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Comparison of 0.1% dexamethasone phosphate eye gel (Dexagel) and 1% prednisolone acetate eye suspension in the treatment of post-operative inflammation after cataract surgery

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Abstract A prospective, multi-centre, clinical parallel group study was conducted to assess the efficacy and safety of a new 0.1% dexamethasone phosphate eye gel (Group 1, *n*=117) compared to 1%prednisolone acetate eye suspension (Group 2I, *n*=119) in a total of 236 patients (safety population), aged 39–92 years, following cataract surgery. Both drugs were given four times a day for 14 days starting 24±4 h after surgery. Criteria for evaluation were the reduction in anterior chamber flare and inflammation severity score (primary efficacy criteria) as well as different secondary efficacy and safety evaluation criteria. Laser photometry (LFM-500, Kowa), slit lamp assessment and the examination of other objective and subjective symptoms of ocular discomfort were performed between the last preoperative and 14th post-operative day. There were no statistically significant differences between the treatment groups concerning primary and secondary efficacy criteria. The mean reduction in anterior chamber flare from day 1 to day 14 post-operatively was 8.34±20.80 photons/ms with 0.1% dexamethasone eye gel and 5.72±16.70 photons/ ms with 1% prednisolone eye suspension. The mean reduction of inflammation severity score was 1.8±1.3 points in Group 1 and 2.0±1.1 points in Group 2. Intra-ocular pressure did not increase after treatment with 0.1% dexamethasone phosphate eye gel. *Conclusion:* the results of the study underline the protective effect of topically applied 0.1% dexamethasone phosphate eye gel on the blood-aqueous barrier. This drug is an effective and safe steroidal anti-inflammatory agent for topical use following cataract surgery and intra-ocular lens implantation.

Introduction

Dexamethasone and prednisolone are halogenated glucocorticoids with a potent anti-inflammatory effect. Both agents are topically applied routinely after intra-ocular surgery to reduce conjunctival, perikeratic and iridal hyperaemia, prevent the breakdown of the blood-aqueous barrier and to inhibit cellular infiltration into target tissues. The clinical utility of corticosteroid eye drops is limited by some known side-effects occurring after prolonged administration. Ocular adverse effects include elevation of intra-ocular pressure, masking of infection, formation of posterior subcapsular cataract, and delay in corneal healing.

Until recently, dexamethasone sodium phosphate was commercially available in Germany in the form of aqueous eye drops only. Now, a new formulation has been developed in the form of a viscous crystal-clear gel (Dexagel, Dr. Mann Pharma GmbH, Berlin) containing the water soluble ester of dexamethasone, dexamethasone sodium phosphate, at a concentration of 0.1%. The addition of a viscoelastic agent (carbomer) increases the viscosity of the formulation. In rabbits, a pharmacokinetic comparison of an aqueous dexamethasone solution versus

dexamethasone gel demonstrated that bioavailability of dexamethasone phosphate in corneal tissue and aqueous humour is increased after application of Dexagel, probably as a result of greater initial saturation of the tear film and a slower rate of elimination [13].

The aim of the present study was to investigate the effects of this 0.1% dexamethasone phosphate eye gel on post-operative inflammation following cataract surgery after a treatment period of 14 days. The reference preparation was an eye suspension containing 1% prednisolone acetate.

Subjects and methods

This prospective, multi-centre, active-controlled, open, clinical parallel group study describes the results of 236 patients (safety population) scheduled for phaco emulsification by the tunnel technique with sclerocorneal incision. The study was reviewed by the appropriate Ethics Committee. The tenets of the World Medical Association Declaration of Helsinki were followed and prior informed consent was obtained from all patients.

After screening on the basis of defined inclusion and exclusion criteria, the total of 236 cataract patients (87 male, 149 female), aged 39–92 years (average age 70.8 years) were included successively in the study in seven different centres between January and October 1999. At each centre, all surgery was performed by one surgeon with comparable surgical experience and surgical technique. The number of examiners was not specified. Patients to be included in the study were at least 40 years of age, suffered from pre-senile or senile cataract and were planned for cataract surgery. The eye concerned had to be free of irritations. Exclusion criteria were a history of hypersensitivity to steroids or other components of the study medication, diabetes mellitus, herpes simplex virus infection, uveitis, glaucoma and surgical interventions of the eye concerned within 2 months preceding surgery. Exclusion criteria regarding present conditions were infections, inflammation, severe dry eye syndrome and corneal lesions of the eye concerned.

Distribution of patients:

Patients were randomly allocated to one of the following therapeutic groups: Group 1 (n=117, 47 males, 70 females); therapy with 0.1% dexamethasone phosphate eye gel (Dexagel) and Group 2 (n=119, 40 males, 79 females); therapy with 1% prednisolone acetate eye suspension. Some 16 patients of the safety population (Group 1: 6; Group 2: 10) were withdrawn from the study after randomisation due to different reasons for premature study termination. As 13 of the 236 patients of the safety population did not meet the criteria for the intention-to-treat (ITT) population and 47 patients had at least one major protocol violation, the ITT population consisted of 223 patients (Group 1: 112, Group 2: 111) and the per protocol (PP) population comprised 189 patients (Group 1: 92, Group 2: 97). BothPP and ITT populations were used for the analysis of clinical efficacy.

Treatments:

From Day 1 (24±4 h after surgery) until Day 14, the study medication (marketed preparations) was to be applied four times a day. At each administration, one drop of study medication was to be instilled into the lower conjunctival fold of the operated eye. Concomitant therapy given in both groups was identical. The following criteria were used for the evaluation of the two preparations from preoperative Day –1 (visit 1), Day 0 (surgery), Day 1 (visit 2), Day 3 (visit 3), Day 7 (visit 4) to Day 14±2 (visit 5) : (1) primary efficacy consisting of, reduction in anterior chamber flare, and reduced inflammation severity score (cells and flare in the anterior chamber), (2) secondary efficacyconsisting of reduced corneal oedema, reduction of Descemet folds, reduction of intraocular debris on lens, change in visual acuity, and global efficacy assessment (frequency of clinical cure);(3) safety evaluation: adverse events, intraocular pressure, local tolerance and vital signs. The following parameters were measured at each visit using the methods described: the Tyndall effect in the anterior chamber using the LFM-500 laser flare photometer (Kowa) based on the method described by Sawa et al. [20] and Oshika et Araie [17], clinical-biomicroscopic parameters assessed by slit lamp examination, visual acuity examined using standard equipment, and intraocular pressure determined by applanation tonometry. The signs and symptoms were scored using different rules and scales. Adverse events were assessed with respect to their intensity using the categories mild, moderate and severe.

Statistics

The statistical analysis procedures, as laid down in the protocol, were described in detail in the analysis plan which was prepared by “staticon international” (Verum Staticon GmbH, Planegg). The study was designed to show one-sided non-inferiority (at the 2.5% significance level) of 0.1% dexamethasone eye gel compared to 1% prednisolone eye suspension. The test preparation 0.1% dexamethasone eye gel was to be considered as not being inferior if the reduction of the main efficacy variable (anterior chamber flare) with 0.1% dexamethasone eye gel was greater than 80% of that with 1% prednisolone eye suspension. The confirmatory analysis was based on the PP population. Additionally, an exploratory analysis based on the ITT population was performed in order to check for internal consistency of the results.

The tests were calculated by t-test (ANCOVA). For the secondary efficacy criteria, two-sided exploratory tests for differences between 0.1% dexamethasone eye gel and 1% prednisolone eye suspension were performed at the 5% significance level (Mantel-Haenszel chi-squared test and analysis of covariance). An exploratory analysis of covariance for the primary efficacy criteria was carried out with additional treatment-by-centre interaction, both for the PP population and ITT population. There was no evidence of centre specific treatment effects either in the PP population or in the ITT population.

Results

Primary efficacy criteria

The mean reduction in anterior chamber flare from Day 1(24±4 h after surgery) to Day 14 was 8.34±20.80 photons/ms (median 4.00 photons/ms) with 0.1% dexamethasone eye gel (Group 1) and 5.72±16.70 photons/ms (median 3.10 photons/ms) with 1% prednisolone eye suspension (Group 2) (Fig.1). The mean reduction in inflammation severity score in the same post-operative period was 1.8±1.3 points (median 2.0 points) in Group 1 and 2.0±1.1 points (median 2.0 points) in Group 2 (Fig.2). Confirmatory testing showed statistically significant non-inferiority of 0.1% dexamethasone eye gel

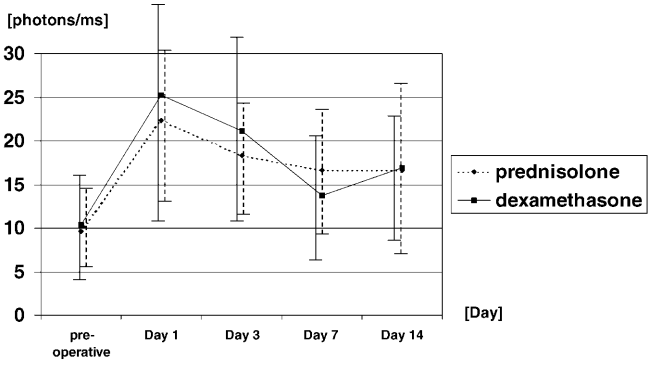

Fig. 1 Anterior chamber flare from preoperative Day –1 (visit 1) to Day 14±2 (visit 5); laser tyndallometry; PPpopulation (*n*=189). Dexamethasone 0.1% eye gel (*dex*), (*n*=92); prednisolone 1% eye suspension (*predn*) (*n*=97)

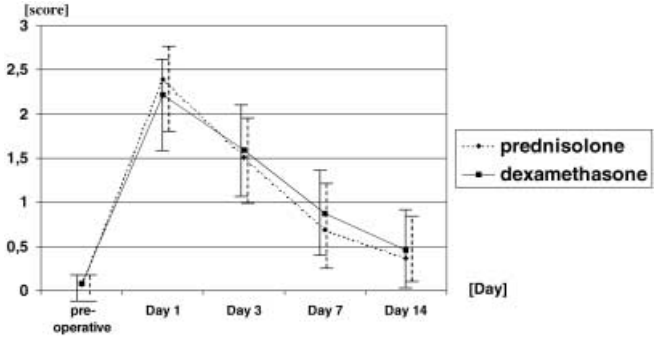

Fig. 2 Inflammation severity score from preoperative Day –1 (visit 1) to Day 14±2 (visit 5); slit lamp examination of cells and flare in the anterior chamber; PPpopulation (*n*=189). Dexamethasone 0.1% eye gel (*dex*) (*n*=92), prednisolone 1% eye suspension (*predn*) (*n*=97)

compared to 1% prednisolone eye suspension with respect to reduction in anterior chamber flare (*P*=0.0019, one-sided) and reduction in inflammation severity score (*P*<0.0001, one-sided). Superiority of 0.1% dexamethasone eye gel over 1% prednisolone eye suspension could not be demonstrated (*P*=0.1927, one-sided, for reduction in anterior chamber flare and *P*=0.6347, one-sided, for reduction in inflammation severity score). These results were supported by the exploratory analysis of the primary efficacy criteria, based on the ITT population, which also showed statistically significant one-sided non-inferiority of 0.1% dexamethasone eye gel compared to 1% prednisolone eye suspension, but not superiority.

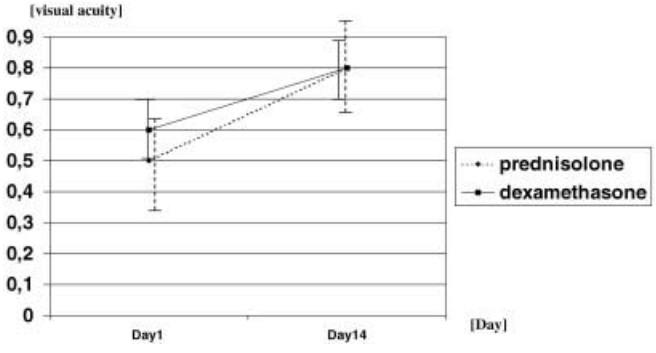

Fig. 3 Change in best corrected visual acuity from Day 1 (visit 2) to Day 14±2 (visit 5): 0.2±0.2 (both groups) PP population (*n*=189). Dexamethasone (*dex*) (*n*=92), prednisolone (*predn*) (*n*=97)

Secondary efficacy criteria

There was no statistically significant difference between the treatment groups from Day 1 to Day 14 with respect to the reduction in corneal oedema (*P*=0.242, two-sided), Descemet folds (*P*=0.682, two-sided) and intraocular debris on lens (*P*=0.168, two-sided), respectively (Table1). Exploratory testing did not show statistically significant differences between the treatment groups with respect to the change in visual acuity (*P*=0.404, two-sided (Fig.3) and the global efficacy assessment (*P*=0.209, two-sided).

It must be taken into consideration that the relative frequency of patients with abnormal baseline conditions (at Day 1) was higher for two criteria in the prednisolone group as compared to the dexamethasone group (reduction in corneal oedema and Descemet folds, respectively) and for the criterion “reduction of intraocular debris on lens” higher in the dexamethasone group as compared to the prednisolone patients.

Table 1 Secondary efficacy criteria (selection) from Day 1 (visit 2) to Day 14±2 (visit 5); slit lamp examination, PP population (*n*=189)

Criterion	Reduced (%)		Unchanged (%)		Increased (%)	
	Dexamethasone (*n*=92)	Prednisolone (*n*=97)	Dexamethasone (*n*=92)	Prednisolone (*n*=97)	Dexamethasone (*n*=92)	Prednisolone (*n*=97)
Change in corneal oedema	37.0	44.3	62.0	54.6	1.1	1.0
Change in Descement folds	29.3	37.1	68.5	60.8	2.2	2.1
Change in intraocular debris on lens	18.5	11.3	81.5	88.7	0	0

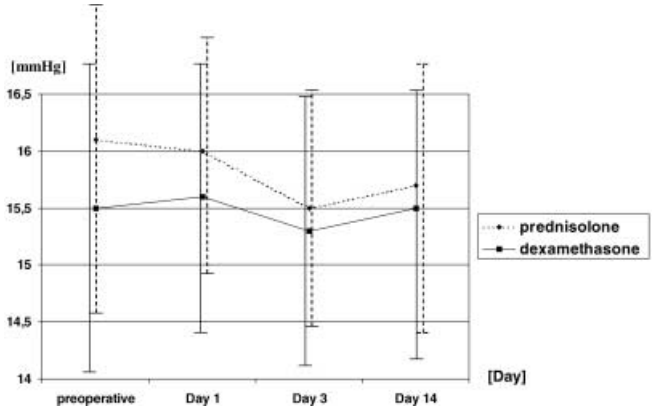

Fig. 4 Intraocular pressure from preoperative Day –1 (visit 1) to Day 14±2 (visit 555]. Applanation tonometry. Safety population (n=236).Dexamethasone (*dex*) (*n*=117), predisolone (*predn*) (*n*=119)

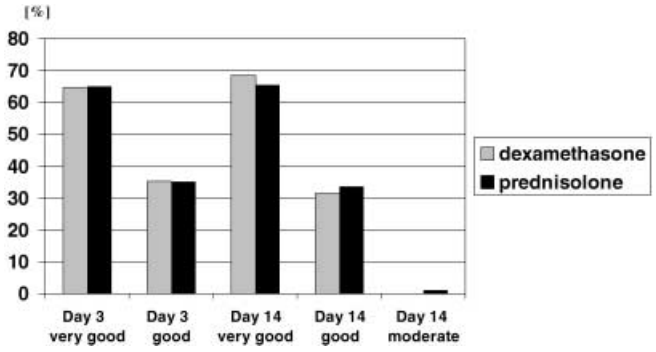

Fig. 5 Subjective local tolerance from Day 3 (visit 3) to Day 14±2 (visit 5); safety population (*n*=236). Dexamethasone (*dex*) (*n*=117), predisolone (*predn*) (*n*=119). Scale: very good = no irritation; good = slight irritation, ≤5 min; moderate = marked irritation, >5 min

The secondary efficacy criteria were additionally analysed for the ITT population using the same test procedures as described for the PP population. Exploratory testing did not show statistical significant differences between both treatment groups with respect to any of the secondary efficacy criteria.

Safety evaluation

The analysis of adverse events, "intraocular pressure", "local tolerance", and "vital signs" (systolic and diastolic blood pressure and pulse) was carried out on the safety population (*n*=236), which was defined as patients who received at least one dose of study medication. The incidence of adverse events assessed as related to the administration of study medication was equal in the treatment groups.

Overall, in four patients (two patients in each treatment group), the adverse events were considered to be related to the administration of study medication (dexamethasone group: face oedema, conjunctivitis, corneal oedema and ulceration; prednisolone group: conjunctivitis and decrease of intraocular pressure). The intraocular pressure was measured at each visit. There were no relevant differences between the treatment groups with respect to the mean values of intraocular pressure. The mean values were within the normal range at each visit. In both treatment groups, the mean intraocular pressure in the operated eye was comparable to that in the not operated eye (Fig.4).

From Day 3 (visit 3) up to the end of treatment, the subjective local tolerance was examined by questioning the patient (Fig.5). At the end of treatment (visit 5), the relative frequency of patients who assessed the local tolerance of the study medication as very good was slightly higher among the patients in the dexamethasone group as compared to the prednisolone group. There were no relevant differences between the treatment groups with respect to mean values of vital signs. The mean values were within the normal range at each visit.

Discussion

Published reports have shown that the post-operative inflammatory response after cataract surgery may be related to such factors such as previous alteration of the blood-aqueous-barrier, surgical equipment and technique, incision size, intraocular lens type, and degree of iris pigmentation [3, 7, 8, 10,16]. The anti-inflammatory effects of topically applied corticosteroids which are administered during the perioperative period have been clearly demonstrated in clinical trials [25]. Our reference preparation, 1% prednisolone acetate eye drops (aqueous suspension), has been shown to readily penetrate the cornea [5], exhibit prolonged bioavailability in the aqueous humour [14] and to have marked anti-inflammatory effects in the post-cataract surgery period [2, 21,23].

With respect to the primary efficacy criteria "reduction in anterior chamber flare" and "reduction in inflammation severity score", the test medication, 0.1% dexamethasone phosphate eye gel, was equivalent to the reference preparation. Concerning the secondary efficacy criteria, the two preparations exhibited practically identical clinical effects. There were no statistically significant differences between 0.1% dexamethasone phosphate eye gel and 1% prednisolone acetate eye suspension with respect to the criteria "reduction in corneal oedema", "reduction in Descemet folds", "reduction of intraocular debris on lens", "change of visual acuity", or "global efficacy assessment". Regarding the baseline values of corneal oedema and Descemet folds (Day 1, post-operative), the number of patients with corneal oedema and

Descemet folds was higher in the prednisolone group as compared to the dexamethasone group. This fact could possibly explain the higher percentage of prednisolone patients with a reduction in corneal oedema and Descemet folds respectively as compared to the dexamethasone patients. On the other hand, the reduction of intraocular debris on lens was more frequent under dexamethasone as compared to prednisolone. The baseline values showed more patients with debris on lens in the dexamethasone group than in the prednisolone group. The increase in visual acuity was equal in both treatment groups.

Corticosteroids vary in their inherent anti-inflammatory potency. Prednisolone is four times more potent than hydrocortisone and dexamethasone is 25 times as potent as hydrocortisone [12]. Dexamethasone has an inherent systemic anti-inflammatory potency which is 5–7 times greater than that of prednisolone. However, it has been suggested that these systemic differences in potency cannot be extrapolated directly to the eye. Lipophilic acetate and alcohol corticosteroid preparations penetrate the intact corneal epithelium better than polar preparations such as sodium salts of the steroid phosphate. Thus, the mean peak concentration in human aqueous humour following the separate topical administration of 50 µl of 1% prednisolone acetate is 669.6±135.5 ng/ml and of 0.5% prednisolone phosphate only 25.6±4.0 ng/ml [6,14]. McGhee et al. [14] reported a mean concentration of 0.67 µg/ml in human aqueous humour 1.5–2 h after instillation of 50 µl of 1% prednisolone acetate in the conjunctival sac. After 20 h, the mean level had fallen to 0.03 µg/ml.

Although 0.1% dexamethasone has a better anti-inflammatory potency and a higher glucocorticoid-receptor binding capacity, it is hardly able to protect the blood-aqueous barrier in a significantly better way than 1% prednisolone acetate. One reason for this might be the better corneal penetration of prednisolone acetate [5]. Midelfart et al. [15] investigated the penetration of dexamethasone phosphate into the aqueous humour and its metabolism using NMR spectroscopy. These investigations have confirmed that dephosphorylation of the prodrug, dexamethasone phosphate, occurred in the cornea. On the other hand, the penetration rate of dexamethasone phosphate increases distinctly in an inflamed eye or when the epithelium of the cornea is no longer intact [4]. Furthermore, it has been documented that the formulation of drugs (particularly vehicle and preservative) can significantly influence the penetration of topically applied steroids [9]. The variables include the concentration of the drug in the vehicle, the volume of the instilled dose, the viscosity of the vehicle, the influence of tear turnover and drainage on the instilled dose, and the absorption and elimination characteristics of the drug. Contact time of a topically administered drug with the eye plays a major role in the concentration that the drug achieves in the cornea and in the aqueous humour, respectively [11]. The contact time of the drug system with the precorneal tear film is largely determined by the viscosity of the vehicle [22]. In a previous study we compared the effect of 0.5% prednisolone acetate eye gel with 1% prednisolone acetate eye suspension in a clinical trial with a total of 63 patients, following cataract surgery. Both evaluated drugs showed equivalence concerning the anti-inflammatory efficacy [24].

In an animal experiment with albino rabbits the concentration-time response curve shows better availability of 50 µl 0.1% dexamethasone phosphate in the cornea and aqueous humour when topically applied as an eye gel in comparison to eye drops [13]. The animal experiment demonstrated that due to the prolonged corneal contact time the gel formulation increases the bioavailability of dexamethasone in the cornea and doubles the area under the concentration-time curve in aqueous humour compared with the same drug applied as an aqueous solution. Maximum concentration (C_{max}) was moderately, but statistically significantly higher in the cornea (2.05 µg/g versus 1.13 µg/g) and aqueous humour (0.22 µg/ml versus 0.14 µg/ml) of the group having received the ophthalmic gel. This would explain, together with the different anti-inflammatory potency and the glucocorticoid-receptor binding capacity, the equivalence of clinical effects of 0.1% dexamethasone phosphate eye gel and 1% prednisolone acetate eye suspension. This effect can be utilised to improve the safety of the corticosteroid during use.

In the study presented here, adverse events assessed as related to the administration of study medication were rare and the incidence was equal in the treatment groups. There was no indication of any ocular side-effect. Ocular adverse effects might also include a rise in the intraocular pressure, especially in steroid-responders, but this effect should be less pronounced for prednisolone than for dexamethasone [1, 18, 19]. We did not observe any influence of the study medication on the mean values of intraocular pressure. The mean values were within the normal range at each visit. For no patient in the dexamethasone group, increase of ocular pressure was reported as an adverse event. Concerning the mean values of intraocular pressure and local tolerance, 0.1% dexamethasone eye gel and 1% prednisolone eye suspension were comparable. The clinical findings together with the results of the patients' reports of symptoms of ocular discomfort correlated well with the objectively evaluated data. In conclusion, the results of the study underline the protective effect of topically applied 0.1% dexamethasone phosphate eye gel on the blood-aqueous barrier after cataract extraction and IOL implantation and the equivalent anti-inflammatory efficacy of 0.1% dexamethasone phosphate eye gel compared to 1% prednisolone acetate eye suspension.

References

1. Akingbehin AO (1983) Comparative study of the intraocular pressure effects of fluorometholone 0.1% versus dexamethasone 0.1%. Br J Ophthalmol 67: 661–663
2. Carriker F, Liebowitz S, Nees O, Siegel E, Duzman E, Cheetham JK, Gruse R (1987) Prednisolone acetate-gentamicin combination following cataract surgery. Ann Ophthalmol 19: 247–250
3. Chee SP, Ti SE, Sivakumar M, Tan DTH (1999) Postoperative inflammation: Extracapsular cataract extraction versus phacoemulsification. J Cataract Refract Surg 25: 1280–1285
4. Cox WV, Kupferman A, Leibowitz HM (1972) Topically applied steroids in corneal disease: the role of inflammation in stromal absorption of dexamethasone. Arch Ophthalmol 88: 308–313
5. Diestelhorst M, Aspacher F, Konen W, Krieglstein GK, Hilgers RD (1992) Effect of dexamethasone 0.1% and prednisolone acetate 1.0% eye drops on the blood-aqueous barrier after cataract surgery: a controlled randomized fluorophotometric study. Graefes Arch Clin Exp Ophthalmol 230: 451–453
6. Flint GR, Morton DJ (1984) Effect of derivatization on the bioavailability of ophthalmic steroids: development of an in vitro method of evaluation. Arch Ophthalmol 102: 1808–1809
7. Hessemer V, Schartner H (1997) Geringer Einfluß antiinflammatorischer Therapie auf den intraokularen Reizzustand nach minimal invasiver Phakoemulsifikation. Ophthalmologe 94: 30–32
8. Hinkelmann L, Struck HG, Lautenschläger C (1998) Untersuchungen zur Entzündungsreaktion des vorderen Augenabschnitts. Kataraktextraktion bei Patienten mit und ohne Diabetes mellitus. Ophthalmologe 95: 213–218
9. Kupferman A, Pratt MV, Suckewer K, Leibowitz HM (1974) Topically applied steroids in corneal disease: 111. The role of drug derivate in stromal absorption of dexamethasone. Arch Ophthalmol 91: 373–376
10. Laurell CG, Zetterström C, Lundgren B, Törngren L, Andersson K (1997) Inflammatory response in the rabbit after phacoemulsification and intraocular lens implantation using a 5.2 or 11.0 mm incision. J Cataract Refract Surg 23: 126–131
11. Leibowitz HM, Kupferman A (1979) Optimal frequency of topical prednisolone administration. Arch Ophthalmol 97: 2154–2156
12. Leibowitz HM, Kupferman A (1980) Anti-inflammatory medications. Int Ophthalmol Clin 20: 117–134
13. Dr. Mann Pharma Study Nr. 008 PHA 94 (1998) Critical assessment report on the pharmaco-toxicological documentation of dexamethasone-21-dihydrogen-phosphate-disodium-salt.
14. McGhee CNJ, Watson DG, Midgley JM, Noble MJ, Dutton GN, Fern AI (1990) Penetration of synthetic corticosteroids into human aqueous humour. Eye 4: 526–530
15. Midelfart A, Dybdahl A, Müller N, Sitter B, Gribbestad IS, Krane J (1999) Dexamethasone and dexamethasone phosphate detected by ^{1}H and ^{19}F NMR spectroscopy in the aqueous humour. Exp Eye Res 66: 327–337
16. Nguyen NX, Tomida I, Küchle M (2000) Blood-aqueous barrier after phacoemulsification with posterior chamber lens implantation; foldable acrylate lens versus PMMA lens – a clinical study on 46 eyes. Klin Monatsbl Augenheilk: 217: 215–218
17. Oshika T, Araie M (1990) Time course of changes in aqueous protein concentration and flow rate after oral acetazolamide. Invest Ophthalmol Vis Sci 31: 527–534
18. Polansky JR, Weinreb RN (1984) Steroids as anti-inflammatory agents. In: Sears ML (ed) Pharmacology of the eye. Springer, Berlin Heidelberg New York, pp 460–538
19. Rubin B, Palestine AG (1989) Complications of corticosteroid and immunsuppressive drugs. Int Ophthalmol Clin 29: 159–171
20. Sawa M, Tsurimaki Y, Tsuru T, Shimizu H (1988) New quantitative method to determine protein concentration and cell number in aqueous in vivo. Jpn J Ophthalmol 32: 132–142
21. Schmitt K, Hessemer V (1995) Ist eine subkonjunktivale Steroidgabe zusätzlich zur Lokaltherapie nach Kataraktoperation notwendig? Ophthalmologe 92: 303–306
22. Sieg JW, Robinson JR (1975) Vehicle effects on ocular drug bioavailability I: evaluation of fluorometholone. J Pharm Sci 64: 931–936
23. Sousa FJ (1991) The bioavailability and therapeutic effectiveness of prednisolone acetate versus prednisolone sodium phosphate: a 20-year review. CLAO J 17: 282–284
24. Struck HG, Stoldt G (1997) The antiinflammatory efficacy of prednisolone eye gel after cataract extraction. In: Süveges I, Follmann P (eds) XIth Congress of the European Society of Ophthalmology. Monduzzi editore, Bologna, pp 245–251
25. Wenzel M, Dahlke C, Tahmaz E, Reim M (1992) Zur Bedeutung der Kortikosteroide in der Nachsorge von Patienten nach Kataraktextraktion und Linsenimplantation. Klin Monatsbl Augenheilk 200: 262–266