

## **The effect of oral clonidine pretreatment on intraocular pressure and hemodynamic stability after succinylcholine injection and intubation in cataract surgery**

H. Zahedi, MD.<sup>1</sup>, M. Nikooseresht, MD.<sup>2</sup>, and M. Rahro-Taban, MD.<sup>3</sup>

*Department of Anesthesiology, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran.*

### **Abstract**

**Background:** Providing better surgical conditions with meticulous control of Intraocular Pressure (IOP) is one of the most important factors that affect the success rate in ophthalmic surgery. Clonidine is a selective central  $\alpha_2$  agonist with analgesic, antianxiety and sedative effects which makes it a good choice in premedication recently. In this study, we compared the effects of oral clonidine with oral diazepam as premedicants on IOP and hemodynamic stability after injection of succinylcholine and intubation in cataract surgery.

**Methods:** 109 patients with physical status 1-2 were randomly assigned in 2 groups. The C Group (54 cases) was treated with oral clonidine (3 mic/kg) and the D group (55 cases) was treated with oral diazepam (0.15 mg/kg), 2 hours before induction of anesthesia. Induction of general anesthesia in all patients was performed with sodium thiopental (5mg/kg), fontanel (2mic/kg) & succinylcholine (1.5mg/kg). Heart rate and mean arterial blood pressure were measured before and immediately after induction and 5 & 10 minutes after intravenous injection of succinylcholine. Measurements of IOP were performed before and 5 and 10 minutes after injection of succinylcholine.

**Results:** IOPs' were always lower in C group as compared with D group but the IOP difference between groups was only significant at 5 minutes after succinylcholine injection.

Mean arterial blood pressure and pulse rate were lower in C group compared with D group and the most significant difference observed was at the time 5 minutes after succinylcholine injection.

**Conclusion:** Small doses of oral clonidine as premedicant can effectively reduce the IOP and provide better hemodynamic stability after intravenous injection of succinylcholine and intubation in cataract surgery.

**Keywords:** clonidine, diazepam, succinylcholine, IOP, cataract.

### **Introduction**

Although many anesthetic drugs can reduce intraocular pressure (IOP), succinylcholine transiently elevates IOP 2-4 minutes after IV injection [1]. Sudden significant rise of IOP can

produce permanent loss of vision perioperatively, so success in ophthalmic surgery mainly depends on meticulous control of IOP [2,3]. Therefore, many drugs and methods have been proposed to prevent IOP rise in ophthalmic surgery [1,4,5].

Clonidine is an imidazoline derivative, selective central  $\alpha_2$  agonist with analgesic, antianxi-

1. Associate Professor of Anesthesiology, Farabi Eye Hospital, Tehran University of Medical Sciences. Cell phone: +98912 5246441, email: hamid\_zahedi@yahoo.com.

2. Corresponding author, Assistant Professor of Anesthesiology. Hamadan University of Medical Sciences. Hamadan, Iran. Cell phone: +98912 3205754, email: nikoo\_mahshid@yahoo.com.

3. Anesthesiologist.

ety and sedative effects which makes it a good choice in premedication recently [6]. The topical form of clonidine (Apraclonidine) effectively prevents IOP rise after intraocular procedures such as: posterior and anterior segment laser surgery and phacoemulsification too [7]. It is confirmed that clonidine effectively decreases the anesthetic drug requirements and neuroendocrine responses to stressors and stimulations. Because of reduced perioperative stress hormones and more hemodynamic stability caused by clonidine, there is more interest to use this drug as a premedicant [8,9].

In Ghignone [2] and Filos' [6] studies, 90-120 minutes after a small oral dose of clonidine (5  $\mu$ g/kg) and lower doses like 2-2.5 $\mu$ g/kg IOP declined dramatically (35-48%) which persisted for 6 hours. Oral diazepam (0.2mg/kg) had no effect on IOP but IV diazepam (0.15mg/kg) or equivalent doses of midazolam can reduce IOP too [8].

In this randomized double blind clinical trial, we compared the effects of oral clonidine (3 $\mu$ g/kg) and diazepam (0.15mg/kg) as premedications on IOP and hemodynamics after induction of anesthesia with succinylcholine and intubation.

## Methods

Ethics Committee approval was obtained and all patients gave informed consent. 109 patients ASA class I, II presenting for elective cataract surgery (with intraocular lens insertion) under general anesthesia in Farabi Eye Hospital were randomly selected. Exclusion criteria included glaucoma or IOP reductant agents' usage, history of allergy to anesthetic drugs, previous eye surgery and sedative or narcotic drug usage during the past 24 hours.

The patients were randomly divided to clonidine (C group, N=54) and diazepam groups (D group, N=55) and respectively received oral clonidine (3 $\mu$ g/kg) and diazepam(0.15mg/kg) as premedicants 2 hours before induction of anesthesia which was performed with fontanel

(2 $\mu$ g/kg), thiopental sodium 5mg/kg and succinylcholione 1.5mg/kg in all patients. Halothane 1-1.5% was used for maintenance of anesthesia. This study was performed in a double blind nature and the investigator that measured IOP and hemodynamic indices was blind of the premedication assigned. IOP measurements were performed 4 times: in ophthalmology clinic, before induction of anesthesia, 5 and 10 minutes after succinyl injection with a Schiotz tonometer device. Blood pressure and pulse rate were measured by a cuffed automated noninvasive device and a pulse oximeter respectively at the times before induction of anesthesia, immediately after intubation and 5 and 10 minutes after induction.

Data was entered and analyzed with SPSS v10 software. Mean of all numeric data (age, blood pressure, IOP and HR) were compared with Students t-test and for comparing sex, Chi-square test was used.

## Results

Patients demographic characteristics including age and gender are presented in Table 1. There were no statistically significant differences among groups.

Patients in C group had lower IOP than D group at all times but the difference between the two groups was only significant at 5 minutes after succinylcholine injection (immediately after tracheal intubation) (P<0.02, Table 2). There was a dramatic decrease of mean IOP from time 1 (before induction) to 10 minutes after induction of anesthesia and mean of IOP at 5 and 10 min were significantly lower than IOP at time 1 (before induction) in the two study groups (T-

Premedicants	Sex		Mean age (year)	Sum
	F	M		
Clonidine	21	33	60.7±14.8	54
Diazepam	30	25	62.7±12.9	55
Sum	51	58	61.7±14	109

Table 1. Sex distribution and mean age of patients in clonidine and diazepam groups.

Premedicants	Mean IOP(mmHg)			
	IOP0	IOP1	IOP5	IOP10
Clonidine	15.32±2.2	15.15±4.6	9.8±4.2*	8±3.2
Diazepam	14.9±2.2	15.9±3.9	11.6±4*	8.96±3.5

\*: Difference between groups statistically significant ( $P<0.02$ )

IOP0=Intra Ocular Pressure before premedication  
IOP1=Intra Ocular Pressure 2 hours after premedication  
IOP5=Intra Ocular Pressure 5 min after IV Succinylcholine  
IOP10=Intra Ocular Pressure 10 min after IV Succinylcholine

Table 2. Mean IOP at different times in clonidine and diazepam groups.

test,  $P<0.000$ , Table 2).

The mean arterial blood pressure (MAP) in clonidine group was significantly lower than diazepam group immediately after intubation (MAP1) ( $P<0.01$ , Table-3).

Heart rate (HR) increased in response to intubation in the two study groups but the difference between mean HR before and after intubation was only significant in D group ( $P<0.001$ ). In addition mean HR after intubation was significantly lower in C group as compared with D group ( $P<0.008$ ) (Table 3).

### Conclusion

Many drugs including carbonic anhydrase inhibitors, myotics, beta blockers, calcium channel blockers, etc. have been used to reduce IOP in ocular surgery [5,10]. Most anesthetic drugs except for succinylcholine and ketamine have a lowering effect on IOP, too [1]. Transient IOP elevation after IV succinylcholine injection may lead to adverse outcome in ocular surgery and several studies have been performed to assess the effectiveness of some drugs or pre-

medicants on reducing IOP and providing better surgical conditions [3]. Low dose oral clonidine (0.15mg) was effective in terms of anxiolysis, sedation, stable hemodynamics, and lowering effect on IOP and perioperative endocrine stress responses [11]. The effectiveness of oral clonidine(300 $\mu$ g) [12] or smaller doses like 2-2.5 $\mu$ g/kg as premedication on prevention of IOP rise following IV succinylcholine was confirmed by other studies [2,6,8,11,12].

In the study, 5 and 10 minutes after induction of anesthesia there was a decline in IOP compared with the time before anesthesia in the two study groups, which could be related to anesthetic drugs, but the difference of mean IOP between the clonidine and diazepam groups was only significant at 5 minutes after IV succinylcholine injection (immediately after intubation). Considering the transient rise of IOP, 2-4 min after IV succinylcholine and significantly lower IOP in the clonidine group at the same time, we conclude that clonidine and not diazepam had successfully prevented the IOP rise after intubation.

	Premedicants	Time			
		Before induction	After intubation	5 min after succ	10 min after succ
MAP (mmHg)	Clonidine	88.6±11	87.3±13 <sup>1</sup>	78.6±12	71.9±12
	Diazepam	95.1±16	94.3±17 <sup>1</sup>	82.2±13	73.1±12
PR (beat/min)	Clonidine	77.5±15	79.5±14 <sup>2</sup>	75.9±14 <sup>3</sup>	71.8±16
	Diazepam	82.1±15	91.1±17 <sup>2</sup>	83±15 <sup>3</sup>	74.7±15

1,2,3. Difference between two study groups are significant, (1:  $P \leq 0.01$ , 2:  $P \leq 0.008$ , 3:  $P \leq 0.05$ ).

SBP=Systolic Blood Pressure, MAP=Mean Arterial Pressure, PR=Pulse Rate.

Table 3. Mean of hemodynamic indices at different times in clonidine and diazepam groups.

In general, IOP was measured indirectly by Indentation tonometry (Schiotz) and Applanation tonometry. There might be errors in two methods and after repeated measurements IOP could be underestimated [6,13], so in a study a placebo group was used to limit the biases caused by repeated IOP measurements.

All hemodynamic indices (HR, MAP) in clonidine group were lower than the diazepam group but the difference between the two groups was only significant at the time immediately after intubation. In other words, the stress response to intubation was significantly lower in the clonidine group as compared with the diazepam group and clonidine was able to provide more hemodynamic stability, although in one study there was no significant discrepancy between clonidine and diazepam in terms of hemodynamic stability after laryngoscopy and tracheal intubation [14].

Complications such as tachyphylaxis, contraction of posterior segment vasculature, depression, syncope, hypotension, and allergy-like syndromes were seen after long-term treatment with  $\alpha_2$ -agonists for IOP control in Robin et al's study [15]. Larger doses of clonidine (5  $\mu\text{g}/\text{kg}$ ) are thought to produce severe hypotension and bradycardia [6,16], but there is no evidence that single clonidine doses of 2-3  $\mu\text{g}/\text{kg}$  could result in major hemodynamic complications [2,6,17]. We had no significant adverse effects like hypotension, syncope, and bradycardia in our patients.

A dose of 3  $\mu\text{g}/\text{kg}$  oral clonidine is a safe and effective premedicant compared with oral diazepam for IOP reduction and provides hemodynamic stability in cataract surgery in elderly patients.

## References

1. Miller RD. *Anesthesia*, 6th ed. New York: Churchill Livingstone; 2005. pp.123-129.
2. Gignone M, Noe C. The effects of clonidine on IOP, perioperative hemodynamic and anesthetic requirement. Anesthesiol 1988; 68:707-16.
3. Rich WJ, Radtke ND, Cohn BE. Early ocular hypertension after cataract extraction. *Br J Ophthalmol* 1974; 58:725-9.
4. Ruitz RS, Wilson CA, Musgrove KH. Management of increased IOP after cataract extraction. *Am J Ophthalmol* 1987;103:487-92.
5. Murphy DF. Anesthesia and IOP. *Anesth Analg* 1985; 64:620-30.
6. Filos KS. A dose response study of orally administered clonidine as premedication in the elderly, evaluating hemodynamic safety. *Anesth Analg* 1993; 77:1185-92.
7. Unal M, Yucel I, et al. Brinzolamide 1% versus apraclonidine 0.5% to prevent intraocular pressure elevation after Nd-YAG laser posterior capsulotomy. *J Cataract Refract Sur* 2006;32(9):1499-502.
8. Kumar A, Bose S. Oral clonidine premedication for elderly patients undergoing intraocular surgery. *Acta Anesth Scan* 1992;36:159-63.
9. Laurito CE, Baughman VL. Oral clonidine blunts the hemodynamic responses to brief but not prolonged laryngoscopy. *J Clin Anesth* 1993; 5:54-7.
10. Al-Sereiti MR, Tummer P. Effects of captopril on IOP in healthy human volunteers. *J Ocular Pharmacol* 1989;5:1-5.
11. Weindler J, Keifer RT. Low dose oral clonidine as premedication before intraocular surgery in retrobulbar anesthesia. *Eur J Ophthalmol* 2000 ;10(3):248-56.
12. Polarz H, Bohrer H. Oral clonidine premedication prevents the rise in IOP following succinylcholine administration. *Ger J Ophthalmol* 1993; 2:97-9.
13. Heilmann K. Glaucoma, tonometry, and anesthesia. *Anesthesist* 1975; 24:97-102.
14. Jakola ML, Ali-Melkilla D, Konto J. Dexmedetomidine reduces IOP, intubation responses & anesthetic requirement in patients undergoing ophthalmologic surgery. *British J Anesth* 1992; 68:570-5.
15. Robin AL (John Hopkins University School of Medicine). The role of alpha-agonists in glaucoma therapy. *Cur Opin Ophthalmol* 1997;8:42-9.
16. Taittne MT. Effect of clonidine and Dexmedetomidine for elderly patients undergoing intraocular surgery. *Acta Anesth Scand* 1992; 36:159-63.
17. Nishikawa T, Taguchi M, Kimara. Effects of clonidine premedication upon hemodynamic changes associated with laryngoscopy and tracheal intubation. *Masui* 1991;40:1083-8