# Efficacy of tobramycin dexamethasone combined with loteprednol in the treatment of anterior uveitis and its impact on serum IgG, IgA, and IgE.

Tingqin Yan<sup>1,2</sup>, Hongsheng Bi<sup>3</sup>\*

<sup>1</sup>Clinical School, Shandong University of Traditional Chinese Medicine, Ji'nan 250355, China

<sup>2</sup> Department of Ophthalmology, Central Hospital of Tai'an City, Tai'an 271000, China

<sup>3</sup> Ophthalmologic Hospital, Shandong University of Traditional Chinese Medicine, Ji'nan 250002, China

#### Abstract

Objective of the present study is to investigate the efficacy of tobramycin dexamethasone combined with loteprednol for the treatment of anterior uveitis and its impact on serum IgG, IgA and IgE. 72 patients with anterior uveitis were randomly divided into study group and control group. The study group was treated with tobramycin dexamethasone and loteprednol, while the control group was only treated with tobramycin dexamethasone. All patients were followed up for six weeks. The clinical efficacy, healing time, side effects, serum IgG, IgA and IgE changes were compared between the two groups. The clinical efficacy of the study group was significantly better than the control group; the healing time of the study group was shorter than the control group; the incidence of adverse reactions of the study group was 2.78% lower than 16.67% of the control group. There were significant differences between the two groups (P<0.05). After the treatment, the serum IgG and IgE levels in the study group were significantly lower than the control group. However, IgA level was higher in the study group (P<0.05). The efficacy of tobramycin dexamethasone combined with loteprednol for treating anterior uveitis is certainly better than tobramycin dexamethasone alone. The serum IgG and IgE levels were significantly reduced and the serum IgA levels were significantly increased, so it should be widely applied in clinical practice.

Keywords: anterior uveitis; tobramycin dexamethasone; chlorine; serum IgG, IgA, and IgE

Accepted January 14 2014

### Introduction

Anterior uveitis is the most common type of uveitis, including mucous membrane inflammation, iridocyclitis and anterior cyclitis and accounting for about > 50% of the total number of uveitis. It can clinically manifest as acute, chronic, granulomatous and non-granulomatous inflammation [1]. The treatment should be performed based on the principle of quickly eliminating the inflammation and preventing posterior synechia. However, it should be first determined whether patients have active inflammation, and then give the patients who are diagnosed with inflammation different medicines based on the severity of the inflammation. Because the vast majority of anterior uveitis is caused by non-infectious factors, treatment with antibiotics is not generally needed; but patients with highly suspected or confirmed pathogen infection should be given an appropriate anti-infective therapy. As for the uveitis caused by non-infectious factors, the effective concentration of the drug can be achieved in the anterior eye segment through local administration; therefore, systemic administration of the medicine is generally not needed. The commonly used medicines including glucocorticoid eve drops, cycloplegic agent, non-steroidal anti-inflammatory eye drops, anti-viral eye drops, antibiotic eye drops and traditional Chinese medicine [2]. It is reported that loteprednol/tobramvcin was significantly less likely to produce elevations in intraocular pressure than was dexamethasone/tobramycin in healthy subjects treated for 28 days. Both loteprednol etabonate/tobramycin and dexamethasone/tobramycin were well tolerated with low risks for systemic and ocular adverse events other than elevation in intraocular pressure for dexamethasone/tobramycin[3]. In this study we combined tobramycin dexamethasone with loteprednol to treat anterior uveitis and investigated the efficacy of this combination and its impact on serum IgG, IgA and IgE.

### **Materials and Methods**

#### **General Information**

A total of 72 patients (39 males and 33 females; mean

Biomed Res- India 2014 Volume 25 Issue 2

age:  $38.54\pm2.92$  years [17-62 years]; mean course:  $3.65\pm$  0.72 days) who were all from those with anterior uveitis admitted into our hospital from July 2010 to December 2011 were enrolled for this observation. They were

randomly divided into the study group and control group. No significant difference was found in gender, age and course of disease between the two groups (P>0.05), but a comparability was observed. See Table 1.

Groups	n _	Gender		Age	Course of disease	
_		Male	Female	(years)	(uays)	
Study group	36	19	17	38.62±2.85	3.64±0.79	
Control group	36	20	16	38.39±2.47	3.71±0.82	

#### **Methods**

72 patients with anterior uveitis were collected and randomly divided into the study group and control group based on the parity of the inclusion number for observation. The study group was treated with tobramycin dexamethasone combined loteprednol (trade name: Lotemax, 1-2 drops once, 4 times daily) while the control group was given with tobramycin dexamethasone alone (trade name: Tobradex, 1-2 drops once, 4-6 times daily). All of the patients were followed up for six weeks. The clinical efficacy, healing time, adverse reaction and serum IgG, IgA and IgE changes before and after treatment were compared between the two groups, and the statistical analysis was performed.

#### Efficacy Evaluation Criteria

1) healing: regressed lesions of ocular region, negative aqueous flare, disappeared fresh KP and eliminated photophobia, pain, weeping and other symptoms; 2) improved: reduced lesions of ocular region, alleviated aqueous flare, decreased fresh KP and mitigated photophobia, pain and weeping; 3) ineffective: unchanged or increased photophobia, pain, weeping and lesion of ocular region [4]. The clinical efficiency = (the number of the patients healed + the number of patients improved)/total number of the patients  $\times 100\%$ .

#### Statistical analysis

All the data obtained from the observation were treated by using the statistical software SPSS18.0, among them, *t* test was used for measurement data, and  $\chi^2$  test was adopted for counting data. *P*<0.05 was considered to statistical significant in the test standard.

#### Results

# Comparison of the clinical efficacy between the two groups

After treatment, the healing, improvement and ineffectiveness was shown in 21, 13 and 2 patients in the study group; while in the control group, the healing, improvement and ineffectiveness was shown in 11, 17 and 8 patients, respectively. The efficacy of the combination drug in the study group was significantly better than that in the control group, and the difference between the two groups was statistically significant (P < 0.05) (See Table 2).

Table 2. Comparison of the clinical efficacy between the two groups

Groups	n	Healed	Improved	Ineffective	Effective rate (%)
Study group	36	21	13	2	94.44*
Control group	36	11	17	8	77.78

*Note:* \**P*<0.05,  $\chi^2 = 4.18$ , *P*=0.039

#### The healing time between the two groups

The mean healing time  $(14.67 \pm 2.92 \text{ days})$  of the study group with tobramycin dexamethasone combined with loteprednol was significantly shorter than that  $(18.25\pm3.46 \text{ days})$  of the control group with tobramycin dexamethasone alone, and the difference between the two groups was statistically significant (t=6.21P= 0.037<0.05).

Comparison of the adverse reactions between the two groups During the treatment, only 1 patient had ocular discomfort after dropping with the incidence of 2.78% in the study group; and 3 patients exhibited ocular discomfort after dropping, and 3 patients had increased intraocular pressure with the incidence of 16.67%. The difference between the two groups was statistically significant ( $\chi$ 2=3.96, P=0.041<0.05).

## Comparison of the changes in serum IgG, IgA and IgE before and after treatment between the two groups

No significant difference was found in serum IgG, IgA and IgE level between the two groups before treatment (P>0.05), however, after treatment, the mean serum IgG

and IgE level of the study group was significantly lower than those of the control group, while the serum IgA level was higher than that of the control group. The difference between the two groups was statistically significant (P<0.05).

 Table 3. Comparison of the changes in serum IgG, IgA and IgE before and after treatment between the two groups (g/L)

Groups	Before treatme	Before treatment			After treatment		
	IgG	IgA	IgE	IgG	IgA	IgE	
Study group	16.78±1.24	1.24±0.17	6.14±0.42	13.08±1.04*	2.35±0.23*	4.09±0.36*	
Control group	16.71±1.32	1.27±0.16	6.11±0.39	$15.26 \pm 1.17$	$1.86\pm0.19$	4.97±0.38	
			-				

*Note:* compared to the control group, \*P < 0.05; before treatment: IgG: t=2.53, P=1.28; IgA: t=2.41, P=1.31; IgE: t=2.72, P=1.15; after treatment: IgG: t=6.22, P=0.035; IgA: t=5.26, P=0.039; IgE: t=5.89, P=0.037.

#### Discussions

Uveitis, an autoimmune eye disease with a high blinding rate, mainly occurs in young adults and has the feature of easy recurrence. It is very difficult to treat this disease, and improper treatment often causes the blindness of the patients. The current clinical therapy is mainly the hormonotherapy, and the local administration of hormones can generally bring an effective control of the inflammation [5]. In the clinical treatment process, the individualized treatment should be performed for the specific conditions of the patients, but the long-term treatment with hormone will lead to a series of adverse reactions and complications, which remains to be resolved. In recent years, the invention and application of the new drugs improve the situation, of which, the compound preparation tobramycin dexamethasone containing 0.3% tobramycin and 0.1% alcohol dexamethasone is the common drug of the ophthalmology and has a good antiinflammatory effect; but it can inevitably bring the adverse reactions and complications in the ocular region and even the whole body [6], for which people have been trying to seek the cortisol medicines with low toxicity. While loteprednol ophthalmic suspension is a new generation of esters steroidal agent and is designed based on the principle of Bodor with a higher potency and safety, solving the problem of the toxicity of cortisol agents, and it has a higher affinity with cortisol receptor and higher lipid solubility to enhance the permeability of the cornea. Moreover, it is quickly converted to the inert metabolite after the onset, reducing the systemic toxicity and the potential adverse effects on the eye [7-8], and also has a stronger anti-inflammatory compared to prednisolone.

The results indicated that the clinical efficacy in the patients of the study group treated with tobramycin dexamethasone combined with loteprednol was significantly better than that of the control group treated with tobramycin dexamethasone alone, and the healing time was significantly shorter than that of the control group, and the incidence of the adverse reaction (2.78%) was significantly lower than that of the control group (16.67%); the differences in all these parameters were significant between the two groups (P < 0.05); after treatment, the serum IgG and IgE level of the study group was significantly lower than those of the control group, and the IgA level was higher than that of the control group; the difference was significant between the two groups (P < 0.05). Loteprednol ophthalmic suspension has little effect on the whole body, and the changes of the serum IgG, IgE and IgA were the manifestations of the improved systemic immune system after the ocular symptoms were alleviated. It can be seen that tobramycin dexamethasone combined with loteprednol has a certain efficacy in treating the anterior uveitis, which is better than that of tobramycin dexamethasone alone. Tobramycin dexamethasone combined with loteprednol is worthy of popularization and application as well as further study clinically.

#### References

- Comstock TL, Decory HH. Advances in corticosteroid therapy for ocular inflammation: loteprednol etabonate. Int J Inflam 2012; 2012: 789-623.
- Cohen AE, Assang C, Patane MA, From S, Korenfeld M; Avion Study Investigators. Evaluation of dexamethasone phosphate delivered by ocular iontophoresis for treating noninfectious anterior uveitis. Ophthalmology. 2012; 119(1): 66-73.
- Holland EJ, Bartlett JD, Paterno MR, Usner DW, Comstock TL.Effects of loteprednol/tobramycin versus dexamethasone/tobramycin on intraocular pressure in healthy volunteers. Cornea. 2008;27(1):50-55.
- Bennett TO, Peyman GA. Use of tobramycin in eradicating experimental bacterial endophthalmitis. Albrecht Von Graefes Arch Klin Exp Ophthalmol 1974; 191(2): 93-107.
- Garzozi HJ, Muallem MS, Harris A. Recurrent anterior uveitis and glaucoma associated with inadvertent

entry of ointment into the anterior chamber after radial keratotomy. J Cataract Refract Surg 1999; 25(12): 1685-1687.

- Ghosn CR, Li Y, Orilla WC, Lin T, Wheeler L, Burke JA, Robinson MR, Whitcup SM. Treatment of experimental anterior and intermediate uveitis by a dexamethasone intravitreal implant. Invest Ophthalmol Vis Sci 2011; 52(6): 2917-2923.
- Suarez E, Torres F, Vieira JC, Ramirez E, Arevalo JF.Anterior uveitis after laser in situ keratomileusis. J Cataract Refract Surg. 2002; 28(10):1793-1798.
- Barraquer RI, Alvarez de Toledo JP, Montané D, Escoto RM, Garcia Torres C, Bennani-Tazzi M. Fixed-dose combination of 0.1% diclofenac plus 0.3% to-bramycin ophthalmic solution for inflammation after cataract surgery: a randomized, comparative, active treatment-controlled trial. Eur J Ophthalmol 1998; 8(3): 173-178.

#### **Correspondence to:**

Hongsheng Bi Ophthalmologic Hospital Shandong University of Traditional Chinese Medicine, Ji'nan 250002, China