EFFECT OF ADMINISTRATION OF NIFEDIPINE OR SUFENTANIL BEFORE INDUCTION OF ANESTHESIA WITH THIOPENTONE OR PROPOFOL ON OCULAR TENTION IN GLUCOMATOUS PATIENTS

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ABSTRACT

This study was designed to assess the effect of nifedipine and sufentanil prior to induction of anesthesia on ocular tension in glaucomatous patients. This study was accomplished on ninety patients of either sex. Their ages ranged from 30-60 years. They were classified into six groups, each comprised fifteen patients. Forty five of the patients (groups I,II,II) received thiopentone 5mg/kg for induction, and the second half (group IV,V,VI) received propofol 2 mg/kg.Patients in group I and IV received no premedication. Patients in groups II and V received sufentanil 0.1 µg/kg IV, patients in groups III and VI received nifedipine 10mg/kg sublingually 20 minutes before induction of anesthesia. Tracheal intubation was facilitated in all patients by suxamethonium 1mg/kg.Anesthesia was maintained by halothane 0.5-1% and nitrous oxide: oxygen (2:1), muscle relaxation was achieved with atracurium 0.6 mg/kg with increments when required, controlled ventilation was carried out to maintain Pco2et between 32-35 mmHg. Heart rate, mean arterial blood pressure, intraocular pressure (IOP) were measured before any medication as a basal value, then it was measured 20 minutes after premedication ,after induction, after succinylcholine ,and at 1,2,3 and 5 minutes after tracheal intubation. The present recorded data revealed that nifedipine and sufentanil prevented the increase in IOP that occurred after succinylcholine, laryngeoscopy and tracheal intubation.The combination

of nifedipine and propofol was found to decrease the IOP below the basal values. The results demonstrated that the increase in IOP was primarily due to laryngoscopy and intubation and not due to succinylcholine and could be prevented by nifedipine and sufentanil. Moreover we found that sufentanil and propofol together not only prevented the increase in IOP, but also decreased it, which is advantageous in glaucomatous patients.

Key words : Intraocular pressure, nifedipine, sufentanil, calcium channel blockers.

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INTRODUCTION

Ophthalmic surgery presents challenges to the anesthesiologist not seen in other surgical specialties. Management of anesthesia for ophthalmic surgery requires judicious perioperative control of intraocular pressure (IOP). Severe perioperative increases in IOP of up to 30 – 40 mm Hg due to blockage of aqueous outflow by acute venous congestion as a result of straining, bucking, breath holding or obstructed airway was reported (1). Endotracheal intubation is a potent stimulus for increasing IOP which is also affected by External pressure from face mask, fingers, contraction of the orbicularis occuli muscle (2).

Most anesthetics reduce IOP, in general, they relax extraocular muscle tone, depress the CNS, reduce outflow of aqueos humour and lower venous and arterial blood pressures (3). Inhalation anesthetics are thought to alter IOP in a number of ways : by an effect on the central controlling areas in the midbrain, altering aqueous outflow facility, altering intra and extraocular muscle tone and by changing venous and arterial blood pressures(4). Most inhalational, and intravenous agents, decrease IOP if such factors as $PaCO_2$ and Pa O_2 are controlled. Halothane, enflurane and isoflurane produce a dose-dependent reduction in IOP (5). All intravenous agents lower IOP, with the exception of ketamine. Both Etomidate and propofol cause a greater reduction than thiopentone (6).

Orally administered diazepam and equipotent intravenous doses of midazolam significantly lower IOP. The nondepolarizing muscle relax-

ants decrease IOP. By contrast, succinylcholine causes a transient (4-6 min) but significant increase in IOP of 10-20 mmHg. Laryngoscopy and tracheal intubation are the anesthesia related practices most likely to increase IOP significantly, That is, at least 10-20 mmHg [4].

Several pretreatment regimens have been advocated to control the increase in IOP after administration of Succinylcholine and tracheal intubation.These include intravenous administration of lidocaine (1.5 mg/kg) [7].

Sufentanil used as a premedication 20 minutes before induction in a dose 0.03, 0.05 µg/kg with tubocurarine pretreatment plus high dose thiopentone or alfentanil induction effectively blocked the increase in IOP from succinylcholine and intubation[8]. Also sufentanil when used in a dose 1 ug/kg in combination with thiopentone and appropriate dose of vecuronium or atracurium did not increase IOP following rapid sequence induction [9].

A single 20 mg dose of nifedipine sublingually lead to acute fall in IOP in glaucomatous patients, while repeated oral doses had no effect in those patients or normal subjects[10].

We hypothesized that preanesthetic administration of sufentanil or nifedipine may decrease IOP in patients subjected to elective surgical treatment of glaucoma.We seek to detect this hypothesis in those glaucomatous patients with the primary outcome to decrease IOP.

PATIENTS AND METHODS

Ninety patients of either sex admitted in Ophthalmology Center in Mansoura Faculty of Medicine were selected for this study. They were suffering from elevated intraocular pressure (IOP) "Glaucoma" and scheduled for surgical treatment. Their age ranged between 30-60 years. The patients were randomly assigned to six groups, each of them comprised of 15 patients with the help of a random chart (using simple randomization method).

All patients underwent thorough clinical examination and laboratory investigations. Patients with respiratory, neuromuscular or intracranial disease were excluded from the study.

In the morning of the operation, patients were monitored for heart rate

and arterial blood pressure. Intravenous access was then accomplished. Basal IOP was measured in the diseased eye, by the same experienced investigator after instillation of benoxate hydrochloride 0.4 % as local anesthetic eye drop. With the patient in supine position and fixing on a target just overhead, the eyelids were separated, and the tonometer footplate rested on the anesthetized cornea in a position that allowed free vertical movement of the plunger. When the tonometer was properly positioned, a fine movement of the indicator needle on the scale would have been observed in response to the ocular pulsations. The scale readings were taken as the average between the extremes of these excursions. We started with the fixed 5.5 gm weight, however if the scale reading was 5 or less, additional weights were added to the plunger. A conversion table was then used to drive IOP in mmHg from the scale reading and plunger weight. This basal value of IOP was the mean of two successive readings.

Group I (Thiopentone, T) : Anesthesia was induced with thiopentone 5 mg/ kg and succinylcholine 1mg/kg.

Group II (Sufentanil and thiopentone, ST): Patients were given sufentanil IV in a dose of 0.1 µg/kg 20 min before induction of anesthesia with thiopentone and succinylcholine as in group I.

Group III (Nifedipine and thiopentone, NT) : Patients were given nifedipine capsule 10 mg sublingually 20 min before induction of anesthesia with thiopentone and succinylcholine as in group I.

Group IV (Propofol, P) : Anesthesia was induced with propofol in a dose of 2 mg/kg and intubation was facilitated with suxamethonium 1mg/kg

Group V (Sufentanil and propofol, SP) : Patients were given sufentanil IV in a dose of 0.1 ug/kg 20 min before induction of anesthesia with propofol and suxamethonium in the same doses as in group IV.

Group VI (Nifedipine and propofol, NP) : Patients were given nifedipine capsule 10 mg sublingually 20 min before induction of anesthesia with propofol and succinylcholine in the same doses as in group IV.

Laryngoscopy was attempted one minute after succinylcholine administration and intubation completed within 30 seconds in all patients. Any patient in whom tracheal intubation proved difficult or who strained or

coughed during intubation was excluded from the study. After tracheal intubation, Anesthesia was maintained with nitrous oxide oxygen 2:1 and halothane 0.5 %. Ventilation was controlled and non depolarizing muscle relaxant (atracurium 0.6 mg/kg initially then increments as required for adequate neuromuscular blockade) wasn't given till all measurements were terminated. Any patient who had respiratory attempt before complete measurement was excluded. Mean blood pressure, heart rate and IOP were measured before any premedication (basal), twenty minutes after pretreatment with either sufentanil or nifedipine (Just before induction), after injection of thiopentone or propofol. after succinylcholine administration and at one, two, three and five minutes respectively following intubation.

Statistical Methods :

Testing the data with Kolmogrov-Smiirnov test revealed parametric pattern. Mean, standard deviation, and sometimes, the range were used to describe the quantitative data. On the other hand, qualitative data were described with number and percentage . One- way ANOVA test was used as a test of significance between more than two groups. Student t test was used as a test of significance between two groups. Paired t test was used to compare two measurements of one group. In qualitative data, Chi square test was used as a test of significance. P value waes considered significant if less than 0.05.

RESULTS

Patient's ages were similar in the studied group (table I) IOP was significantly decreased ($P < 0.05$) after thiopentone, but increased significantly ($P < 0.05$) after intubation at all times of measurements when compared with basal value in group I while significant decrease in IOP (P, 0.001) after sufentanil, thiopentone; It was also significantly decreased ($P < 0.05$) at 3 and 5 min. after intubation. Also, IOP was significantly decreased ($P < 0.05$) after nifedipine, thiopentone, succinylcholine, and at 5 min post intubation in group III.

In patients receiving propofol as an induction agent (group IV) there was significant decrease in IOP after propofol ($P< 0.001$) but increased significantly ($P < 0.05$) after intubation at all times of measurements when compared with basal values. In Group V who received sufentanil, IOP was significantly decreased at all times of

measurements as compared to basal values ($P < 0.001$) after sufentanil, thiopentone, at 1, 2, 3 and 5 min. after intubation. While in group in which nifidipene was given (group VI) IOP was significantly decreased after propofol, succinylcholine ($P < 0.01$) with no significant change in the 1st and 2nd min immediately after intubation, to be decreased again significantly ($P < 0.001$) at 3, 5 min.

On comparing the IOP values in the whole 6 groups of the present study: there was no significant difference in the basal values of IOP between the six groups. After premedication; IOP decreased significantly ($P <0.05$) in group II compared to group VI .and after administration of the induction agents; there was significant decrease ($P < 0.05$) of IOP in group V compared to groups III and IV.Also after succinylcholine; the values of IOP showed significant decrease in group V compared to group IV ($P < 0.01$).

After intubation; groups I and IV showed significant increase in IOP compared to groups III ($P < 0.05$) and V ($P<0.01$). Two minutes post-intubation; IOP was significantly decreased in group V compared to groups I ($P < 0.01$), III ($P < 0.05$), IV ($P < 0.001$), and VI ($P < 0.01$).

At 3 min. post-intubation; there was a significant increase in IOP of group I compared to groups II ($P < 0.01$), III ($P < 0.05$), V ($P < 0.01$), and VI ($P < 0.01$). Also IOP in group IV was increased significantly compared to the same groups mentioned above while IOP in group V was decreased significantly compared to groups III, and VI only.

At 5 min. post-intubation; IOP was significantly increased in group I ($P < 0.001$) compared to groups II, III, and VI. There was increase in group IV compared to group III and VI . In group V IOP was decreased significantly ($P < 0.05$) in comparison to groups III, IV , and VI (table1) .

Mean arterial blood pressure (MBP) in group I showed statistically significant decrease after thiopentone but significantly increased in the 1st and 2nd min. post intubation and showed significant decrease after sufentanil, thiopentone, succinylcholine, and 5-min post intubation in group II while in group III who received nifidipene there was statistically significant decrease after nifedipine, thiopentone, and succinylcholine with no

significant change after intubation.Moreover in group IV There was significant decrease in MAP after propofol and succinylcholine, but significantly increased immediately after intubation to be decreased again at 3, and 5 min. post-intubation and showed statistically significant decrease at all times of measurements compared to the basal values in patients given sufentanil and also showed statistically significant decrease at all times of measurements except after 1 min. post-intubation compared to the basal values when nifidipene used as premedicant. (Fig I).

Heart rate showed significant increase in the 1st three min after intubation in group I while in group II significant increase occurred only after succinylcholine with no significant change after intubation and in patient received nifidipene there was significant increase after succinylcholine and only 1 min after intubation. In propofol group heart rate increased significantly in the 1st three min after intubation,with sufentanil a significant decrease in heart rate occurred after propofol and at 3 and 5 min after intubation and significant increase in the 1st min after intubation only in nifidipene propofol group (Fig2).

Table (1)Age (ys) and Intraocular pressure (IOP) (mmHg) of the study groups (Values are mean ± SD (n=15)

	Group I (T)	Group II (ST)	Group III (NT)	Group IV (P)	Group V (SP)	Group VI (NP)
Age(ys)	43.8±8.62	47.8±9.08	46.46±9.18	47.4±9.71	46.8±8.52	46.13±9.05
IOP(mmHg)						
Basal	32.52 ± 11.8	31.19 ± 9.9	34.58 ± 7.2	34.21 ± 8.13	34.21 ± 8.13	35.85 ± 7.27
		27.08 ± 9.*•	30.85 ± 7.6•		31.84 ± 7.76•	34.82 ± 7.69
After premedication						
After induction agent	27.35 ± 9.7•	24.61 ± 10.8•	30.85 ± 7.6•	27.67 ± 7.96•	25.46 ± 5.93**•	28.55 ± 5.61•
After succinyl	33.23 ± 10.8	28.97 ± 10.9	30.85 ± 7.6•	34.28 ± 7.6	27.73 ± 7.04¤•	31.74 ± 6.41•
After intubation :						
1 min	40.52 ± 11.2•▲	33.30 ± 11.8	32.41 ± 9.9	41.7 ± 10.π▲	29.9 ± 6.81•	37.56 ± 7.71
2 min	36.98 ± 11.4▲	30.63 ±12.3	32.41 ± 9.9	38.73 ± 9.75▲	26.18 ± 1.14#•	34.21 ± 8.17
3 min	38.35 ± 5.8¥▲	27.39 ± 10.6•	32.4 ± 7.6	39.2 ± 9.48£▲	23.97 ± 9.23©•	31.21 ± 7.22•
5 min	37.35 ± 4.5¶▲	25.04 ± 9.8•	29.05 ± 8.6•	38.7 ± 6.13◊▲	22.91 ± 6.52∞•	28.56 ± 6.63•

• Significant increase in group I as compared to III & V

¥ Significant increase in group I as compared to II, III, V & VI

¶ Significant increase in group I as compared to II, III & VI

* Significant decrease in group II as compared to group VI

π Significant increase in group IV as compared to III & V

◊ Significant increase in group IV as compared to III & VI

£ Significant increase in group IV as compared to II, III, V & VI

© Significant decrease in group V as compared to III & VI

∞ Significant decrease in group V as compared to III, IV & VI

Significant decrease in group V as compared to I, III, IV & VI

** Significant decrease in group V as compared to group III & IV

¤ Significant decrease in group V as compared to I & IV

•Significant decrease in comparison to basal values in each group

▲Significant increase in comparison to basal values in each group

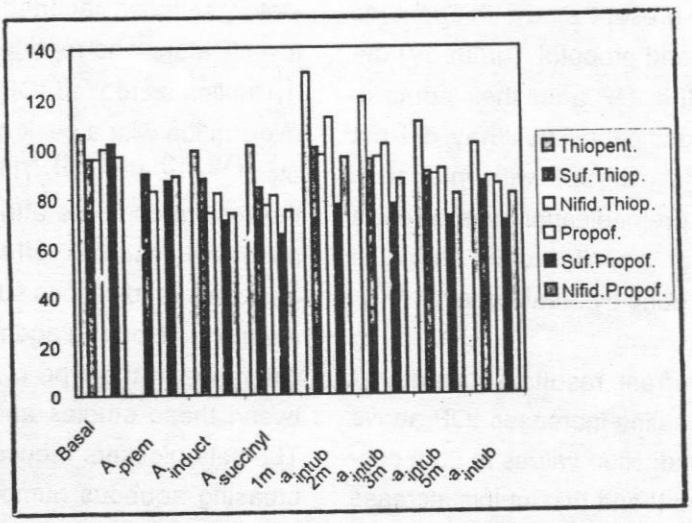

Fig. 1 : Mean arterial blood pressure in the study groups.

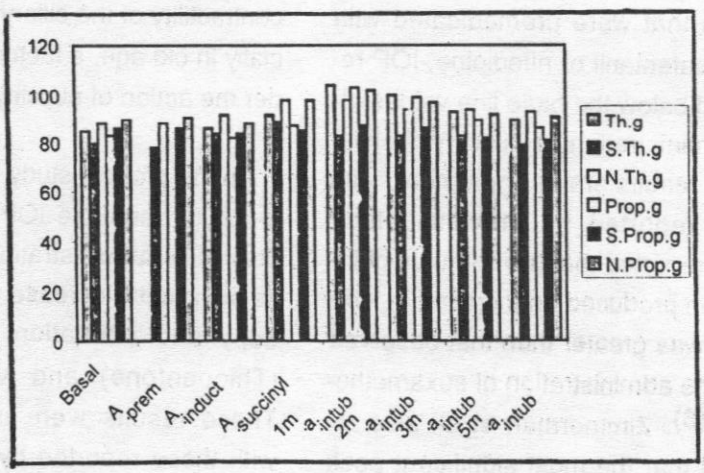

Fig. 2 : Heart rate in the study groups.

DISCUSSION

In the present study, thiopentone (group I) and propofol (group IV) decreased the IOP after their administration significantly but they did not prevent its increase with intubation when no premedication was given, a finding that is similar to the results of the study done by Mirakhur et al, (6)

The current results showed that Succinylcholine increases IOP above the post-induction values in both control groups (I and IV) but this increase was statistically insignificant. There was no significant increase in IOP after succinylcholine compared to baseline values in these two control groups mentioned. In the other groups that were premedicated with either sufentanil or nifedipine, IOP remained below the base line values after administration of succinylcholine. These results are in agreement with those reported by previous study which reported that the stimulus of intubation produced an increase in IOP which was greater than that observed after the administration of suxamethonium (6). Zimmerman et al, also reported that the most significant peak increase in IOP was with laryngoscopy and intubation and not with succinylcholine (11).

However; our results are contradictory to those reported by previous investigators who reported that succinylcholine increased IOP after its administration with a peak after 2-4 minutes (12, 13, and 14). This variation in the results could be attributed to the possible residual effect of anti-glaucoma medications such as the B-adrenergic blocking agents and to the difference in the type of patients between these studies and our study. The beta-blockers reduce IOP by decreasing aqueous humor production and their effect could remain up to 12-24 hours (15). Moreover, the patients in our study were glaucomatous patients in whom one of the possible pathologic changes is the reduction in contractility of the ciliary muscle especially in old age, a factor that may hinder the action of succinylcholine (16).

In the present study nifedipine was found to decrease IOP after 20 minutes of its administration and prevent its significant increase with laryngoscopy and intubation in groups III (Thiopentone) and VI (Propofol). These results were in accordance with those reported by Indu et al. in their study they use 10 mg nifedipine sublingual 20 min. before induction of anesthesia in normal patients and

they found that it is effective in attenuating the IOP response after succinylcholine administration, laryngoscopy and intubation [17]. They suggested that the mechanism of this response could be due to obtunded haemodynamic response or direct effect of nifedipine on aqueous flow dynamics. A previously published clinical study also found that a single 20 mg dose of nifedipine sublingually caused an acute fall in IOP in glaucomatous patients, while repeated oral doses had no effect in these patients or normal subjects (10) . However, in contrast to the present study, previous investigators studied three calcium antagonists in rabbits and normal humans and found that an intravenous bolus of verapamil or diltiazem increased the IOP acutely in rabbits. Topical verapamil, diltiazem, or nifedipine also increased IOP in humans and rabbits, but oral verapamil had no effect [18]. They considered that the increase in IOP could be due to ocular vasodilatation because whole eye and ciliary body blood flow were increased in rabbits on topical verapamil.

Sufentanil in the present study decreased IOP significantly in group II after its administration and prevent its increase that occur after intubation with thiopentone as induction drug, sufentanil significantly decreased the IOP allover the period of measurements even with succinylcholine and intubation in group V when propofol was the induction drug. These results seems to be parallel with those reported by other authers who used 0.05 µg/Kg sufentanil with d- tubocurarine and thiopentone for induction of anaesthesia in non glaucomatous patients and they found it to be effective in blocking the increase in IOP after succinylcholine and intubation [8]. Another study used sufentanil in a dose of 1 ug/Kg and found it to be effective in blocking the response of IOP to intubation [9]. The mechanism by which sufentanil or opioids in general decrease IOP was suggested to be due to relaxation of intra- or extraocular muscles, facilitation of outflow or a decrease in production of aqueous humor [19].

On the other hand, nifedipine decreased the mean blood pressure after its administration and prevented its increase with intubation in group II (with thiopentone), but in group VI (when propofol was used as induction drug) the mean blood pressure showed significant decrease all over the period of the study. The heart rate

showed no significant change following nifedipine administration but it increased significantly after succinylcholine in group III (nifedipine and thiopentone) and with intubation in groups III (nifedipine and thiopentone) and VI (nifedipine and propofol) These results confirm those reported by Kale et al in which they concluded that sublingual nifedipine administration 5-7 min before tracheal intubation is a safe, convenient and effective way to prevent the pressor response associated with laryngoscopy and intubation [20].

Sufentanil in combination with thiopentone (group II) prevented the increase in mean arterial blood pressure with laryngoscopy and intubation. While its combination with propofol (group V) led to significant decrease in mean arterial blood pressure all over our measurements period. Sufentanil also prevented the increase in heart rate after intubation whether thiopentone (group II) or propofol (group V) was the induction drug. As a result, sufentanil was useful to block the stress response for intubation. These results coincide with those reported by other investigators who reported that sufentanil 0.5ug and 1 ug/kg sufentanil 2 minutes before induction of anesthesia [21], and those used 1 and 2 ug/kg sufentanil with induction [22] and they found that these doses attenuated the stress response to intubation.

The over all results of the present study indicate that laryngoscopy and tracheal intubation increased IOP and not succinylcholine. These effects could be prevented by nifedipine and sufentanil. Moreover sufentanil and propofol together not only prevent the increase in IOP, but also decrease it, which is useful in glaucomatous patients.

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أجرى هذا البحث على تسعين مريضاً من الجنسين تتراوح أعمارهم بين ثلاثين وستين عاماً. وقد تم تقسيم المرضى إلى ستة مجموعات كل منها يضم خمس عشر مريضاً. أعطى نصف المرضى عقار الشايوبنتون ٥ مجم/كجم كمخدر (المجموعة الأولى والثانية والثالثة) وأعطى النصف الآخر عقار البروبوفول كمخدر بجرعة ٢ مجم/كجم (المجموعة الرابعة والخامسة والسادسة).

مرضى المجموعة الأولى والرابعة لم يتلقوا أى أدوية قبل التخدير أما مرضى المجموعة الثانية والخامسة فقد تم حقنهم بعقار السوفنتانيل عن طريق الوريد بجرعة ١ر٠ ميكروجرام/ كجم ومرضى المجموعة الثالثة والسادسة قد تم إعطائها كبسولة من عقار نيفيديبن ١٠ مجم تحت اللسان. وتم إستخدام عقار السوكشاميثونيوم لتسهيل إدخال أنبوبة القصبة الهوائية ثم استمر التخدير بالهالوثان ٥ر٠-١٪ محملا بأكسيد النيتروز والأكسچين بنسبة ١:٢ وقد تم تسجيل عدد نبضات القلب ومتوسط ضغط الدم وتوتر العين قبل إعطاء أى عقاقير ثم بعد إعطاء السوفنتانيل أو النفيديبين بعشرين دقيقة قبل التخدير مباشرة ثم بعد عقار الشايوبنتون أو البروبوفول ثم بعد عقار السوكشاميثوننيوم ثم بعد تركيب أنبوبة القصبة الهوائية كل دقيقة لمدة خمس دقائق.

وقد لوحظ أن عقار النيفيدين والسوفنتانيل قادرين على منع توتر العين مع عقار السوكشاميثونيوم وتركيب أنبوبة القصبة الهوائية مقارنة بالمجموعات التى لم تتلقى هذه العقاقير كما وجد أن استخدام عقار السوفنتانيل مع عقار البروبوفول يؤدى إلى إنخفاض توتر العين عن القيم الأساسية مما قد يكون مفيداً فى المرضى المصابين بالمياه الزرقاء.