Original Article

Brimonidine in Reducing Peroperative Bleeding in Pterygium Surgery

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Abstract

Objective: To assess efficacy of brimonidine 0.2% in the control of per-operative bleeding in pterygium surgery. **Methodology:** This quasi-experimental study was conducted was in the department of Cornea, National Institute of Ophthalmology from January, 2019 to December, 2020 on 196 diagnosed patients of primary progressive pterygium. They were grouped into group-A (experimental group-brimonidine 0.2% used as per-operative bleeding control agent) and group-B (control group- only pressure was applied to control per-operative bleeding). Patients were selected based on specific selection criteria. Selected patients underwent detail ocular and systemic evaluation as well as relevant investigations. Excision of pterygium with conjunctival limbal autograft was done in all patients by a single competent surgeon. In patients of group A, topical brimonidine 0.2% were applied 3 times prior to surgery (15 minutes, 10 minutes and 5 minutes prior to surgery). Per-operative bleeding was quantified by counting the number of micro-sponges (weck cel) used. Grading of haemorrhage was done based on number of microsponge used during surgery and grouped into Grade-I, where 1-3 microsponge used per-operatively to control bleeding, grade-II where 4-6 microsponge used per-operatively to control bleeding and Grade-III, where 1-3 microsponge used per-operatively to control bleeding. **Results:** Mean age of patients were 40.6±10.2 (SD) years in group-A and 39.8±13.22 (SD) years in group-B respectively. Out of 98 patients in group A, 61.2% were male and 38.8% were female and in group B, 63.3% were male and 36.7% were female. In group-A, 60(61.3%) patients belong to grade-I, 22(22.4%) patients belong to grade-II, 16(16.3) patients belong to grade-III. In group-B, 28(28.6%) patients belong to grade-I, 34(34.7%) patients belong to grade-II, 36(36.7%) patients belong to grade-III. In group-A and B, mean operation time were 15.5±0.99 (SD) min. and 22.3±1.77 (SD) minutes respectively(p value <0.001). In group-A, the mean pre-operative value of IOP was 15.04±1.46 (SD) mm of Hg and at the end of surgery, 13.6±2.02 (SD) mm of Hg (p value >0.06). In group-B, the mean pre-operative value of IOP was14.94±1.81 mm of Hg and at the end of surgery, 14.6±1.62 (SD) mm of Hg (p value >0.076). **Conclusion:** Analysis of the study findings shows that topical brimonidine 0.2% significantly reduces per-operative bleeding in pterygium surgery without affecting IOP.

Keywards: Brimonidine 0.2%, Per-operative bleeding, Pterygium surgery

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Background:

Pterygium is a triangular fibrovascular sub-epithelial in growth of degenerative bulbar conjunctival tissue over the limbus on to the cornea (Taylor, 1992). Its three parts are apex or head, body and tail. Pterygium may lead to reduction of visual acuity either because of induced astigmatism or encroachment onto the visual axis, marked cosmetic deformity, marked discomfort and irritation unrelieved by medical management, limitation of ocular motility secondary to restriction, or documented progressive growth toward the visual axis and ultimately loss of vision. Prevalence of pterygium ranges from 0.7% to 31% in various populations around the world, and the condition is more common in warm, dry climates (Tasman and Jaeger, 2002). A leading theory proposes that the increased prevalence of pterygium among people in equatorial regions is due to the damaging effects of ultraviolet radiation,

specifically UV-B radiation. The working hypothesis is that this radiation causes mutations in the p53 tumor suppressor gene, thus facilitating the abnormal proliferation of limbal epithelium (Ang, Chua and Tan, 2007).

Treatment of pterygium is medical and surgical, medical treatment only for symptomatic improvement. For further consequences, surgical intervention is required . There are numerous modalities of surgical approaches are practiced[2,3,4,5] according to the method of excision and the method of dealing with the defect created. After excision, the resulting defect can be left exposed (bare sclera excision)[6,7] or covered by surrounding conjunctiva (primary closure) or a pedicle flap[5,6,7] or by transposition of the pterygium head. The defect can also be covered by a conjunctival autograft without the limbus or with the limbus or using other tissue sources such as buccal mucous membrane grafts, lamellar keratoplasty, penetrating keratoplasty or sclerokeratoplasty. The other techniques include yttrium–aluminium–garnet (YAG) laser treatment and a polishing technique as advocated by Barraquer[8,9,10,11,12,13]

Most commonly encountered problem during pterygium surgery is bleeding. Source of which is from episcleral and conjunctival vessels. Commonly practiced measure to control per-operative hemorrhage is use of cautery (Ball or bipolar electric) and application of adrenaline-soaked micro-sponge. Adrenaline controls bleeding by its vaso-constrictive properties, but it has some adverse effects as it absorbed systemically via the nasopharyngeal mucosa and can cause cardiovascular side effects such as tachycardia and increased in blood pressure. These effects may deteriorate the physical condition of patients with cardiovascular risk factors. On the other hand, adrenaline can cause mydriasis (via α1a receptor) and mild inhibition of accommodation (via β2 receptor) which may lead to angle closure glaucoma.

For effective and optimum surgical outcome proper visualization is mandatory during operation, which is often hampered due to per-operative bleeding in pterygium surgery. Considering the unwanted side effects of topical adrenaline, brimonidine is being used in many centers in the world for control of per-operative hemorrhage in different ocular surgery such as pterygium, strabismus etc.

Brimonidine is a selective α 2-adrenergic agonist that has been widely used to lower intraocular pressure in glaucoma patients. Brimonidine induces conjunctival blanching and this has been used in cataract, laser refractive and glaucoma filtration procedure. It has supposed to have vaso-constrictive property..

Topical brimonidine is used successfully in some parts of the world in control of per- operative bleeding in strabismus surgery and small incision cataract surgery[14]. This study was done to explore the efficacy of topical brimonidine as an agent to control Preoperative bleeding in pterigium surgery.

Study procedure: This study was conducted was in the department of Cornea, National Institute of Ophthalmology on 196 diagnosed patients of primary progressive pterygium. Patients were selected based on specific selection criteria. Those who had been suffering from other intraocular or ocular surface disease, uncontrolled diabetes a, hypertension or other systemic diseases, known patient of bleeding disorder, taking anti-platelet or blood-thinner agents, having history of ocular surgery or trauma in the previous six months were excluded from the study. Selected patients underwent detail ocular and systemic evaluation as well as relevant investigations. They were grouped in to group-A (experimental group-whom brimonidine 0.2% used as per- operative bleeding control agent) and group-B (control group- whom only pressure was applied to control per-operative bleeding). Excision of pterygium with conjunctival limbal autograft was done in all patients by a single competent surgeon. In patients of group A, topical brimonidine 0.2% were applied 3 times prior to surgery (15 minutes, 10 minutes and 5 minutes prior to surgery). Per-operative bleeding was quantified by counting the number of micro-sponges (weck cel) used and were compared between two groups and analyzed statistically to assess the level of significance. All the relevant data were recorded in a pre-designed data collection sheet.

Results were presented by appropriate tables and figures.

Statistical analysis:

Data were processed by using window software SPSS program version 25. Descriptive analysis was presented by frequencies or percentages for qualitative values and mean (± SD) for quantitative values with normal distribution. Inferential analysis was done by paired t-test, unpaired t-test and chi-square test as applicable. At 95% CI, p-value < 0.05 was considered as significant.

Results and observations

Table 1: Socio-demographic distribution

		Group-A (n=98)	Group-B (n=98)	p-value*
Age		40.6±10.27	39.8±13.22	0.724a
Gender distribution	Male	60(61.2%)	62(63.3%)	0.924b
	Female	38(38.8%)	36(36.7%)	

ns=not significant, p value obtained by a= unpaired t rest and b= chisquare test.

Table 1 shows that there is no significant statistical difference between the group A and group B regarding age and gender (p value > 0.05)

Distribution of grading of haemorrhage

Table-2: Distribution of grading of haemorrhage (based on number microsponge used) of the study subjects

Grading	Group-A	Group-B	p value
Grade-I (1-3 microsponge)	60(61.2%)	28 (28.6%)	
Grade-II (4-6 microsponge)	22 (22.4%)	34 (3474%)	<0.001s
Grade-III (7-9 microsponge)	16 (16.3%)	36 (36.7%)	

s= significant, p value obtained by $\chi 2$ test

Table-2 shows grade 1 bleeding was significant more in group A compared to group B (p value <0.001).

Distribution of mean duration of haemorrhage

Table-3: Distribution of mean duration of per-operative haemorrhage (in minutes) of the study subjects

Group-A	Group-B	p value
3.4±0.87 min.	5.8±1.31 min.	<0.001[s]

s= significant, p value obtained by unpaired t test

Table-3 shows the distribution of mean duration of per-operative haemorrhage (in minutes) of the two groups. In group-A (experimental group) the mean duration of per-operative haemorrhage was 3.4±0.87 (SD) minutes. and in group-B (control group) mean operation time was 5.8±1.31 (SD) minutes (p value < 0.001).

Distribution of mean operation time

Table-4: Distribution of mean operation time (in minutes) of the study subjects

Group-A	Group-B	p value
15.5±0.99 min.	22.3±1.77 min.	<0.001[s]

s= significant, p value obtained by unpaired t test

Table-4 shows the distribution of mean operation time (in minutes) of the two groups. In group-A mean operation time was 15.5±0.99 (SD) min. and in group-B mean operation time was 22.3±1.77 (SD) min (p value <0.001).

Table-5: Distribution of changes of mean IOP of the study subjects

	Pre-operative mean IOP	Mean IOP at the end of surgery	p value
GroupA	15.04±1.46	13.64±2.02	0.066
Group B	14.94±1.81	14.32±1.62	0.762

ns= non-significant, p value obtained by paired t test, IOP was measured in mm of Hg

Table-5 shows the distribution of changes of mean IOP between pre-operative value and at the end of surgery. In group-A, the mean pre-operative value of IOP was 15.0±1.46 (SD) mm of Hg and 13.6±2.02 (SD) mm of Hg at the end of surgery. In group-B, the mean pre-operative value of IOP was 14.94±1.81 mm of Hg and 14.64±1.62 (SD) mm of Hg at the end of surgery (p value >0.005).

Discussion

Pterygium is a proliferative, fibrovascular disease that extends from the conjunctiva to the cornea, showing prominent vascularity. It is treated with steroid and artificial tear eye drops, but if it affects vision, it is excised surgically (American Academy of Ophthalmology, 2009; Liu et al., 2013). Brimonidine tartrate, which is a selective alpha-2 adrenergic receptor (AR) agonist, is used for ocular hypertension and glaucoma. It decreases aqueous humor production and increases uveoscleral outflow. In decreased concentration brimonidine causes conjunctival whitening (blanching) and reduces bleeding; for this reason, it is used in intravitreal injections and ophthalmic surgeries (Derick et al., 1997; Adkins and Balfour, 1998; Annegret H. Dahlmann-Noor et al., 2009; Mamun Q. Rahman, Ramaesh and Montgomery, 2010). Its affinity to α-2 receptors is 790-fold more than to that of α-1 receptors. Now a day's, topical brimonidine is used as an agent to control haemorrhage in many ocular surgeries. This study was designed to evaluate the efficacy of topical brimonidine as an agent to control per-operative bleeding during pterygium surgery.

In the present study, regarding age distribution mean age of patients was 40.6 in group A and 39.8 in group B. Similar observations were made by Rohatgi et al, Viso et al. and Yoon et al. showing that, prevalence of pterygium increases with advancement of age (Viso, Gude and Rodríguez-Ares, 2011; Yoon et al., 2011; Rohatgi, 2013)

In this study males (61.0%) were affected more than females (39.0%). Among cases the frequency of male was 60% and among control it was 62.0%. Higher incidence in males is due to more exposure to dust, wind, heat and sun to which they are exposed while outdoor activities for their livelihood and the chief factor in the etiology was exposure to atmospheric irritants leading to chronic irritation of the conjunctiva (Rohatgi, 2013). Rajiv et al. had also found that pterygium was most commonly seen in males 64.29% as compared to females 35.71% (Rajiv, Mithal and Sood, no date). Similar observations were made by Saleem et al. in their study of 120 patients where 79.16% were males and only 20.84% were females (Saleem, Muhammad and Islam, 2004).

In this study, per-operative haemorrhage was measured qualitatively by counting the microsponge (Omni sponge 2/5) used to control haemorrhage. In group-A, 61.2% (60) patients belongs to grade-I, 22.4% (22) patients belongs to grade-II and 16.3% (16) patients belongs to grade-III and in group-B, 28.6% (28) patients belongs to grade-I, 34.7% (34) patients belongs to grade-II and 36.7% (36) patients belongs to grade-III. The quantity of microsponge used per-operatively in two groups were compared statistically and were found significant. Study done by Fikret Ucar and Servet Cetinkaya, 2020 observed that the vasoconstriction effects of topical brimonidine tartrate on surface vessels. The surface area of blood vessels was reduced 60% within 5 min; this effect was observed with the help of Photoshop and ImageJ programs and it lasted for 20 min. The surgery lasts for 7 min, on average, so the conjunctival whitening formed by brimonidine tartrate provides a safe and comfortable operative area throughout the surgery. This finding supports the present study findings.

Moreover, brimonidine is used a bleeding control agent in different ophthalmic surgical procedure in different concentrations. Study done by Samin Hong , Chan Yun Kim, Gong Je Seong and Sueng-Han Han on 2007 to investigate the effects of preoperative brimonidine-purite 0.15% instillation on intraoperative bleeding and postoperative subconjunctival hemorrhage during strabismus surgery in adult patients. In this study, one hundred and eighteen eyes of 90 consecutive adult patients were instilled with either a single drop of brimonidine-purite 0.15% (42 eyes), phenylephrine 1% (38 eyes), or sodium hyaluronate 0.1% (38 eyes) 15 minutes prior to strabismus surgery. Intraoperative bleeding and postoperative subconjunctival hemorrhage were graded on a scale of one to three. The scores were compared among the study groups. Scores of the intraoperative bleeding and the postoperative subconjunctival hemorrhage of the treatment groups were significantly less than that of the control group ($p < .001$). The scores of the

brimonidine group were similar to those of the phenylephrine group (intraoperative bleeding score, p = 0.405; subconjunctival hemorrhage score, p = 0.722). Another study done by Sang Beom Han and Jeong-Min Hwang published on 2021 to investigate the effects of topical brimonidine 0.15% instillation on conjunctival injection after strabismus surgery in children. This study was conducted on 63 Korean children who underwent strabismus surgery for intermittent exotropia. Patients received topical brimonidine 0.15% after surgery for up to 4 weeks. Conjunctival injection was objectively assessed using a software that automatically scored the region of interest from the image of the bulbar conjunctiva. Conjunctival injection scores were compared with those of the control group who were not prescribed topical brimonidine. The mean scores of conjunctival injection after rectus muscle recession and resection were significantly lower in the brimonidine group than the controls at 4 weeks after surgery (respectively). There was no significant difference in intraocular pressure between the two groups. No adverse effects, such as dry mouth, fatigue/drowsiness, headache, sedation, hypotension, or bradycardia, were reported. Administration of topical brimonidine 0.15% after strabismus surgery is efficacious and safe in reducing postoperative conjunctival injection.

The mean pre-operative IOP (intra-ocular pressure) in group-A was 15.0±1.46 (SD) mm of Hg and group-B was 14.9±1.81 (SD) mm of Hg and mean post-operative IOP (intra-ocular pressure) in group-A was 13.6±2.02 (SD) mm of Hg and group-B was 14.3±1.6 (SD) mm of Hg. Brimonidine is commonly used as anti-glaucoma agents to lower IOP. In this study though the mean IOP is reduced in study group, it was statistically non-significant to IOP.

Mean operation time between group A and group B were 15.5±0.99 min and 22.3±1.77 min, this difference is significant statistically ($p<0.001$). Ucar et al in their study entitled “The Results of Preoperative Topical Brimonidine Usage in Pterygium Surgery” showed similar findings (Ucar and Cetinkaya, 2020b). They stated that, application of brimonidine before surgery causes reduction of surface area of blood

vessel by 60% within 5 minutes which causes conjunctival whitening that provides safe and comfortable operative area throughout the surgery (Ucar and Cetinkaya, 2020b).

Per-operative haemorrhage often hampers quality of surgery as well as causes wastage of time especially in microsurgery like excision of pterygium followed by conjunctival autograft. Proper agent should be looked for which control per-operative bleeding with minimum adverse effects. Topical brimonidine may be a choice for control of bleeding.

Conclusion

Analysis of the study findings shows that topical brimonidine significantly reduces per- operative bleeding in pterygium surgery without significantly influences on intra- ocular pressure.

Limitations

Long-term IOP reducing effects were not studied, Influence on recurrence rate of pterygium was not compared between two groups and Study was done in only in primary progressive pteygium, the efficacy on other types of pterygium were not studied.

Recommendations

Long term follow-up should be done to compare the recurrence rate and Study should be done in all forms of pterygium to draw global conclusion about the efficacy of the drug in controlling per-operative haemorrhage.

Conflict of interest: Nothing to declare

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