COMPARATIVE STUDY OF THE INTRAOCULAR PRESSURE ELEVATION POTENTIALS OF DEXAMETHASONE PHOSPHATE AND FLUORO-METHOLONE ACETATE ON NORMOTNSIVE NIGERIA

BY
AMAECHI, O. U.
DEPARTMENT OF OPTOMETRY, ABIA STATE UNIVERSITY
UTURU, ABIA STATE, NIGERIA
Email:okamaechi@yahoo.com
*Corresponding author

ABSTRACT

Corticosteroids provide a non-specific mode of therapy for suppressing inflammation without eliminating the cause; and their local ophthalmic use entails a degree of risk for serious ocular complications like steroid induced glaucoma, cataract formation, rebound inflammation, etcetera. The risk of elevated intraocular pressure (IOP) was compared for dexamethasone phosphate (Decadron®) and fluorometholone acetate (Flarex®) on 32 normotensive volunteers, comprising 12 males and 20 females of the age range 18-40 years. However, age and sex were not considered in the study. An IOP increase of > 5mmHg was recorded in 44 eyes (68.8%) for Decadron® as against 2 eyes (3.1%) for Flarex®; and this difference was found to be highly significant when analyzed statistically using the Z-test at 95% confidence interval. Fluoromentholone acetate, therefore, has a low propensity for increasing IOP, and is recommended for treating most ocular inflammations in patients where an increased IOP is considered an urgent visual risk.

KEYWORDS: Intraocular Pressure, Steroids, Fluorometholone acetate, Dexamethasone phosphate, Indentation tonometry, Normotensive.

INTRODUCTION

The delicate and exposed nature of the eye makes it prone to infections and inflammation. Corticosteroid as anti-inflammatory agent is the drug of choice for treatment of ocular inflammations[1]. They are however, anti-inflammatory without removing the cause of the inflammation: hence are found mainly useful in decreasing inflammation in a self- limited disease process. Topical and systemic steroids are invaluable agents in the treatment of a wide range of ocular disorders, but they are fraught with a lot of complications. Ocular side effects of corticosteroids may follow topical, peri- ocular or systemic administration. The complications of steroids are highly dependent on dose schedule and total cumulative effect. Ocular side effects include glaucoma, cataract, delayed corneal epithelia healing, ocular muscle palsy and etcetera. Glaucoma, however, is more often associated with topical or peri-ocular steroid than with systemic steroid[2].

Glaucoma is a syndrome that causes progressive excavation of the optic disc, optic atrophy and characteristic loss of visual field. A diagnosis is confirmed when any of the above two are present. It primarily results from intraocular pressure (IOP) shoot-up due to excess aqueous production, alteration in composition of aqueous, and obstruction of aqueous outflow. The level of IOP associated with optic nerve damage is not the same in every eye as some individuals may tolerate a pressure that will rapidly blind another. The internal or intraocular pressure is the pressure maintained in the eyeball by constant formation and drainage of aqueous humour[3]. The pressure of the fluid content of the eyeball serves to maintain its shape for optical purposes. A balance between aqueous humour production and outflow regulates IOP, which normally varies between 15mmHg and 21mmHg. The normal IOP in man is that pressure which the eye tolerates over a period of time without damage to its integrity, and it varies from individual to individual. Normal individuals have a mean IOP of about 15±3mmHg[1]. Hourly variations known as diurnal variations may be greater in individuals with glaucoma than in healthy individuals. Factors that affect the IOP includes blockage of aqueous circulation, abnormalities within the trabecular meshwork, and physiological variables such as age, sex, weight, refractive errors. The pressure may be increased by consumption of

corticosteroids.

Whereas steroids increase the intraocular pressure, some other compounds are known to decrease it such as alcohol[4,5], oral isorbide[6], beta-adrenergic blockers[7,8], and alpha 2- agonists[9].

The intraocular pressure is clinically measured using a tonometer by determining the resistance of the eye to an applied force. A single normal reading with either the indentation or applanation tonometer does not rule out glaucoma, whereas a single ñhigh normalò reading (24-32mmHg) is suggestive of glaucoma, but requires repeated testing before a definite diagnosis is made[3].

Fluorometholone is said to have good excellent anti-inflammatory potential, while having diminished propensity to cause secondary IOP increase. Its two derivatives are fluorometholone alcohol and fluorometholone acetate (the one under study). The latter has greater efficacy than the former, while still enjoying intraocular pressure sparing properties. Dexamethasone and prednisolone have great potency, but are said to be the easiest to induce steroid glaucoma as against rimexolone or fluorometholone[10].

This comparative study would establish if the foregoing holds true for normotensive Nigerians, thus highlighting the need to employ the use of the steroid that has lower propensity of elevating IOP in treating most ocular inflammations.

It is important to note that treatment of corticosteroid-induced glaucoma is immediate discontinuation of the steroid, and use of anti-glaucoma medication if necessary.

MATERIALS AND METHOD

A randomly selected sample of 40 subjects of the age range 18 to 40 years from a Nigerian community was used for the study. These subjects had previously been screened and found to be free of ocular or systemic medications that would compromise the study, and did not have glaucoma. Pregnant subjects were also ruled out from the study. Medical histories were taken and ocular examinations including visual acuity, external examination, ophthalmoscopy, visual field charting using Bjerrum tangent screen, and Schiotz indentation tonometry were performed. All examinations were done in the morning.

The research design was a prospective, randomized, controlled clinical trial adopting the pre-test, post-test method of research. The materials used for the research were the visual acuity chart, the pen light, ophthalmoscope, Bjerrum tangent screen, and Schiotz indentation tonometer. The test medications used were 0.1% dexamethasone sodium phosphate (Decatron®) as drug1, and 0.1% fluorometholone acetate (Flarex®) as drug 2.

The details of study including possible risks were explained to each subject and consent obtained. The baseline IOP (i.e. IOP before drug instillation) was measured. One drop of study drug 1 was instilled into the lower fornix of the subject. The drug was to be instilled after shaking the bottle, one drop 4 times daily for 4 weeks, or until there was an IOP response of ≥10mmHg relative to the baseline IOP.

The subject was advised on the need for 100% compliance. The medication bottle was marked without the patient's knowledge at each visit to monitor compliance. The IOP was monitored weekly, and at each visit a total of three measurements were taken and the lowest recorded. Once the subject completed 4 weeks of treatment, he was withdrawn from the medication for approximately one month (washout). At the completion of the washout period, IOP was measured as on day 1 of the first course of treatment. The subject was then issued the second medication (Flarex®) and followed up in an identical fashion as for the first study drug (Decadron®).

A statistical comparison of dexamethasone sodium phosphate (Decadron®) and fluorometholone acetate (Flarex®) was based on the number (percentage) of subjects that record an IOP change of ≥5mmHg at the expiration of 4 weeks. To test for significance, the Z-test was employed.

RESULTS

Of the 40 subjects enrolled in the study, 32 i.e. 64 eyes (80%) completed both courses of treatment. No IOP change of ≥ 10mmHg was observed before the expiration of 4 weeks. The average baseline IOP of the eyes was 14.8mmHg for Decadron® and 14.5mmHg for Flarex®.

The mean change in baseline IOP at the end of 4 weeks was 9.9mmHg for Decadron® and

5.8mmHg for Flarex® (tables 1 and 2). The number of eyes that demonstrated a mean change in IOP ≥ 5mmHg was 44 (68.8%) for Decadron® and 2 (3.1%) for Flarex® (table 3).

The number of eyes that demonstrated a mean change in IOP ≥ 5mmHg was 44 (68.8%) for Decadron? and 2 (3.1%) for Flarex (Table 3). The ratio of the mean change in IOP for Decadron® to Flarex® was 9.9 to 5.8 which is approximately 2:1.

DISCUSSION

The mean baseline IOP of the eyes for Decadron® and Flarex®

was 14.8mmHg and 14.5mmHg respectively. There was no significant statistical difference between the baseline IOPs.

At the expiration of 4 weeks, a mean change in IOP from the mean baseline IOP was 9.9mmHg for Decadron® and 5.8mmHg for Flarex®; a change of 66.9% and 40% respectively. A graphical presentation of this, showed a steeper slope for Decadron® and Flarex® (fig. 1). The difference recorded between the two drugs was found to be significant when analyzed statistically using the Z-test at 95% confidence interval. The Z_{cal}(6.95) is greater than the Z_{tab}(1.98), indicating that the IOP elevation potential of Decadron® was significantly higher than that of Flarex® in the same steroid responders. A similar study by Stewart et al[11], but carried out for a 6 weeks duration recorded a mean change in IOP of 13.6 mmHg for Decadron® and 6.5mmHg for Flarex®. He established that fluorometholone takes significantly longer to raise IOP than dexamethasone in the 17 subjects used for that study. Of the 64 eyes used in this study, 44 eyes recorded a mean change in IOP of ≥ 5 mmHg for Decadron®, as against 2 eyes for Flarex® i.e a mean change of 68.8% and 3.1% respectively, which was also found to be statistically significant. The ratio of the mean change in IOP for dexamethasone and fluorometholone was approximately 2:1; in other words dexamethasone raised IOP about 2 times more than fluorometholone within the same time period. Many writers have established that dexamethasone produced a significant increase in IOP[11,12], and a marked reduction in outflow facility in all the age groups studied[12].

Fluorometholone acetate has a significantly lower propensity for raising intraocular pressure than dexamethasone. It is therefore recommended as a drug of choice for treating ocular inflammations especially when long term therapy with steroids is required.

TABLE 1: MEAN CHANGE IN IOP IN WEEKS FOR DECADRON®

Mean baseline IOP= 14.8mmHg	Induced IOP (mmHg)			
	Week 1	Week 2	Week 3	Week 4
Mean IOP (mmHg)	18.0	21.3	24.3	24.7
Mean ɑin IOP (mmHg)	3.2	6.5	9.5	9.9

TABLE 2: MEAN CHANGE IN IOP IN WEEKS FOR FLAREX®

Mean baseline IOP= 14.8mmHg	Induced IOP (mmHg)			
	Week 1	Week 2	Week 3	Week 4
Mean IOP (mmHg)	15.6	16.8	18.2	20.3
Mean ɑin IOP (mmHg)	1.1	2.3	3.7	5.8

TABLE 3: MEAN IOP DEMONSTRATED BY THE EYES FOR DECADRO N® AND FLAREX®

	Number of eyes	
Mean Δ in IOP (mmHg)	Decadron®	Flarex®
<5mmHg	20 (31.2%)	62 (96.9%)
≥5mmHg	44 (68.8%)	2 (3.1%)

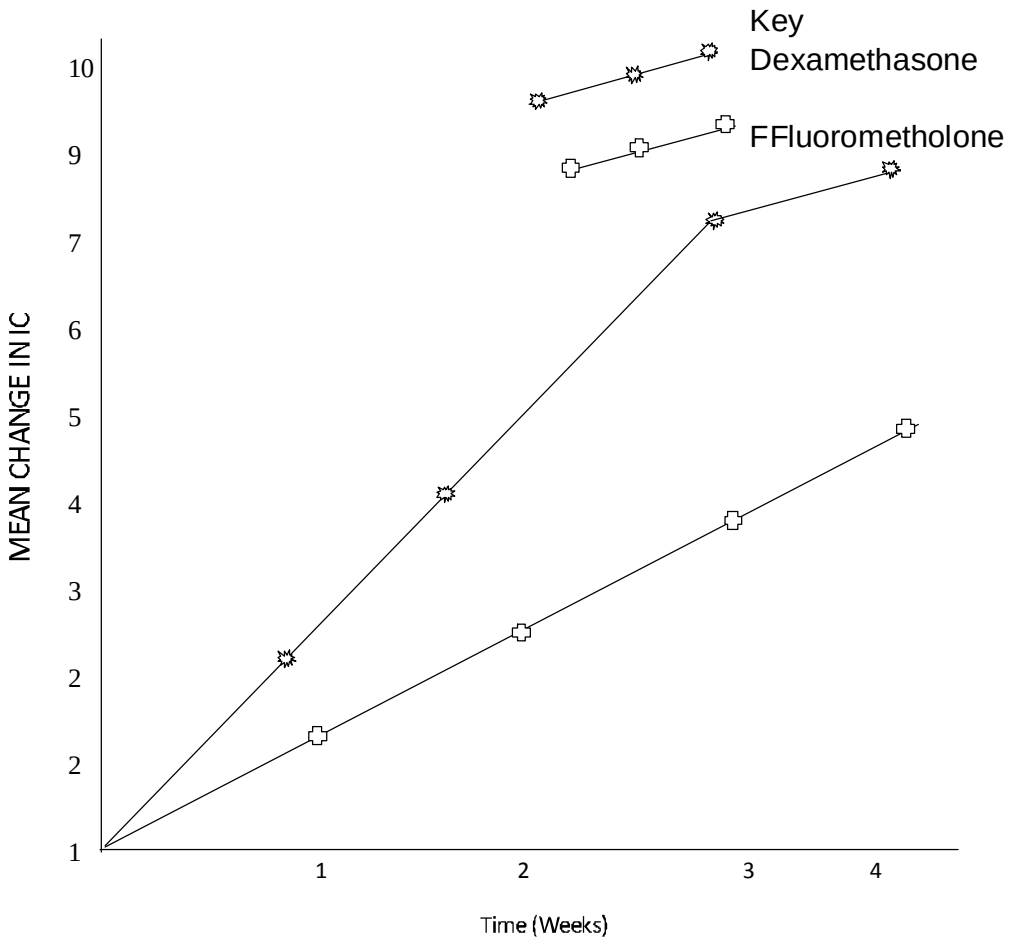

FIG. 1: MEAN CHANGE IN IOP IN WEEKS FOR DEXAMETHASONE AND FLUOROMETHOLONE

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