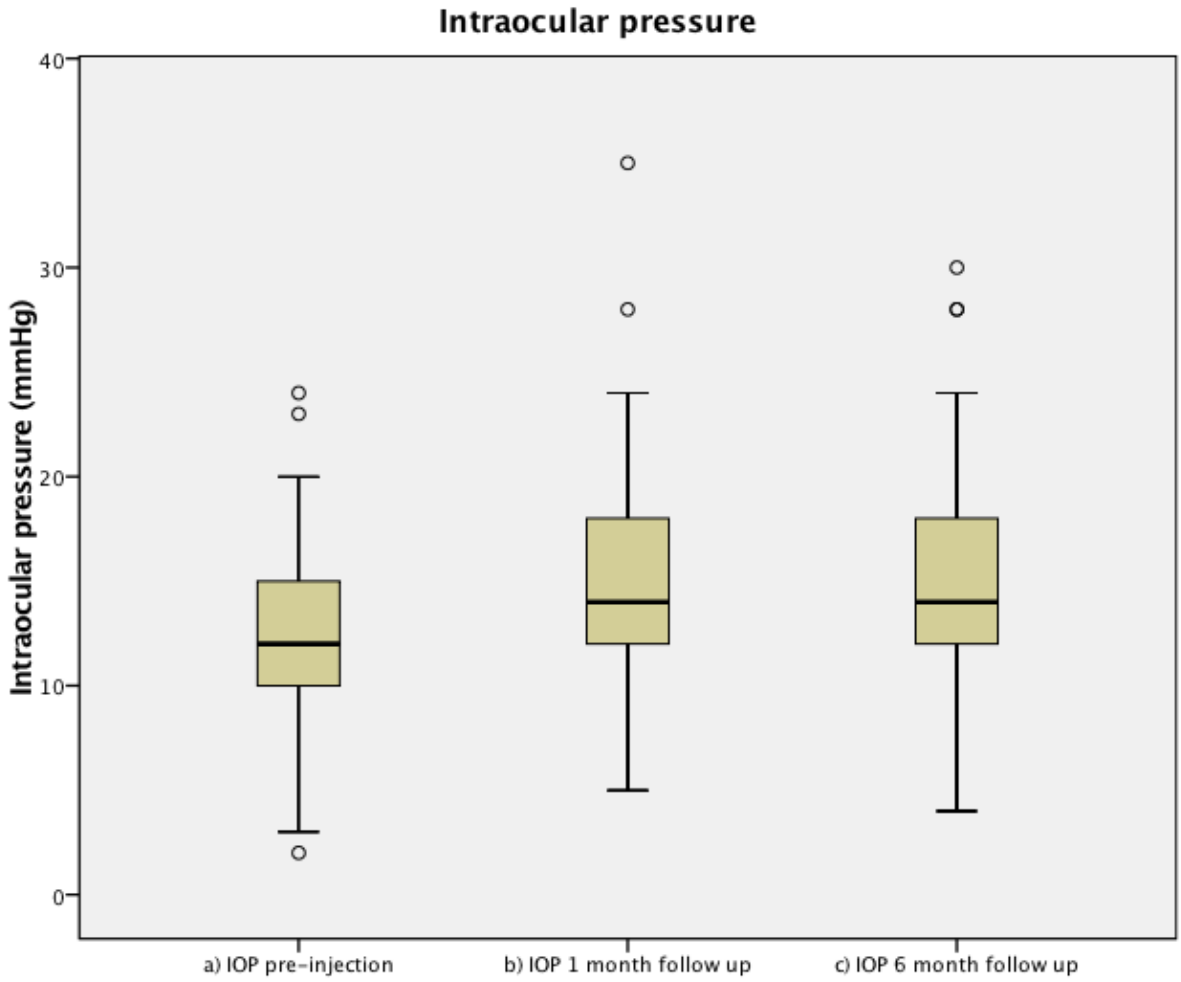

Figure 1: Mean intraocular pressure (IOP)

(a) Mean intraocular pressure (IOP) pre-injection 12.5±4.4 mmHg (n=97); (b) Mean intraocular pressure (IOP) one month post injection 15.1±4.8 mmHg (n=83); (c) Mean intraocular pressure (IOP) six months post injection 15.1±5.0 mmHg (n=64)

	IOP pre-injection (mmHg)	IOP 1 month post injection (mmHg)	IOP 6 months post injection (mmHg)	significance
1 month follow up (n=82)	12.7±4.3	15.1±4.8	-	p<0.001
6 months follow up (n=63)	12.7±4.3	-	15.1±5.0	p<0.001
Comparison of both follow ups (n=58)	-	15.36±4.99	14.95±4.96	p=0.578
Comparison of all examinations (n=58)	12.7±4.2	15.4±5.0	15.0±5.0	p=0.001*

Table 8: Comparing intraocular pressure (IOP)

Comparison of intraocular pressure (IOP) in 1 month and 6 months follow up examination. Tested with paired T-Test. (*Tested with repeated measures ANOVA and Greenhouse-Geisser correction)

In the 6 months follow up 16 out of 63 patients (25.4%) showed an increase of intraocular pressure of 5 mmHg or more, 7 out of 63 patients (11.11%) showed an increase of intraocular pressure of 10 mmHg or more (maximum 20 mmHg). No significant difference concerning intraocular pressure was detected whether Triamcinolone acetate or Dexamethasone was injected (data not shown).

3.2. Best visual acuity

A repeated measures ANOVA with a Greenhouse-Geisser correction determined that the mean best visual acuity differed statistically between the baseline (0.27±0.29 LogMAR), the one month (0.15±0.22 LogMAR), and the six months follow-up examination (0.14±0.22 LogMAR) (n=41, p>0.001). The comparison of the mean pre-injection best visual acuity of 0.27±0.27 LogMAR and the mean best visual acuity in the one month follow up of 0.15±0.21 LogMAR (n=58, p<0.001, paired t-test) as well as the six months follow up of 0.14±0.22 LogMAR (n=49, p<0.001, paired t-test) did show a statistically significant improvement. No significant improvement in best visual acuity was shown between the two follow ups (n=46, p=0.638, paired t-test). (see figure 3 and table 10)

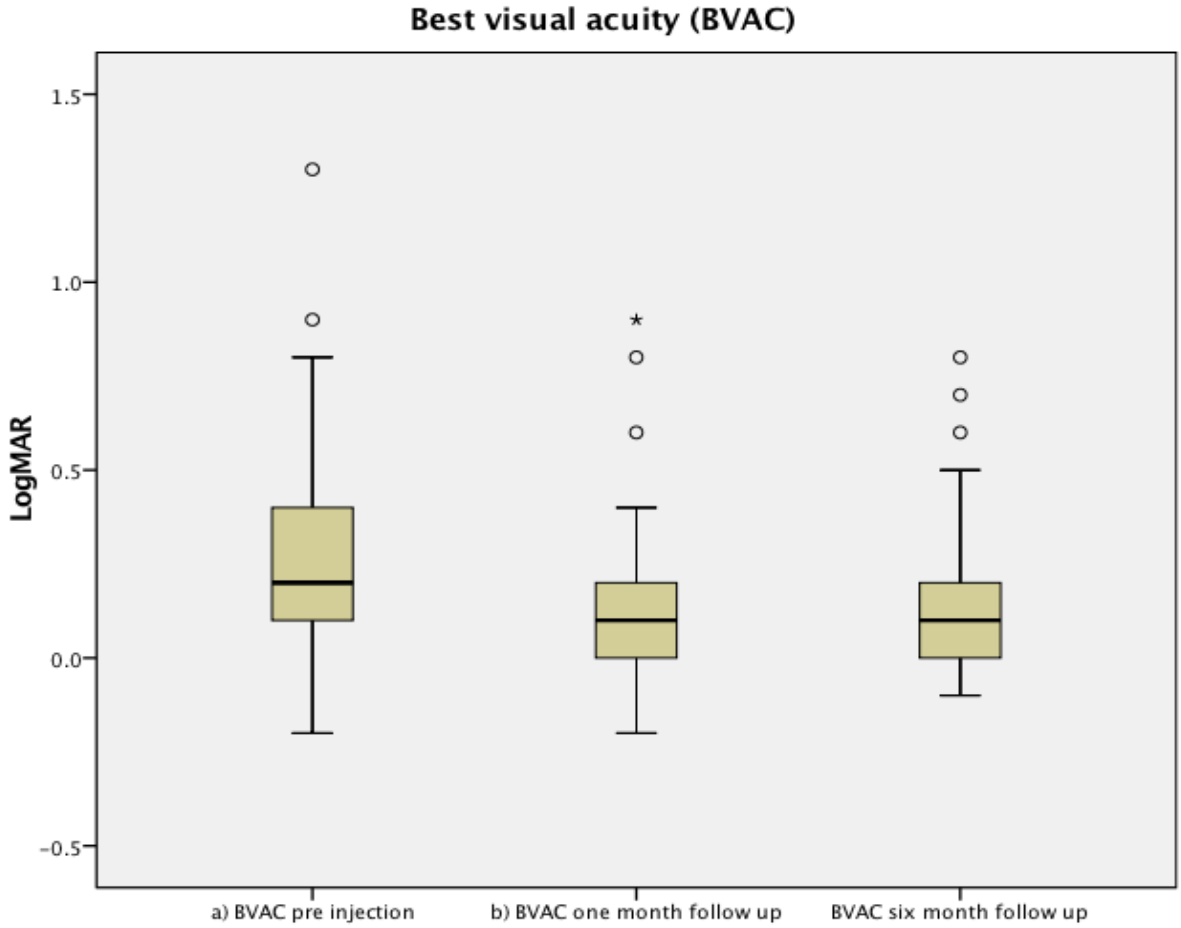

Figure 2: Mean best visual acuity (BVAC)

(a) Mean best visual acuity (BVAC) pre-injection 0.26±0.26 LogMAR (n=79); (b) Mean best visual acuity one month post injection 0.15±0.21 LogMAR (n=66); (c) mean best visual acuity six months post injection 0.18±0.28 LogMAR (n=55).

	BVAC pre-injection (LogMAR)	BVAC 1 month post injection (LogMAR)	BVAC 6 months post injection (LogMAR)	Significance
1 month follow up (n=58)	0.27±0.27	0.15±0.21	-	p<0.001
6 months follow up (n=49)	0.26±0.28	-	0.14±0.22	p<0.001
Comparison of both follow ups (n=46)	-	0.16±0.23	0.16±0.24	p=0.817
Comparison of all examinations (n=41)	0.27±0.29	0.15±0.22	0.14±0.22	p<0.001*

Table 9: Comparing best visual acuity (BVAC). Tested with paired T-Test. (*Tested with repeated measures ANOVA and Greenhouse-Geisser correction)

Comparison of best visual acuity (BVAC) at the one month and six months follow up examination. Tested with paired t-test.

3.3. Systemic corticosteroids and autoimmune diagnosis

Patients with systemic corticosteroids as well as patients with a diagnosed autoimmune disease showed a different outcome concerning intraocular pressure and best visual acuity. Of those receiving systemic steroids (n=19) the mean dosage was 43±39.17 milligram prednisolone per day. Repeated measures ANOVA with a Greenhouse-Geisser correction showed that the mean intraocular pressure of patients receiving systemic corticosteroids did not statistically differ between the baseline (13.9±5.4 mmHg), the one month (14.3±4.7 mmHg), and the six months follow examination (15.2±6.9 mmHg) (n=15, p=0.657). The comparison of the mean pre-injection intraocular pressure of 12.6±3.9 mmHg and the one month post injection intraocular pressure of 14.4±4.5 mmHg (n=16, p=0.413, paired t-test) as well as the six months post-injection intraocular pressure of 15.2±6.9 mmHg (n=15, p=0.194, paired t-test) did not show a significant increase. Patients with no current systemic corticosteroid therapy, however, did show a significant intraocular pressure increase. (see table 11) Similar results can be found in patients with a diagnosed autoimmune disease. (see table 12)

Immunosuppression	IOP pre-injection (mmHg)	IOP 1 month post injection (mmHg)	IOP 6 months post injection (mmHg)	Number of eyes (n)	Significance
No	12.6±3.9	15.3±4.9	-	66	p<0,001
	12.4±3.8	-	14.8±4.2	47	p<0,001
	-	15.7±5.1	14.9±4.2	43	p=0.294
	12.4±3.6	15.7±5.1	14.9±4.2	43	p>0.001*
Yes	13.2±5.9	14.4±4.5	-	16	p=0.413
	13.6±5.3	-	15.8±7.1	16	p=0.194
	-	14.3±4.7	15.2±6.9	15	p=0.615
	13.9±5.4	14.3±4.7	15.2±6.9	15	p=0.657*

Table 10: Intraocular pressure (IOP) and systemic corticosteroids

Comparison of intraocular pressure (IOP) in patients treated with systemic corticosteroids at the one month and the six months follow up examination. Tested with paired t-test. (*Tested with repeated measures ANOVA and Greenhouse-Geisser correction)

Autoimmune Diagnosis	IOP pre-injection (mmHg)	IOP 1 month post injection (mmHg)	IOP 6 months post injection (mmHg)	Number of eyes (n)	Significance
No	12.6±4.3	15.2±4.8	-	71	p<0.001
	12.5±4.0	-	15.0±4.7	56	p<0.001
	-	15.2±5.0	14.8±4.6	51	p=0.581
	12.6±4.0	15.2±5.0	14.8±4.6	51	p=0.001*
Yes	13.4±4.5	15.0±5.3	-	11	p=0.480
	14.0±5.6	-	15.9±7.5	7	p=0.368
	-	16.4±4.9	15.9±7.5	7	p=0.879
	13.9±5.4	14.3±4.7	15.2±6.9	15	p=0.657

Table 11: Intraocular pressure (IOP) and autoimmune diseases

Comparison of intraocular pressure (IOP) in patients with a diagnosed autoimmune disease at the one month and the six months follow up examination. Tested with paired t-test. (*Tested with repeated measures ANOVA and Greenhouse-Geisser correction)

Repeated measures ANOVA with a Greenhouse-Geisser correction showed that the mean best visual acuity of patients treated with systemic corticosteroids did also not statistically differ between the baseline (0.19±0.33 LogMAR), the one month (0.11±0.31 LogMAR), and the six months follow examination (0.13±0.28 LogMAR) (n=32, p=0.274). The mean best visual acuity prior to the first injection in immunosuppressed patients was 0.20±0.32 LogMAR. The comparison of the mean pre-injection best visual acuity and the one month post-injection best visual acuity of 0.11±0.32 LogMAR (n=10, p=0.054, paired t-test) as well as the six months post-injection best visual acuity of 0.13±0.28 LogMAR (n=9, p=0.276, paired t-test) did not show a significant improvement, whereas patients with no current systemic corticosteroid therapy did show a significant visual acuity improvement. (table 13) Again, similar results can be found in patients with a diagnosis autoimmune disease. (table 14)

Immunosuppression	BVAC pre-injection (LogMAR)	BVAC 1 month post injection (LogMAR)	BVAC 6 months post injection (LogMAR)	Number of eyes (n)	Significance
No	0.29±0.26	0.16±0.19	-	48	p<0.001
	0.28±0.27	-	0.14±0.21	39	p<0.001
	-	0.16±0.19	0.14±0.20	36	p=0.492
	0.29±0.27	0.16±0.19	0.14±0.21	32	p>0.001*
Yes	0.20±0.32	0.11±0.32	-	10	p=0.054
	0.19±0.33	-	0.13±0.28	9	p=0.276
	-	0.17±0.35	0.20±0.34	10	p=0.541
	0.19±0.33	0.11±0.31	0.13±0.28	9	p=0.274*

Table 12: Best visual acuity (BVAC) and systemic corticosteroids

Comparison of best visual acuity (BVAC) in patients treated with systemic corticosteroids at the one month and six months follow up examination. Tested with paired t-test. (*Tested with repeated measures ANOVA and Greenhouse-Geisser correction)

Autoimmune Diagnosis	BVAC pre-injection (LogMAR)	BVAC 1 month post injection (LogMAR)	BVAC 6 months post injection (LogMAR)	Number of eyes (n)	Significance
No	0.31±0.27	0.16±0.21	-	49	p<0,001
	0.29±0.28	-	0.13±0.22	41	p<0,001
	-	0.18±0.23	0.17±0.25	40	p=0.629
	0.31±0.28	0.17±0.22	0.15±0.23	35	p>0.001*
Yes	0.10±0.22	0.11±0.21	-	9	p=0.347
	0.10±0.25	-	0.16±0.24	7	p=0.172
	-	0.05±0.18	0.08±0.16	6	p=0.465
	0.03±0.19	0.05±0.18	0.08±0.16	6	p=0.376*

Table 13: Best visual acuity and autoimmune disease

Comparison of best visual acuity (BVAC) in patients with a diagnosed autoimmune disease at the one month and the six months follow up examination. Tested with paired t-test. (*Tested with repeated measures ANOVA and Greenhouse-Geisser correction)

4. Discussion

Because large randomized controlled trials regarding the efficacy of periocular steroids are lacking, physicians have to rely on data from single case reports and small case series for evidence of efficacy and safety of this treatment. In addition to scarce data, both of these outcomes might differ from one population to another. The aim of this diploma thesis was to evaluate effectiveness and safety of periocular steroids in a European tertiary centre.

Our data show a significant improvement in visual acuity one and six months after treatment, but also a rise in intraocular pressure. Even though the latter was on average small, 11 patients experienced an increase of more than 10 mmHg. Still all pressure spikes were controllable with topical steroids and none needed glaucoma surgery. These results corroborate previous studies mentioned in section 1. The maximal improvement after treatment was reached after one month and remained relatively stable throughout the rest of the follow up. The intraocular pressure increase reached its peak one month after treatment, but only decreased slightly after 6 months not reaching its baseline value. This could be due to a decreased intraocular pressure during a more active inflammation and a normalization of the intraocular pressure in a quiescent eye.

Eyes of patients treated with concurrent systemic corticosteroids seem to show a less favourable response than patients without systemic corticosteroid treatment. No statistically significant visual acuity improvement could be shown in the one month or the six months follow up. Also, no statistically significant intraocular pressure increase was observed. This could reflect a more severe inflammation in eyes where systemic treatment is necessary. This is supported by the similar poor response in patients diagnosed with an autoimmune disease. Albeit there is significant overlap between the groups receiving systemic treatment and a diagnosed autoimmune disease. Generally, these results may be biased by the small number of patients in this category.

Besides the periocular corticosteroid injections there are other factors possibly contributing to the observed intraocular pressure increase. These include other drugs, fluid intake, heart rate, respiration, general fitness, or simple daily variations.

(80–82) In our cohort only 11.11% showed a relevant intraocular pressure increase according to the “Standardization of Uveitis Nomenclature Project” working group, which is of more than 10 mmHg. The average rise in intraocular pressure was small.

4.1. Limitations

The inhomogeneity of the patients with uveitis of varying severity and varying location of inflammation is responsible for much variability and complicates the interpretation of our data. For a more detailed subgroup analysis a larger data set would be required.

Another problem arises from the retrospective nature of this review. Many patients did not show up at the follow up examinations as indented. There may be various reasons for this. First, the treatment seems to show quick improvement. Therefore, many patients are less motivated to consulate a doctor for a follow up examination. Second, some patients may have consulted doctors in an extramural setting for their follow ups instead of doctors at the hospital, therefore no data would be stored at the local database. In some cases, important data such as intraocular pressure or best visual acuity was either not examined or not sufficiently documented. This reduced the number of patients available for a complete evaluation but still a sizable fraction of eyes remained in analysis.

4.2. Further reflection

This study shows safety and efficacy of periocular steroids in patients with a non-infectious uveitis. In order to elucidate the feasibility and safety of periocular steroids in more detail a prospective multi-centre cohort study would be desirable.

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