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Effect of Topical 1% Pilocarpine on the Ocular Tear Film pH

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Abstract

Ocular tear film pH contributes to the health and function of the anterior ocular tissues. Pilocarpine is a cholinergic drug used for the management of angle closure glaucoma. This study was carried out to investigate the effect of 1% pilocarpine on the tear film pH. A total of 84 glaucoma patients were examined at the Optometry Teaching Clinic, Federal University of Technology, Owerri, Nigeria. Ocular examination included taking the case history, visual acuity, visual field assessment, ophthalmoscopy, slit lamp biomicroscopy, intraocular pressure measurement and tear film pH measurement using sterile pH strips. The base line tear film pH was taken first. Then one drop of pilocarpine 1% was instilled into the eye and the tear film pH was measured 4 hours later and measured again after 24 hours. Results showed that before pilocarpine instillation, 16 (19.05%) of the subjects had a tear film pH between 6 and 6.9; 60 (71.43%) between 7 and 7.9; 8 (9.52%) between 8 and 8.9. After 4 hours of pilocarpine instillation, 22 (26.19%) had a pH between 5 and 5.9; 48 (57.14%) between 6 and 6.9; 14 (16.67%) between 7 and 7.9. Twenty-four hours after instillation of pilocapine, 16 (19.05%) had a pH between 6 and 6.9; 62 (73.81%) between 7 and 7.9; 6 (7.14%) between 8 and 8.9. The mean pH value before instillation of pilocarpine was 6.98±0.51. After 4 hours, the mean value became 6.14±0.57 and 6.95±0.48 after 24 hours. SPSS data analysis using the Paired sample T-test at 0.05 level of significance showed that 1% pilocarpine (1%) had a significant change (P<0.05) on the tear film pH. Eye care professionals who prescribe pilocarpine are advised to monitor the tear film pH values of their patients.

Keywords: Tear film, pH, Pilocarpine, Intraocular pressure, glaucoma

Introduction

In chemistry, pH is a logarithmic scale used to specify the acidity or basicity of an aqueous

solution[1]. At 25 °C, solutions with a pH less than 7 are acidic and solutions with a pH greater than 7 are basic. The neutral value of the pH depends on the temperature, being lower than 7 if the temperature increases. Pure water is neutral with a pH of 7 at 25 °C, being neither an acid nor a base[2]. The tear film is the fluid covering the cornea and conjunctiva. It is also called the pre-corneal film[3]. The tear film is responsible for providing a smooth refractive surface for clear vision, maintaining the health of the corneal and conjunctival epithelia and acting as the first line of defense against microbial infections. The tear film composition is dynamic and is in a constant state of flux responding to environmental conditions in other to maintain ocular surface homeostasis[4].

The pH of the tear fluid is one of its physico-chemical properties that contribute to the health and function of the anterior ocular tissues. Although fluctuations in the normal pH of the pre-ocular tear fluid have been noted[5], this fluid usually maintains a relatively stable pH environment for the anterior ocular tissues. The tear pH has a broad spectrum of values. Even with the exclusions of disease conditions, a span of a pH 5.2- 8.6 has remained. The tear pH has a population average of 7.45[6]. The tear pH tends to shift towards the alkaline side as the day progresses but is more acidic following prolonged eye closure as seen during sleep.

Chemical agents with the potential to reduce or increase the tear film pH are often found at home, at work or in the environment[7]. Damage from pH changes is usually limited to the front segment of the eye including the cornea. Each ocular structure responds uniquely to a chemical insult with different manifestations of signs and symptoms[8]. Acidic pH causes less harm to the ocular surface when compared to alkaline pH. This is because acids precipitate the tissue proteins thereby creating a barrier that shields the eye from much damage[9].

Severe reduction in tear film pH by acids can cause shortening of collagen fibres of the cornea and sclera causing a contraction of the eyeball and an increase in intra ocular pressure. Alkaline tear pH can increase IOP due to accumulation of inflammatory debris within the trabecular meshwork[10]. When the eye comes in contact with pH reducing agents, these agents react with the water in the aqueous portion of the tear film producing heat. This heat can also affect the corneal and conjunctival epithelium[8]. Low or high tear pH can destroy the conjunctival goblet cells leading to a reduction or even absence of mucus in the tear film thereby compromising the proper

dispersion of tear film over the ocular surface. This results in kerato-conjunctivitis sicca (dry eye). This can cause an increase in flourescein staining scores and decreased schirmer scores[11].

Eye drops are saline-containing drops that rely on absorption through the epithelium of the conjunctival sac to produce their effects[12]. Eye drops sometimes do not have medications in them and are only lubricating and tear-replacing solutions. Desirable local effects within the eye can be achieved without causing systemic side effects. Some systemic absorption from the eye occurs, however and can result in unwanted effects. Eye drops commonly used in clinics do have varying pH values. The use of such drops in the initial management of chemical eye injury may influence the accuracy of pH measurement of the eye, and subsequently influence its management. Pilocarpine is a cholinergic drug used in the management of angle closure glaucoma. Its onset of action is rapid. Peak effect occurs between 30-60 minutes and lasts for 4 to 8 hours[13]. Occasionally drug resistance can develop which is reversible. Ocular side effects are common with pilocarpine and can interfere with the patient's quality of life and compliance with recommended therapy. Superficial punctate keratitis is the most troublesome acute toxic effect of pilocarpine. Other side effects include ciliary muscle spasm which can lead to brow ache, induced myopia and miosis[14]. The pH of pilocarpine eye drops ranges from 3.5 to 5.5[13]. The objective of this study is to investigate the effect of pilocarpine eye drop on the tear film pH.

Materials and Methods

This study was a clinical study carried out at the Optometry Teaching Clinic, Federal University of Technology, Owerri, Nigeria. Patients who were diagnosed of primary open angle or closed angle glaucoma were used for this study. Ethical approval for this study was obtained from the ethical committee of School of Health Technology, Federal University of Technology, Owerri, Nigeria. An informed consent was also obtained from the subjects who participated in the study. Examination procedures included taking the case history, visual acuity, visual field assessment, ophthalmoscopy, slit lamp biomicroscopy and intraocular pressure measurement using Perkins applanation tonometer. The tear film pH was measured using sterile pH strips. The base line tear film pH was taken first. One drop of pilocarpine 1% was instilled into the eye and the tear film pH was measured 4 hours after application of pilocarpine. This is the peak concentration time of

the drug. The tear film pH was also measured again after 24 hours.

Results

A total of 84 glaucoma patients were used for the study. Table 1 showed the age distribution of the subjects. There were 4 (4.76%) people between the ages of 21 and 30 years; 19 (22.62%) between 31 and 40; 32 (38.10%) between 41 and 50; 23 (27.38%) between 51 and 60; and 6 (7.14%) between 61 and 70. The intraocular pressure (IOP) was measured on both eyes of the 84 subjects (168 eyes). Out of this number, 62 (36.90%) eyes had an IOP between 11 and 20 mmHg; 97 (57.74%) between 21 and 30; 6 (3.66%) between 31 and 40; 2 (1.22%) between 41 and 50; and 1 (0.61%) between 51 and 60 mmHg (table 2). The pH of the 1% pilocarpine eye drop was measured with the pH strip and found to be 4.5. The base line tear film pH was taken before instillation of pilocarpine. Sixteen (19.05%) of the subjects had a tear film pH between 6 and 6.9; 60 (71.43%) between 7 and 7.9; 8 (9.52%) between 8 and 8.9. After 4 hours of pilocarpine instillation, 22 (26.19%) had a pH between 5 and 5.9; 48 (57.14%) between 6 and 6.9; 14 (16.67%) between 7 and 7.9. Twenty-four hours after instillation of pilocapine, 16 (19.05%) had a pH between 6 and 6.9; 62 (73.81%) between 7 and 7.9; 6 (7.14%) between 8 and 8.9 (table 3). Table 4 showed that the mean value before instillation of pilocarpine was 6.98 with a standard deviation of 0.51. After 4 hours, the mean value became 6.14 with a standard deviation of 0.57. After 24 hours, the mean value was 6.95 with a standard deviation of 0.48. From SPSS version 21 data output, data analysis using the Paired sample T-test at 0.05 level of significance and 95% confidence interval revealed a P value of 0.00. Since P (0.00) < 0.05, the null hypothesis is rejected and the alternative is accepted. Thus, pilocarpine (1%) had a significant change on the tear film pH.

Table 1: Age distribution of glaucoma subjects

Age group	n	%
21 – 30	4	4.76
31 – 40	19	22.62
41 – 50	32	38.10

51 – 60	23	27.38
61 – 70	6	7.14
Total	84	100.00

Table 2: Distribution of Intraocular Pressure of glaucoma subjetcts

Intraocular Pressure (mmHg)	**n**	**%**
11 – 20	62	36.90
21 – 30	97	57.74
31 – 40	6	3.66
41 – 50	2	1.22
51 – 60	1	0.61
Total	168	100.00

Table 3: Tear film pH distribution of glaucoma subjects before and after administration of Pilocarpine (1%)

pH	**Before**		**After 4 hours**		**After 24 hours**	
	n	**%**	**n**	**%**	**n**	**%**
5 – 5.9	0	0.00	22	26.19	0	0.00
6 – 6.9	16	19.05	48	57.14	16	19.05
7 – 7.9	60	71.43	14	16.67	62	73.81
8 – 8.9	8	9.52	0	0.00	6	7.14
Total	84	100.00	84	100.00	84	100.00

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Table 4: Descriptive Statistics of tear film pH values with instillation of Pilocarpine (1%)

Time	n	Min. value	Max. value	Mean	Std. Dev.
Before	84	6	8	6.98	0.51
After 4 hours	84	5	7	6.14	0.57
After 24 hours	84	6	8	6.95	0.48

*N = Number; Min = Minimum; Max = Maximum; Std. Dev. = Standard Deviation

Discussion

Primary open angle glaucoma is an ocular disorder that does not present with any symptoms that would alert the patient to the problem, rather it will quietly reduce the visual acuity and visual field of the patient until total blindness ensues. Primary open angle glaucoma manifests at any age and an increasing number of cases are being observed in juveniles and young adults[15]. Table 1 showed over 28% of the glaucoma cases were people below 40 years. At this age, the intraocular pressure may be high but no serious damage has occurred to the eye. When diagnosed at this age, the patient can enjoy normal vision for the rest of their life as long as they take their anti-glaucoma medications and pay regular follow-up visits to the eye clinic in order to monitor their intraocular pressure.

An elevated intraocular pressure remains the known cause of optic nerve damage which occurs in glaucoma[16]. This means that by constantly keeping the intraocular pressure within normal levels, the glaucoma patient is expected to live a healthy life. For patients who do not take regular medications, their visual acuity and visual field begin to reduce and when they get to middle or late adulthood, the disease has progressed so much that they eventually go blind or become low vision patients. Azuamah, et al.[17] reported glaucoma as making up 23% of the causes of low vision and blindness and over 99% of them were from 40 years and above. Studies[18,19] have shown that most cases of visual field loss from glaucoma manifests in people above 40 years. Table 1 showed that most of the glaucoma patients were above 40 years and from this study, these people had poorer vision than the younger ones. Age is obviously a risk factor as reported by Esenwah et al.[20] in a study on the aging eye. Anti-glaucoma drugs aim at controlling the intraocular pressure of the eye and this is the goal of eye care professionals when managing the disease. Table 2 showed that over 60% of the glaucoma patients had an IOP over 21mmHg. Most of these patients only became aware of their condition for the first time. Others

were aware and were previously on anti-glaucoma medication, though they admitted that they have not gone for check-up in a while. Without their medication, their vision and visual field will deteriorate and this could lead to blindness.

Pilocarpine is a direct-acting cholinergic drug that reduces IOP by enhancing aqueous outflow[21]. The drug is usually not the first drug of choice by Optometrists in reducing IOP because it causes miosis. Prolonged usage of the drug can result in permanent miosis. When prescribed, most Optometrist combine it with another topical drug or with a systemic anti-glaucoma drug. Table 4 showed that after 4 hours of pilocarpine administration, the mean tear film pH reduced from 6.98 to 6.14. It then increased back to 6.95 after 24 hours. The reduction in pH values after the peak period of 4 hours was found to be statistically significant ($P<0.05$) when analyzed using the Paired sample T test (table 4.28). Longwell, et al.[22] reported changes in tear film pH within 1 hour of pilocarpine instillation. Pilocarpine has localized side effects such as brow aches, accommodative spasms and reduced vision secondary to miosis.

In conclusion, pilocarpine eye drop significantly reduces the tear film pH when instilled into the eye. However, the pH gradually returns to its normal within 24 hours. Pilocarpine therefore should not be used for long term treatment of glaucoma. In addition to causing miosis, it can disrupt the normal pH levels and shift it toward increased acidity. Eye care professionals who prescribe pilocarpine should monitor the tear film pH values of their patients.

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