

## Effect of Oral Clonidine on Acute Intraocular Pressure rise after cataract Extraction under General Anaesthesia

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### Abstract

**Objective:** To evaluate the efficacy of preoperative oral clonidine (5 g/kg) in preventing ocular hypertension in the early period after cataract surgery with posterior chamber intraocular lens implantation under general anaesthesia.

**Methods:** This was a randomized double-blind clinical trial comprising of 62 eyes in 62 patients with senile cataract without using any viscoelastics. They were randomly assigned into two groups for preoperative oral clonidine (5 g/kg) and placebo. Intraocular pressure (IOP) was measured 6, 12 and 24 hours postoperatively.

**Results:** Mean differences of IOPs at 6 and 12 hours after surgery were significantly lower in clonidine group [+0.41 4.55(p=0.612), 0.06 3.62(p=0.922)] than placebo group [5.77 4.25 (p=<0.001), 4.70 3.19p<0.001)] but was more than preoperative intraocular pressures in both. There was no statistically significant difference between the mean IOP 24hours post operatively in the two groups. But compared to preoperative IOP less increase in mean IOP was seen in clonidine group when compared to placebo group.

**Conclusion:** A single dose of oral clonidine (5 g/kg) preoperatively can produce a significant IOP-lowering effect in early period after cataract surgery, specially in the first 12 hours.

**Keywords:** Clonidine, Intraocular pressure, Cataract. (JPMA 62: 1285; 2012)

## Introduction

Transient elevation of intraocular pressure (IOP) following cataract extraction is a well-recognized complication.<sup>1</sup> The mechanisms causing this problem are multifactorial. Maximum IOP rise usually occurs between 6 and 8 hours after surgery.<sup>1</sup> The important sequelae of this complication are central retinal artery obstruction (CRAO) and Ischaemic optic Neuropathy.<sup>2</sup> There is more optic nerve damage in glaucomatous eyes,<sup>3</sup> post-operative ocular pain,<sup>4</sup> and corneal oedema.<sup>5</sup>

There are no general agreements about expected IOP after cataract extraction<sup>6</sup> but many, though not all, use ocular hypotensive agents at the time of cataract surgery to prevent or lessen IOP increase. However, there is no standard accepted regimen, and the results reported in the literature have been contradictory.<sup>4</sup>

Clonidine is prototype of  $\alpha_2$  agonist adrenergic drugs. It can reduce intra-ocular pressure (IOP) and attenuates the increase in IOP after ophthalmologic procedures as pre-operative medication, because clonidine is able to decrease IOP via multiple mechanisms such as laryngoscopy and tracheal intubation.<sup>7</sup>

This study was done to evaluate the ocular hypotensive effect of clonidine after cataract surgery.

## Patients and Methods

This consort study comprised of 62 eyes in 62 patients according to block randomization scheduled for conventional extracapsular cataract extraction with posterior chamber intraocular lens implantation (ECCE PCIOL) under general anaesthesia. No viscoelastic material was used during surgery.

The sample size was calculated using the formula:

$$(Z_1 - \alpha/2 + Z_1 - \beta)2 (S_1^2 + S_2^2) / (m_1 - m_2)^2 = \text{for each group } 31.$$

$Z_1 - \alpha/2 = 1.96$ ,  $Z_1 - \beta = 0.67$ ,  $S_1 = 2.76$ ,  $S_2 = 1.34$ ,  $M_1 = 13.66$ ,  $M_2 = 15.01$ , Power: 75% (26,27).

Ophthalmic exclusion criteria were history of any ocular trauma and surgery, pseudoexfoliation syndrome, pigment dispersion syndrome, uveitis, glaucoma, usage of viscoelastic material during surgery and the duration of operation more than one hour. Systemic exclusion criteria were hypertension, diabetes, chronic obstructive pulmonary disease (COPD), any opioid addictions, clonidine contraindications and change of anaesthetic protocol during surgery.

The patients in each group were randomly assigned to receive clonidine tablets 5  $\mu\text{g}/\text{kg}$  (31 patients) or placebo (31 patients) two hours before surgery. All patients were operated by the same surgeon who was masked to treatment

assignment. All patients were operated under general anaesthesia by the same technique. Indication of general anaesthesia was requested by the patient due to phobia of surgery. Surgical incision was secured by 5 interrupted 10-0nylon sutures. The baseline IOP was measured by Goldman applanation tonometer 1 day before surgery. The IOP was measured with the same Goldman applanation tonometer (mean measurement calculated from 90 and 180 degree of applanation surface axis) 6, 12 and 24 hours after operation by the surgeon himself. If measured IOP was more than 21 mmHg, an antiglaucoma agent was given, first with timolol maleate 0.5% twice daily. If this could not control the IOP then systemic acetazolamid and other ocular hypotensive drugs were prescribed.

ANOVA was used to compare preoperative and postoperative IOP between and in groups by using SPSS version 17 package.

## Results

Sixty-two eyes of 62 patients were included in this randomized clinical trial study. There was no significant difference in mean age and gender distribution between clonidine and placebo groups (Table-1).

Table-2 shows the mean preoperative and postoperative IOPs 6, 12 and 24 hours after surgery in both groups. At 6 hours after operation there were significant difference between mean IOPs in clonidine group: 13.61 4.09 and placebo group. However there was no significant difference ( $p=0.539$ ) in clonidine group 15.41 3.96 and placebo group 16.00 3.41 at 24 hours post operation.

**Table-1: Mean age and gender distribution of clonidine and placebo groups.**

	No of cases	Mean age in years	P-value
Group 1 (Placebo)	31	66.12±8.03	0.883
Group 2 (Clonidine)	31	64.19±7.59	
Total		Female	Male
Group 1 (Placebo)	31	13	18
Group 2 (Clonidine)	31	13	18
Total	62 (100%)	26 (41.9%)	36 (58.1%)

**Table-2: IOPs in Clonidine and placebo groups.**

Time	Group1 (Placebo) Mean±SD	Group2 (Clonidine) Mean±SD	P value (t student test)
Preoperative IOP	12.19±1.88	14.03±2.42	0.001
Postoperative IOP:			
6h	17.96±5.49	13.61±4.09	0.001
12h	16.90±4.11	13.96±3.25	0.003
24h	16.00±3.41	15.41±3.96	0.539

IOP: Intraocular Pressure.

**Table-3: Mean difference of postoperative IOP changes in Clonidine and placebo groups.**

Change of IOP	Mean difference	P Value (Paired t test) value
6hours post.op to preop.	G1*= $5.77 \pm 4.25$ G2**= $0.41 \pm 4.55$	<0.001 (0.612)
12hours post.op to preop	G1= $4.70 \pm 3.19$ G2= $0.06 \pm 3.62$	<0.001 (0.922)
24hours post.op to preop.	G1= $3.80 \pm 2.92$ G2= $1.38 \pm 4.64$	<0.001 (0.107)
12hours to 6hours post.op.	G1= $1.06 \pm 4.65$ G2= $-0.35 \pm 2.47$	0.213 (0.430)
24hours to 12hours post.op	G1= $0.90 \pm 2.37$ G2= $1.45 \pm 2.27$	0.042 (0.001)

\* G1= Group 1 (Placebo)

\*\* G2=Group 2 (clonidine).

Table-3 shows postoperative mean IOP changes at 6,12 and 24 hours compared to each other and with preoperative IOP. In placebo group at 6, 12 and 24 hours postoperative there was a significant rise ( $P < 0.001$ ) compared to preoperative IOP. From 6 to 12 hours postoperative no significant change occurred ( $P = 0.213$ ) and from 12 to 24 hours postoperative, it was significant ( $P = 0.042$ ).

In clonidine group, at any time after surgery no significant IOP rises occurred compared to preoperative IOPs. From 6 to 12 hours no meaningful change was seen. However, 12 to 24 hours after surgery, there was significant increase in mean IOPs ( $P = 0.001$ ). Therefore, preoperative oral clonidine prevented IOP increase after cataract extraction surgery efficiently. This effect was prominent especially during 12 hours after operation.

In placebo group, 8 cases (25.8%) and in clonidine group 3 cases (9.7%) had postoperative IOP greater than 21mmHg and hypotensive agents were given to them. There was no significant statistical difference between the two groups ( $P = 0.09$ ). Patient's need for Hypotensive agents in clonidine group was less than placebo group.

In clonidine group all 3 patients were controlled by one drug (Timolol maleate 0.5%, bid) but in placebo group only 2 patients required one drug (Timolol maleate 0.5%, bid). Six patients required two drugs (Timolol maleate 0.5%, bid and oral Acetazolamide 250 mg qid). IOP was stabilized in clonidine group more easily compared to the placebo group. Every 7 out of 8 patients with IOP rise in the placebo group was noted 6 hours postoperatively.

### Discussion

Acute postoperative intraocular pressure rises after cataract surgery can result in CRAO and ischaemic optic neuropathy,<sup>2</sup> more optic nerve damage in glaucomatous eyes,<sup>3</sup> postoperative pain<sup>4</sup> and corneal oedema.<sup>5</sup>

Although preoperative mean IOPs in placebo group were lower than clonidine group but our study demonstrated that a single dose of preoperative oral clonidine (5g/kg) in cataract surgery under general anaesthesia can prevent acute postoperative IOP rise effectively, especially in first 12 hours after surgery. Maximum IOP rises usually occur

between 6 and 8 hours after surgery<sup>1</sup> and in this study most cases of IOP rise in the placebo group was detected 6 hours postoperative. We found that if IOP rise occurred after surgery, with preoperative clonidine, a smaller dose of ocular hypotensive agents could control it rapidly.

Few studies have been done on oral clonidine usage in ophthalmic surgeries. Scuderi G et al had used apraclonidine topically and observed that post-operative IOP was significantly reduced compared to oral acetazolamide or placebo.<sup>9</sup> Mjehed et al studied effect of lidocaine and clonidine combination in retrobulbar anaesthesia and concluded that it can decrease post injection IOP and can enhance sedation and analgesia and akinesia.<sup>10</sup> In one comparative study of clonidine and lidocaine by Nunes et al, it was concluded that oral clonidine prevented post-endotracheal intubation induced IOP rises, more effectively than lidocaine.<sup>11</sup> Kumar et al found that oral clonidine (300 g) as premedication could decrease IOP rises after retrobulbar injection.<sup>12</sup>

Roquennedy Souza Cruz et al showed that 200 g Oral clonidine decreases IOP in the preoperative and postoperative phase more than 100 g.<sup>13</sup>

Poley et al stated that IOP decreases one year after cataract surgery and intraocular lens implantation because of removal of crystallized lens, but they did not measure post operative IOP and its acute complications.<sup>14</sup>

Shrivastava A et al referred to articles in literature which demonstrated a modest, long-lasting decrease in IOP following phacoemulsification and posterior chamber intraocular lens implantation in patients with primary open-angle glaucoma and ocular hypertension. The mechanism of this average pressure-lowering effect has yet to be elucidated. The IOP reductions obtained in patients with angle closure glaucoma are often more pronounced than those seen in patients with open angles. Patients with higher levels of preoperative IOP obtain greater average reductions in IOP, although this phenomenon may partially be explained by a statistical effect known as regression to the mean.<sup>15</sup> Antao SF et al stated that post cataract surgery IOP remained within acceptable range of 10-30mm Hg in about 90% of cases.<sup>16</sup> Shingleton BJ et al demonstrated that IOP>30mmHg 24 hrs

after cataract surgery was observed in 15% and 8% glaucoma eyes and normal eyes respectively.<sup>17</sup> Fraser S et al speculated a measurable relation between IOP, volume of the anterior segment, lens size, and possibly corneal thickness.<sup>18</sup> Issa S A et al described a ratio that incorporates preoperative ocular parameters, which can be easily measured in a clinical setting, and appears to be strongly predictive for IOP reduction following cataract surgery in non-glaucomatous eyes. Eyes with a higher PD ratio, (pressure to depth ratio) exhibited a greater reduction in IOP. Further studies, with longer follow up, is needed to investigate the potential role of the PD ratio in non-glaucomatous and glaucomatous eyes if its value in surgical decision making is to be confirmed or refuted.<sup>19</sup> Usha Zamvar et al stated there is no consensus among UK ophthalmologists about IOP increase and its treatment or prophylaxis.<sup>20</sup> Alysia W et al were of the opinion that AS-OCT (anterior segment optical coherence tomography imaging) is a quick and non-invasive tool to demonstrate changes in the anterior segment after cataract extraction, including the effects on the anterior chamber angle. Preoperative angle width does not appear to be correlated with the degree of IOP reduction after cataract surgery and cannot be used at this time to predict a patient's IOP response to cataract surgery.<sup>21</sup> J Y Kim observed that IOP elevation on the first postoperative day following resident-performed cataract surgery occurred frequently (22.0%). Increased early postoperative IOP was associated with presence of glaucoma and ocular hypertension, higher preoperative IOP, and longer axial length.<sup>22</sup>

## Conclusion

In conclusion, our study showed that single dose oral clonidine (5g/kg), two hours before cataract surgery under general anaesthesia could prevent acute post operative IOP rise effectively. Clonidine has benefits with general anaesthesia such as haemodynamic stability, preventive effect of IOP rise after laryngoscopy and endotracheal intubation and improved patient's condition after recovery, which are all advantageous for the ophthalmic surgeon for successful cataract extraction surgery.

More studies on the use of clonidine in ophthalmic surgery especially in patients with complicated systemic problems such as cardiovascular disease and hypertension and other ocular conditions as glaucomatous eyes and pseudoexfoliation syndrome would establish the efficacy of this drug in prevention of postoperative IOP rise.

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