ORİJİNAL ARAŞTIRMA / *ORIGINAL RESEARCH*

The Effects of Low Dose Intravenous Nitroglycerin Infusion on Intraocular Pressure in Laparoscopic Cholecystectomy

DÜŞÜK DOZ NİTROGLİSERİN İNFÜZYONUNUN LAPAROSKOPİK KOLESİSTEKTOMİ OPERASYONLARINDA GÖZ İÇİ BASINCI ÜZERİNE ETKİSİ

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Abstract

Objective: The aim of our study was to evaluate the effects of low dose intravenous nitroglycerin infusion on intraocular pressure during pneumoperitoneum period in laparoscopic cholecystectomy.

Material and Methods: Sixty patients with no pre-existing eye disease were divided into two groups as nitroglycerin and control groups in this prospective, randomized, and double-blind study. Anesthesia was induced with propofol, fentanyl, lidocaine and rocuronium in all patients and maintained with isoflurane and N_2O in oxygen. Intravenous nitroglycerin infusion 0.5µg kg^{-1} min^{-1} was given to the nitroglycerin group during pneumoperitoneum period. Intraocular pressure, mean arterial pressure, heart rate, peak and plateau airway pressure, end tidal CO_2 pressure, and peripheral oxygen saturation measurements were recorded before induction of anesthesia (T_0), post-intubation (T_1), before insufflations of CO_2 (T_2), 10 min (T_3), and 30 (T_4) min of pneumoperitoneum and 5 (T_5) min after exsufflation.

Results: After induction of anesthesia, there was a significant decrease in intraocular pressure compared with basic values in both groups. Mean arterial pressure and intraocular pressure were significantly higher in control group compared to nitroglycerin group during the period of pneumoperitoneum (23.7 ± 3.1 and 15.6 ± 2.9 at T_3 and 19.1 ± 2.7 and 14.5 ± 2.8 at T_4, respectively, in control and nitroglycerin groups, for intraocular pressure).

Conclusion: We concluded that intravenous low-dose nitroglycerin infusion might prevent the increase of intraocular pressure during pneumoperitoneum period in patient with no pre-existing eye disease.

Key Words: Nitroglycerin; cholecystectomy, laparoscopic; intraocular pressure

Özet

Amaç: Çalışmamızın amacı, laparoskopik kolesistektomi operasyonlarında, düşük doz intravenöz nitrogliserin infüzyonunun pnömoperitonyum süresince göz içi basıncı üzerine etkisini değerlendirmektir.

Gereç ve Yöntemler: Prospektif, randomize ve çift kör olarak planlanan bu çalışmada, daha önceden göz hastalığı olmayan 60 hasta "nitrogliserin" ve "kontrol" grubu olarak 2 gruba ayrıldı. Anestezi indüksiyonu tüm hastalarda propofol, fentanil, lidokain ve rokuronyum ile yapıldı. Anestezinin idamesi için izofluran ile N_2O-O_2 kullanıldı. Nitrogliserin grubunda pnömoperitonyum süresince intravenöz olarak nitrogliserin 0.5 µg kg^{-1} min^{-1} verildi. Göz içi basıncı, ortalama arteriyal basınç, kalp hızı, periferik O_2 saturasyonu, hava yolu basınçları ve end-tidal CO_2 basıncı değerleri; anestezi öncesi (bazal değer) (T_0), entübasyon sonrası (T_1), karın içine CO_2 gazı verilmeden önce (T_2), pnömoperitonyumun 10. (T_3) ve 30. (T_4) dakikalarında ve gaz boşaltıldıktan sonraki 5. (T_5) dakikada kaydedildi.

Bulgular: Anestezi indüksiyonu sonrasında, her iki grupta da göz içi basıncı değerleri bazal değerlere göre azaldı. Ortalama arteriyal basınç ve göz içi basıncı değerleri, pnömoperitonyum süresince, kontrol grubunda nitrogliserin grubuna göre daha yüksek bulundu (göz içi basıncı; T_3 ölçümünde 23.7 ± 3.1 ile 15.6 ± 2.9 ve T_4 ölçümünde 19.1 ± 2.7 ile 14.5 ± 2.8, sırasıyla kontrol ve nitrogliserin gruplarında).

Sonuç: Düşük doz intravenöz nitrogliserin infüzyonunun, pnömoperitonyum süresince, göz içi basıncındaki artışı önleyebileceği sonucuna varıldı.

Anahtar Kelimeler: Nitrogliserin; kolesistektomi, laparoskopik; göz içi basıncı

Turkiye Klinikleri J Anest Reanim 2006, 4:101-105

Geliş Tarihi/*Received:* 27.02.2006 **Kabul Tarihi/*Accepted:*** 12.07.2006

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The normal range of intraocular pressure (IOP) is 10-22 mmHg and maintained by several factors. Some of these factors are venous congestion of the orbital veins, the volume of intraocular fluid such as blood, aqueous humor, and the semisolid structures, which include the lens, the vitreous, and intraocular tumors.[1]

During laparoscopic surgery, many physiological changes cause the increase in IOP. These changes include the increase of blood pressure, end tidal carbon dioxide pressure and central venous pressure, which are the results of the increase in intrathoracic pressure and postural changes.[2]

The effects of nitroglycerin on the eye and specifically on IOP have been investigated with diverse results. Various investigators reported that the nitrates were used in normal and glaucomatous patients.[3-6] Hessemer and Schmidt[4] found a minimal drop in IOP by using oral nitrates. Chronic nitrate treatment causes retinal venous dilatation and lead to improvement in perfusion of the retina and optic nerve head in patients with glaucoma [5]. Wizemann and Wizemann[6] also reported that the usage of systemic nitrate therapy lowered IOP both in glaucoma patients and healthy patients. The effect was dose-dependent. Jantzen et al[7] suggested the usage of intravenous nitroglycerin to prevent IOP increase, which is the result of succinylcholine in anesthetized patients.

Therefore, we designed a randomized controlled study to evaluate the effects of intravenous low dose nitroglycerin infusion on the IOP during the pneumoperitoneum period.

Material and Methods

With ethic committee approval and written informed consent, 60 patients (ASA I-II) undergoing elective laparoscopic cholecystectomy were included in the study. The patients who were younger than 18 years and older than 60 years and had acute or chronic eye disease, pre-existing ocular hypertension and chronic obstructive lung diseases were the exclusion criteria. The patients were randomly divided into two groups: Nitroglycerin (NTG) and Control (C) groups. Randomization of the patients was achieved using a computer-generated table.

Anesthesia was induced by propofol 2 mg kg[1], fentanyl 1 μg kg^{-1}, lidocaine 2% 1 mg kg^{-1} and maintained with isoflurane 1.2% and N_2O 65 % in O_2. Tracheal intubations were facilitated by rocuronium 0.6 mg kg.[1] The lungs of the patients were mechanically ventilated with a volume-cycled ventilator (Datex-Ohmeda Inc, Helsinki, Finland). Through the procedure, minute volume was set to maintain end tidal-CO_2 at 35-45 mmHg. Pneumoperitoneum was applied by intraperitoneal CO_2 insufflations with the patient in supine position. Through surgery intraperitoneal pressure was maintained automatically at 12-15 mmHg by CO_2 insufflators. While intravenous nitroglycerin 0.5 μg kg^{-1} min^{-1} was being infused in the beginning of the intraperitoneal CO_2 insufflations, and continued throughout the pneumoperitoneum period in NTG group, saline was being infused same amount in Group C. Datex A/S3 (Helsinki, Finland) were used to monitor inspired and expired anesthetic gases and ventilator variables in addition to plethysmographic oxygen saturation. Heart rate (HR), mean arterial pressure (MAP), arterial oxygen saturation (SaO_2), end tidal CO_2 pressure ($ETCO_2$), expiratory isoflurane concentration, peak and plateau airway pressure (Paw) and intraocular pressure (IOP) were recorded initially (before induction of anesthesia) (T_0), post intubations (T_1), before insufflations of CO_2 (T_2), at the 10 min (T_3) and 30 min of pneumoperitoneum (T_4) and 5 min after exsufflation (T_5).

Intraocular pressure values were obtained by an ophthalmologist with using a hand-held Perkins applanation tonometer. Both the ophthalmologist and anesthesiologist who performed the IOP and MAP measurements were blinded to the study.

Statistical analysis

The power of this study was calculated using G Power analysis program (http://www.physcho.-uni-duesseldorf.de/aap/projects/gpower/index.html) Using a *post hoc* power analysis with accuracy mode calculation and assuming type 1 error protection of 0.05 and effect size convention of 0.5, a total sample size of 60 patients yields a power of 0.97.

All values are presented as mean ± SD. Comparison of different observations within groups were analyzed using paired t-test. Differences between variable data were analyzed with one-way variance of analysis (ANOVA). When significant difference existed, Bonferroni correction was applied to detect the exact location between groups. Analysis was performed using SPSS software version 10.0 for windows. p< 0.05 was considered statistically significant.

Results

There were no significant differences between two groups with respect to age, weight, gender, and duration of the procedure (Table 1). There were also no significant differences in the basic values of HR, MAP and IOP.

After induction of anesthesia (T_1), there was a significant decrease in IOP and MAP compared with basic values (T_0) in both groups (fig 1 and fig 2). While in Group C, MAP significantly increased at T_3 and T_4 measurements compared to T_0 measurement (p= 0.001 at T_3 and p= 0.022 at T_4 with respectively), there was no difference in Group NTG at T_0 compared to T_3 and T_4 measurements (fig 1). In control group, IOP was higher than nitroglycerin group during pneumoperitoneum period (at T_3 and T_4) (23.7 ± 3.1 and 15.6 ± 2.9 at T_3 and 19.1 ± 2.7 and 14.5 ± 2.8 at T_4, in Group C and Group NTG, respectively) (fig 2).

There was no significant difference in heart rate, $ETCO_2$, expiratory isoflurane concentration and SaO_2 between the groups during the study. Peak and plateau airway pressures slightly increased at T_3 and T_4 when compared with T_2.

Table 1. Demographic data and duration of surgery.

	Nitroglycerin Group	Control Group
	n= 30	n= 30
Age (year)	53.1 ± 6.6	54.2 ± 7.4
Weight (kg)	75.1 ± 9.3	73.2 ± 10.4
Duration of surgery (min)	54.3 ± 11.2	51.1 ± 8.9
Gender (male/female)	18/12	16/14

Data are means ± SD or numbers
*There was no statistically significant difference between two groups.

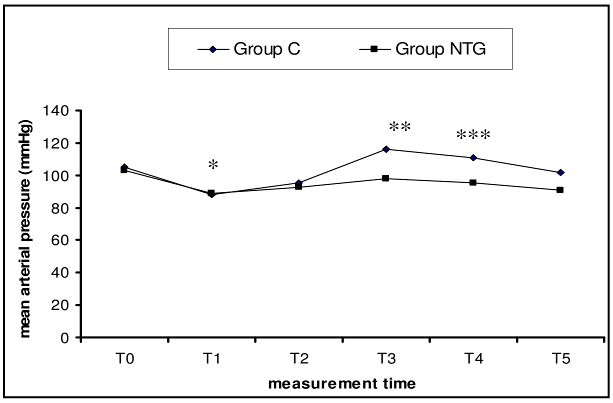

Figure 1. Mean arterial pressure changes in groups

Measurements were made before induction of anesthesia (T_0), post-intubations (T_1), before insufflations of CO_2 (T_2), after 10 min (T_3) and 30 min (T_4) of pneumoperitoneum and 5 min after exsufflation (T_5) in Group NTG (nitroglycerin group) and Group C (control group).

* p=0.043, and p=0.044, respectively in Group C and Group NTG at T_0, compared to after induction of anaesthesia.

** p=0.033, *** p=0.041 in Group C, respectively at T_3 and T_4, compared to Group NTG.

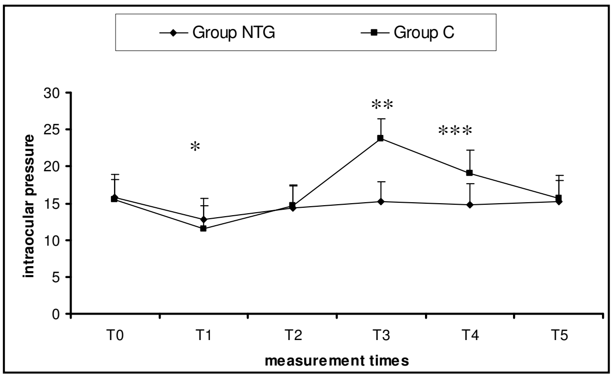

Figure 2. Intraocular pressure changes in groups

Measurements were made before induction of anesthesia (T_0), post-intubations (T_1), before insufflations of CO_2 (T_2), after 10 min (T_3) and 30 min (T_4) of pneumoperitoneum and 5 min after exsufflation (T_5) in Group NTG (nitroglycerin group) and Group C (control group).

*p<0.05, after induction of anaesthesia, there was a significant decrease in IOP compared with basic values in both groups at T_1.

**p= 0.031 and ***: p=0.041 at T_3 and T_4, respectively between the groups.

Compliance values also slightly decreased at same times in both groups. But there was no significantly difference between the groups.

Discussion

The main finding of this study was that intravenous nitroglycerin infusion might prevent the increase of IOP during the pneumoperitoneum period in the patients who have no pre-existing ocular hypertension.

During laparoscopic surgery intraperitoneal CO_2 insufflations and changes in patient position lead to several haemodynamic, ocular, pulmonary and endocrine effects.[2] Creation of pneumoperitoneum in the supine position may increase the intravascular volume, probably as a result of compression of the abdominal organs (eg, liver and spleen) by increasing intraabdominal pressure.[8] Furthermore, the increased sympathetic output and neurohormonal response to systemically absorbed CO_2 may also be contributing factors.[9] On the other hand, pooling of blood in the lower extremities from the head-up position and compression of the inferior vena cava resulting from increased intraabdominal pressure may decrease venous return.[10] Peritoneal insufflations also result in significant increases of MAP, systemic vascular resistances (SVR), pulmonary vascular resistances (PVR), central venous pressure (CVP), and pulmonary capillary wedge pressure (PCWP).[11,12] Odeberg et al.[13] suggested that the combination of pneumoperitoneum and a head up tilt was only associated with the elevation of afterload. Arterial pressure basically represents the afterload opposing left ventricular ejection.[8] In the present study MAP was significantly higher during carbon dioxide pneumoperitoneum compared to basic value in control group. Several studies have also shown that carbondioxide pneumoperitoneum increases MAP.[8-13]

Glyceryl trinitrate infusion is a relatively simple and adjustable technique for relaxing vascular smooth muscle and rapidly produced a marked haemodynamic improvement in laparoscopic surgery, presumably mainly as a result of a decrease in afterload.[14] Several investigators have recommended intraoperative administration of nitroglycerin infusion (0.5-1 $\mu g\ kg^{-1}\ min^{-1}$) in patients with cardiac dysfunction to avoid the changes in SVR and related decrease in cardiac index (CI) during laparoscopic cholecystectomy.[15-18] The nitroglycerin group did not cause increasing of MAP during pneumoperitoneum period in our study. It might be related to the prevention of increase in SVR.

Although IOP is maintained at a relatively uniform level regardless of the degree of hypertension, an acute rise of arterial blood pressure may increase IOP. Over time, if arterial hypertension is chronic, IOP will normalize after adaptation of choroidal vessel compression.[1] During pneumoperitoneum period the measurement of MAP and IOP extensively increased compare with the basic values in control group. Higher IOP might be related an acute rise of arterial blood pressure during pneumoperitoneum period in our study.

There were many conflicting reports about nitrates therapy and IOP in the past, however the recently studies suggested that concomitant use of systemic nitrates in glaucoma patients might be offered for their protective effects against glaucomatous optic neuropathy.[3]

Nitric oxide (NO) is produced from nitroglycerin in the eye, which may contribute to the improved perfusion of the retina and optic nerve associated with nitroglycerin treatment. There are various sites of action for the NO donors in the eye, including ciliary's muscle, the trabecular meshwork and the endothelial and vascular smooth muscle cells in the aqueous drainage system.[19,20] Nathanson et al.[21] concluded that in both young and older rabbits, topically applied nitroglycerin lowered IOP rapidly, but this was dose dependent. Higher doses of nitroglycerine were less effective to decrease IOP.[21] Furthermore, Mahajan et al.[22] suggested that intranasal administration of nitroglycerine decreased IOP in anaesthetized patients. In nitroglycerine group, IOP did not increase during pneumoperitoneum period in our study. It might be related to the effect of nitric oxide on aqueous humor dynamics.

Although a good correlation was found between $ETCO_2$ and IOP,[23] $ETCO_2$ was maintained constant in our study by varying the minute volume ventilation.

Several studies have showed that the usage of propofol, fentanyl, lidocaine and rocuronium prevent the increase in IOP, which is the result of laryngoscopy and endotracheal intubation.[1,2,24] There are a lot of conflicting reports about the correlation of isoflurane and IOP. Some authors suggested that isoflurane decreased IOP by lowering the formation rate of aqueous humour and increasing the trabecular outflow facility.[25] The others demonstrated that isoflurane increased IOP in laparoscopic surgery but it remained within the normal diurnal range in no pre-existing eye disease of patients.[2] The common effects of anesthetics agents and intravenous low dose nitroglycerin might be effective to decrease IOP in patients with normal IOP.

We concluded that low dose nitroglycerin infusion during the period of pneumoperitoneum might be effective to stabilize IOP by preventing increase of SVR and modulating aqueous humor dynamics in laparoscopic cholecystectomy. Further studies are required to prove the effects of low dose nitroglycerin infusion during laparoscopy in patients with preexisting eye disease.

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