A comparison of esmolol and dexmedetomidine for attenuation of intraocular pressure and haemodynamic responses to laryngoscopy and tracheal intubation

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EDITOR:

Laryngoscopy and tracheal intubation may cause undesirable increases in blood pressure (BP), heart rate (HR) and intraocular pressure (IOP). Esmolol, a short-acting β_1-adrenoceptor antagonist, and dexmedetomidine, a selective α_2-adrenoceptor agonist, have been used to modify the IOP increases and cardiovascular responses after laryngoscopy and tracheal intubation. However, data comparing the aforementioned effects of these drugs to each other are not available in the literature. Here we present the data comparison of the effects of a single pre-induction intravenous (i.v.) dose of dexmedetomidine vs. esmolol on IOP and haemodynamic changes due to tracheal intubation.

After obtaining Hospital Ethics Committee approval and informed written consent from the patients, we studied 60 ASA Grade I–II patients, aged 18–60 yr, who required tracheal intubation for elective non-ophthalmic surgery. Exclusion criteria included any known allergies or contraindications to the drugs used, pre-existing eye disease, predicted difficulty in intubation and pregnancy.

After routine monitoring, patients were premedicated with midazolam $0.03\,mg\,kg^{-1}$ 30 min before induction of anaesthesia. Patients were assigned randomly, in a double-blind fashion, to receive either saline as placebo (20 mL) (Group P, $n = 20$), esmolol ($0.5\,mg\,kg^{-1}$) (Group E, $n = 20$) or dexmedetomidine ($0.5\,\mu g\,kg^{-1}$) (Group D, $n = 20$) diluted in saline, using 20 mL syringes, 2 min before anaesthesia induction. Anaesthesia was induced with fentanyl ($2\,\mu g\,kg^{-1}$), rocuronium ($0.6\,mg\,kg^{-1}$) and propofol (titrated until the eyelash reflex was lost), and maintained with sevoflurane and nitrous oxide 50% in oxygen. HR, mean arterial pressure (MAP) and IOP values were recorded before and 2 min after the administration of the drug, 1 min after induction, and at 1, 3, 5 and 10 min after intubation.

After topical application of local anaesthetic, IOP was measured with a Tono-pen® XL hand-held tonometer (Medtronicsolan, Jacksonville, FL, USA). Possible adverse effects during and after administration of esmolol or dexmedetomidine and during the postoperative period such as arrhythmia, bradycardia, tachycardia, hypotension or hypertension were recorded.

The decision to include 20 patients in each group was based on a power analysis ($\alpha = 0.05$, $\beta = 0.1$), which revealed that at least 19 patients should be included in each group. Differences between three groups were compared with the Mann-Whitney *U*-test. Differences from baseline within groups were evaluated using the Wilcoxon signed rank test. Categorical variables were analysed using the χ^2-test. Statistical analysis was performed using SPSS version 10.0 for windows (SPSS, Chicago, IL, USA). Statistical significance was accepted as $P < 0.05$. All the 60 patients who were recruited completed the study.

Patient characteristics were comparable in all groups. The induction dose of propofol at which the eyelash reflex was lost was lower in the dexmedetomidine group (61.3 ± 10.2 mg) than in the esmolol (137.5 ± 16.3 mg) and placebo (144.0 ± 14.1 mg) groups ($P < 0.001$ for both groups). None of the patients needed active treatment for cardiac problems during the study period.

After administration of study drugs, IOP, MAP and HR were lower in Groups D and E when compared with Group P (IOP: $P < 0.001$ for Groups D and E; MAP: $P < 0.001$ for Group D, $P = 0.028$ for Group E; HR: $P < 0.001$ for Group D and $P = 0.014$ for Group E). Following induction, there were no differences in IOP values among groups but MAP was significantly decreased in Group D compared with Group P ($P = 0.043$), while HR was lower in Groups D and E than in Group P ($P < 0.001$ for both groups). The amount of reduction in HR in Group D was higher than that in Group E ($P = 0.046$). IOP and HR at 1, 3, 5 and 10 min after intubation were lower in Group D compared with Groups E and P (IOP: $P < 0.001$ for all variables; HR: $P < 0.001$, $P < 0.001$, $P < 0.001$ and $P = 0.020$ for Group E and $P < 0.001$, $P < 0.001$, $P < 0.001$ and $P = 0.005$ for Group P, respectively). Additionally, in patients receiving esmolol, decreases in IOP at time points of 1, 3 and 5 min after intubation were higher when compared with the patients in Group P ($P = 0.001$, $P < 0.001$ and $P = 0.008$, respectively). MAP at 1 min after intubation in Group D was significantly

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Table 1. Changes in intraocular pressure, mean arterial pressure and heart rate.

				After intubation			
	Baseline	After pretreatment	After induction	1 min	3 min	5 min	10 min
IOP (mmHg)							
Group D ($n = 2020$)	13.5 ± 2.9	10.9 ± 2.4‡	9.4 ± 2.1	10.4 ± 2.5*‡	9.4 ± 1.8*‡	8.7 ± 1.8*‡	8.1 ± 1.5*‡
Group E ($n = 20$)	13.3 ± 3.4	11.5 ± 2.8$^{\sharp}$	9.7 ± 2.9	15.2 ± 3.6†	12.4 ± 2.7‡	11.2 ± 2.5†	10.3 ± 2.3
Group P ($n = 20$)	13.3 ± 2.8	13.2 ± 3.2	9.8 ± 2.3	19.0 ± 3.5	16.3 ± 3.0	13.7 ± 2.6	11.1 ± 2.5
MAP (mmHg)							
Group D ($n = 20$)	89.8 ± 13.2	81.9 ± 11.4‡	76.3 ± 11.2$^{\sharp}$	80.5 ± 12.7§†	77.4 ± 10.1	76.7 ± 10.0	76.6 ± 8.4
Group E ($n = 20$)	93.8 ± 13.1	87.7 ± 9.8$^{\sharp}$	79.6 ± 10.3	91.9 ± 7.7	86.1 ± 10.1	84.6 ± 9.0	80.3 ± 7.5
Group P ($n = 20$)	91.1 ± 8.8	90.6 ± 8.8	82.1 ± 8.2	90.4 ± 9.9	83.8 ± 8.2	83.2 ± 5.8	82.1 ± 8.2
HR (beats min^{-1})							
Group D ($n = 20$)	83.4 ± 7.5	69.5 ± 8.1‡	65.7 ± 8.4§‡	72.6 ± 8.5*‡	71.3 ± 6.4*‡	70.4 ± 7.2*‡	67.8 ± 11.6§†
Group E ($n = 20$)	81.8 ± 10.9	71.5 ± 10.3‡	71.1 ± 9.8‡	88.1 ± 8.4	83.5 ± 7.9	81.9 ± 8.3	75.5 ± 5.1
Group P ($n = 20$)	86.6 ± 11.2	87.6 ± 12.2	83.0 ± 13.9	97.2 ± 14.1	89.4 ± 11.1	88.2 ± 12.3	86.9 ± 9.8

IOP: intraocular pressure; MAP: mean arterial pressure; HR: heart rate.
Data are presented as mean ± SD.
$^{\S}P < 0.05$ and $^{*}P < 0.001$ vs. Group E; $^{\sharp}P < 0.05$, $^{\dagger}P < 0.01$ and $^{\ddagger}P < 0.001$ vs. Group P.

less than that in Groups E and P ($P = 0.012$ and $P = 0.005$, respectively) (Table 1).

Both esmolol and dexmedetomidine have been used for the attenuation of the adrenergic response to laryngoscopy and tracheal intubation. There is a dose-dependent risk of hypotension and bradycardia before laryngoscopy when esmolol and dexmedetomidine are combined with anaesthesia induction agents. We preferred single-bolus low doses for both drugs in our study instead of an infusion or higher dose administration in order to prevent the potential risk of bradycardia or hypotension. However, especially for esmolol, no consensus has been reached regarding the optimum dose nor the mode and timing of its delivery [1]. Bensky and colleagues [2] suggested that small doses of esmolol (0.2 or 0.4 mg kg^{-1}) may block the increases in HR and BP resulting from laryngoscopy and intubation. Nevertheless, Kovac and colleagues [3] reported that esmolol 1.5 mg kg^{-1} given 30 s prior to induction was found to blunt the maximum increase in HR but not MAP or IOP. Regarding dexmedetomidine, Jaakola and colleagues [4] have reported attenuation of the increase in the HR and arterial pressure during intubation by a bolus injection of 0.6 μg kg^{-1} dexmedetomidine, 10 min before anaesthesia induction, which also decreased intra-operative IOP and anaesthetic requirements for thiopentone and isoflurane. The continuous i.v. infusion of dexmedetomidine has been shown to decrease propofol requirements in volunteers and patients [5,6]. In our study, single i.v. dose of dexmedetomidine (0.5 μg kg^{-1}) blunted the haemodynamic and IOP responses to tracheal intubation. Secondarily, the single-bolus dose administration of dexmedetomidine in contrast to the continuous i.v. infusion used in previous studies also proved to reduce the propofol requirements for induction of anaesthesia. However, esmolol, with the dose of 0.5 mg kg^{-1} used in this study, was shown to be ineffective in the attenuation of IOP and haemodynamic responses to tracheal intubation.

In conclusion, the results of this study emphasise that dexmedetomidine is more effective than esmolol in preventing the haemodynamic and IOP responses to tracheal intubation in ASA I–II patients. In order to further evaluate the effects of esmolol, additional studies should be planned to assess the optimum dose, mode and delivery timing of this drug. Furthermore, it should be noted that this study included only healthy patients and does not reflect the effects of these drugs on patients with a history of hypertension or glaucoma.

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Postoperative deep venous thrombosis in a woman with congenital afibrinogenaemia treated with fibrinogen concentrates

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EDITOR:
Congenital afibrinogenaemia is a rare coagulation disorder with an estimated prevalence of one in one million [1]. The risk of abnormal bleeding during a surgical procedure is high but can be avoided by the administration of fibrinogen concentrates [2,3]. The administration of coagulation proteins in patients deficient in coagulation factors can be complicated by venous or arterial thrombosis [1]. We describe the case of a patient with congenital afibrinogenaemia admitted for enucleation of her right eye whose postoperative course was complicated by a deep venous thrombosis.

Case report

A 30-yr-old Algerian female (height 1.62 m, weight 56 kg), known to have congenital afibrinogenaemia, was referred to the ophthalmology department for the enucleation of her right eye. At birth she had suffered from an umbilical cord haemorrhage. The diagnosis of congenital afibrinogenaemia had been made at the age of 5 yr when she presented with a large musculocutaneous haematoma. The parents were asymptomatic. The patient had seven siblings: one sister died from haemorrhage at birth, two brothers were affected with the same haemorrhagic disease and one brother and three sisters were asymptomatic. In 1986, 1997 and 2006 the patient underwent dental extractions without complication after administration of fresh frozen plasma. She was being treated for menorrhagia with normegestrol and an oral iron preparation for the associated iron-deficiency anaemia. At the age of 5 yr she had suffered trauma to the right eye complicated by intraocular haemorrhage. Since then her vision had been poor and in recent months she had suffered from chronic pain. The ocular pain was not relieved by the usual analgesics and enucleation was suggested and accepted by the patient.

The preoperative haematological tests' results are shown in Table 1. Fibrinogen, determined by a functional assay (von Clauss method), was $<0.30\,g\,L^{-1}$, and the level determined by an immunological assay was $<0.50\,g\,L^{-1}$. The plasma concentrations of the other coagulation factors were normal. Immediately before the surgical procedure, the patient received 4.5 g of fibrinogen (Clottagen®; LFB, Lille, France), the target being a plasma concentration of fibrinogen $\geqslant 1\,g\,L^{-1}$.

The enucleation of the right eye was carried out under general anaesthesia. The eye content was replaced by a polymer-coated hydroxyapatite implant. The surgical procedure was uneventful, without abnormal surgical bleeding. She received a further 1.5 g of fibrinogen on the first and the second postoperative days (Table 1). On the fourth postoperative day, she complained of pain in her left calf. Compression ultrasound examination of the lower limb veins revealed thrombosis of the left fibular veins at the mid-calf extending over 3 cm. Contrary to proximal thrombosis, the therapeutic

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