Ephedrine, dopamine, or dobutamine to treat hypotension with propofol during epidural anesthesia

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Purpose: To compare the efficacy of ephedrine, dopamine and dobutamine for circulatory support during thoracic epidural anesthesia after anesthetic induction with propofol.

Methods: Forty patients undergoing lobectomy or mastectomy were divided into four groups of 10: a control group received no vasopressor; an ephedrine group received 5 mg ephedrine when the mean arterial pressure (MAP), measured every 2.5 min, decreased by 10% from baseline; dopamine and dobutamine groups received 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dopamine or 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dobutamine from five minutes after epidural injection of local anesthetic to the end of tracheal intubation. Anesthesia was induced with 2 $mg \cdot kg^{-1}$ propofol. The MAP and heart rate (HR) were measured at baseline, 20 min after epidural injection, three minutes after propofol, and one minute after tracheal intubation.

Results: In the control group, MAP and HR decreased from 86 ± 9 mmHg, 74 ± 8 bpm to 62 ± 9 mmHg; $P < 0.0001$, 60 ± 8 bpm; $P = 0.0003$ after propofol. After tracheal intubation, MAP was restored to (81 ± 13 mmHg, 70 ± 13 bpm). In the ephedrine, dopamine, and dobutamine groups, MAP and HR remained unchanged during epidural anesthesia and propofol induction. However, after tracheal intubation, MAP and HR increased in the ephedrine (104 ± 11 mmHg; $P = 0.004$, 87 ± 11 bpm; $P < 0.0001$) and dobutamine (117 ± 13 mmHg; $P = 0.0005$, 100 ± 11 bpm; $P < 0.0001$) groups, but not in the dopamine group compared with baseline.

Conclusion: Dopamine is preferable to ephedrine and dobutamine in providing hemodynamic stability during propofol induction and tracheal intubation following epidural anesthesia.

Objectif : Comparer les qualités cardiotoniques de l'éphédrine, de la dopamine et de la dobutamine pendant l'anesthésie péridurale thoracique suivant une induction au propofol.

Méthode : Quarante patients devant subir une lobectomie ou une mastectomie sont répartis en quatre groupes de 10 : un groupe témoin, sans vasopresseur; un groupe éphédrine, avec 5 mg d'éphédrine quand la tension artérielle moyenne (TAM), mesurée toutes les 2,5 min, baisse de 10 % comparée à la mesure de base; des groupes dopamine et dobutamine, avec 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ de dopamine ou 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ de dobutamine 5 minutes après l'injection péridurale d'anesthésique local et jusqu'à la fin de l'intubation endotrachéale. L'anesthésie est induite avec 2 $mg \cdot kg^{-1}$ de propofol. La TAM et la FC sont mesurées au début, 20 min après l'injection péridurale, 3 minutes après la dose de propofol et une minute après l'intubation.

Résultats : Dans le groupe témoin, la TAM et la FC diminuent de 86 ± 9 mmHg, 74 ± 8 bpm à 62 ± 9 mmHg; $P < 0{,}0001$, 60 ± 8 bpm; $P = 0{,}0003$ après le propofol. Après l'intubation, la TAM revient aux valeurs de base (81 ± 13 mmHg, 70 ± 13 bpm). Avec l'éphédrine, la dopamine et la dobutamine, la TAM et la FC ne changent pas pendant l'anesthésie péridurale et l'induction au propofol. Mais, après l'intubation, la TAM et la FC s'élèvent, comparées aux mesures de base, avec l'éphédrine (104 ± 11 mmHg; $P = 0{,}004$, 87 ± 11 bpm; $P < 0{,}0001$) et la dobutamine (117 ± 13 mmHg; $P = 0{,}0005$, 100 ± 11 bpm; $P < 0{,}0001$), mais non avec la dopamine.

Conclusion : À la suite d'une anesthésie péridurale, la dopamine est préférable à l'éphédrine et à la dobutamine pour assurer la stabilité hémodynamique pendant l'induction au propofol et l'intubation.

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AN anesthetic technique combining epidural anesthesia with light general anesthesia for thoracic surgery is well-known. We previously reported that the hypotensive effects of propofol add to those of epidural anesthesia, resulting in a profound decrease in mean arterial pressure.[1] Both epidural anesthesia[2] and propofol[3] decrease sympathetic nerve activity, producing marked hypotension; propofol also directly reduces vascular smooth muscle tone and cardiac contractility.[4–6] To prevent these hypotensive effects, many drugs were used to maintain hemodynamic stability. Ephedrine is conventionally given by for bolus injection[7] whereas dopamine and dobutamine are usually administered by continuous infusion.[7–9] The purpose of the study was to compare the efficacy of ephedrine, dopamine, and dobutamine for circulatory support when propofol is used as an induction agent during thoracic epidural anesthesia.

Methods

With approval from our Human Research Review Committee and informed consent from each patient, 40 patients of ASA classification I or II to undergo lobectomy or mastectomy were studied. Patients with hypertension, diabetes mellitus, or those undergoing anticoagulant therapy, were excluded. All patients received premedication with 0.5 mg benzodiazepine *po* 1.5 hr before induction of anesthesia. Arterial blood pressure was measured by oscillometer every 2.5 min using a cuff, and MAP was calculated electronically (BSM-8500, Nihon-Koden, Tokyo, Japan). Heart rate (HR) was determined electrocardiographically (BSM-8500, Nihon-Koden, Tokyo, Japan).

Patients were randomly divided into four groups of 10: a control group which received no vasopressor. An ephedrine group received 5 mg ephedrine when mean arterial pressure (MAP) decreased by 10% from the baseline after epidural injection of local anesthetic. When arterial pressure was still decreased by 10% from baseline value 2.5 min after receiving 5 mg ephedrine, the dose was repeated. Dopamine and dobutamine groups received 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dopamine or 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dobutamine continuously, starting five minutes after epidural injection of local anesthetic and continuing to the end of tracheal intubation. After this study, vasopressors were given as needed to maintain hemodynamic stability.

Epidural technique

All patients received 500 mL hydroxyethyl starch (HES) solution *iv* at a rate of 15 $mL \cdot kg^{-1} \cdot hr^{-1}$ for volume loading beginning 20 min before epidural anesthesia. This was followed by infusion of acetated Ringer's solution. With patients in the lateral decubitus position, infiltration of 3-5 mL lidocaine 1% for local anesthesia before insertion of a 17-gauge Tuohy needle at the T_{5-6} or T_{6-7} interspace. An epidural catheter was inserted 3 cm cephalad and the patient was placed supine. A volume of 10 mL mepivacaine 2% was injected epidurally over one minute. Twenty minutes after epidural injection, the spread of analgesia was determined by response to pin-prick.

Induction of general anesthesia with propofol

General anesthesia was induced with 2 $mg \cdot kg^{-1}$ propofol given at a rate of 200 $mg \cdot min^{-1}$ followed by a continuous infusion of 4 $mg \cdot kg^{-1} \cdot min^{-1}$ via a constant infusion pump (STC-525X, Terumo, Tokyo, Japan). Vecuronium, 0.15 $mg \cdot kg^{-1}$ *iv*, was administered after the bolus of propofol, and the trachea was intubated three minutes later.

Measurements

In all groups, MAP and HR were measured at baseline, 20 min after epidural injection, three minutes after propofol induction, and one minute after tracheal intubation. Once measurements were obtained, the administration of anesthesia was left to the discretion of the attending anesthesiologist.

Data analysis

The spread of epidural block was compared using the Mann-Whitney U test, and the values for the upper and lower levels of analgesia were presented as the median and range. MAP and HR data were analyzed by two factor ANOVA and comparisons among the four groups were followed by Scheffe's post hoc procedure. Sex was compared using chi-square analysis. All analyses were performed using StatView (Abacus, Berkeley, CA), and values were expressed as means ± SD. A value of $P < 0.05$ was considered significant.

TABLE Demographic characteristics of the four groups

	Control (n=10)	*Ephedrine (n=10)*	*Dopamine (n=10)*	*Dobutamine (n=10)*
Age (yr)	59 ± 14	54 ± 10	58 ± 13	52 ± 14
Sex (M/F)	5/5	4/6	5/5	5/5
Height (cm)	158 ± 9	161 ± 8	154 ± 10	161 ± 9
Weight (kg)	56 ± 6	61 ± 8	55 ± 10	59 ± 11
MAP (mmHg)	86 ± 9	87 ± 14	84 ± 8	87 ± 17
HR (bpm)	74 ± 8	67 ± 8	68 ± 14	71 ± 13

Values are expressed as means ± SD.
MAP= mean arterial pressure. HR= heart rate.
There were no significant differences among the four groups.

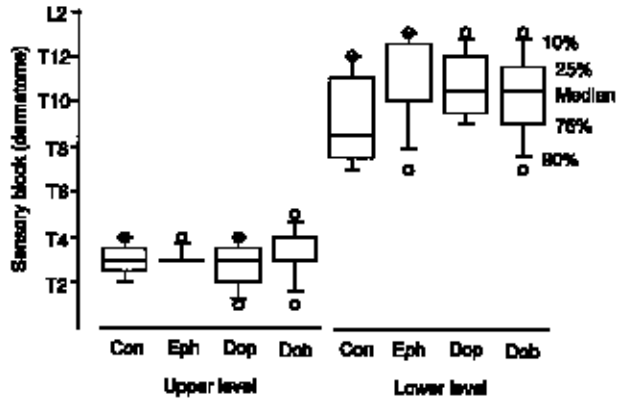

FIGURE 1 The upper and lower levels of the four groups are shown compared by box plot. The median and range of blockade for each group are noted, as is the % of patients obtaining the noted level of block. Open circles indicate n of 10 or 90% of patients.
Con: control group; Eph: ephedrine group; Dop: dopamine group; Dob: dobutamine group.

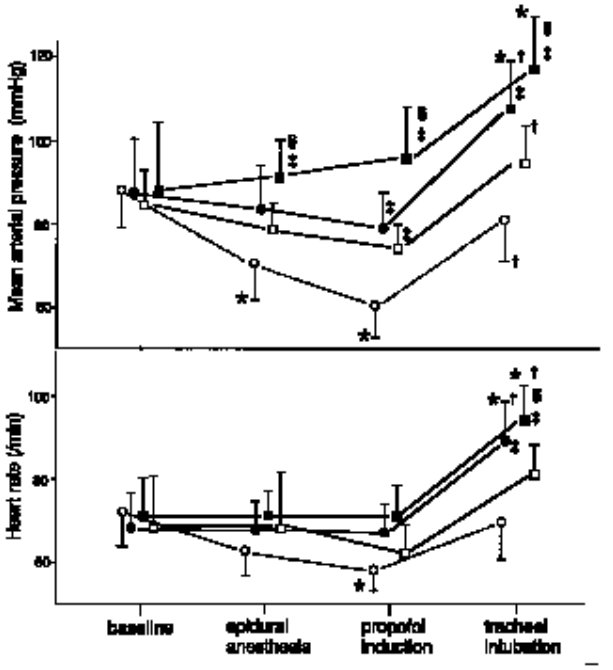

FIGURE 2 Comparative changes in mean arterial pressure (upper figure) and heart rate (lower figure) during propofol induction in the control, ephedrine, dopamine, dobutamine groups.
Open circle = control group, solid circle = ephedrine group, open square = dopamine group; solid square = dobutamine group. Mean ± SD. * $P < 0.05$ *vs* baseline; † $P < 0.05$ *vs* propofol induction; † $P < 0.05$ *vs* control group; § $P < 0.05$ *vs* dopamine group.

Results

There were no differences among study groups in the distribution of age, sex, height, weight, baseline mean arterial pressure, or heart rate (Table). The magnitudes and distributions of sensory block were also not different among study groups (Figure 1). In the ephedrine group, the doses of ephedrine were 15 mg (three times) in one of 10 patients, 10 mg (two times) in three patients, 5 mg in five patients, and 0 mg in one patient. In the dopamine and dobutamine groups, all patients received dopamine and dobutamine continuously.

Comparative changes in MAP and HR are shown in Figure 2. In the control group, MAP decreased from 86 ± 9 mmHg to 72 ± 8 mmHg ($P = 0.0038$) following epidural anesthesia, and to 62 ± 9 mmHg ($P < 0.0001$) following propofol induction. After tracheal intubation, MAP was restored to 81 ± 13 mmHg. In the ephedrine, dopamine, and dobutamine groups, MAP remained unchanged during epidural anesthesia and propofol induction. However, after tracheal intubation, MAP increased in the ephedrine (104 ± 11 mmHg) ($P = 0.004$) and dobutamine (117 ± 13 mmHg) ($P = 0.0005$) groups, but not in the dopamine group (93 ± 8 mmHg) compared with baseline values. Differences were found between the control group and ephedrine ($P = 0.0005$) and dobutamine ($P < 0.0001$) groups after tracheal intubation.

In the control group, HR decreased from 74 ± 8 to 60 ± 8 bpm ($P = 0.0003$) following propofol induction. After tracheal intubation, HR recovered to 70 ± 13 bpm. In the ephedrine, dopamine, and dobutamine groups, HR remained unchanged during epidural anesthesia and propofol induction. After tracheal intubation, HR also increased in the ephedrine (87 ± 11 bpm) ($P < 0.0001$) and dobutamine (100 ± 11 bpm) ($P < 0.0001$) groups, but remained unchanged in the dopamine group (80 ± 9 bpm).

Discussion

This study demonstrated that ephedrine, dopamine, and dobutamine are useful in preventing the hypotension produced by the use of propofol as an induction agent during thoracic epidural anesthesia. Furthermore, dopamine is preferable to maintain hemodynamic stability of MAP and HR for induction and tracheal intubation with propofol during epidural anesthesia.

Our previous findings indicated that the use of propofol for induction of general anesthesia during epidural anesthesia augments the hypotension introduced by epidural anesthesia.[1] Ephedrine, dopamine, and dobutamine are vasoactive drugs commonly used for the treatment of hypotension during spinal or epidural anesthesia.[9–13] To prevent hypotension during combined propofol and epidural block, we selected a dopamine infusion at a rate of 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, or dobutamine infusion at 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$, based on reports by Lundberg *et al.*,[13,14] Takasaki *et al.*[7] and our preliminary study. We selected bolus *iv* injection of ephedrine, which is our usual clinical practice.[10,11]

Ephedrine is a mixed-receptor-activating drug:[15] it improves left ventricular contractility during thoracic epidural anesthesia.[12] The MAP was maintained easily at a total dose up to ephedrine (15 mg *iv*) independent of the magnitude of hypotension. When ephedrine was given intravenously, MAP recovered to the preanesthetic level, and no further decrease of MAP occurred in combined propofol induction during epidural anesthesia.

Dopamine acts at alpha-, beta-, and dopaminergic receptors; it also releases norepinephrine and, therefore, has mixed direct and indirect effects. Dopamine, with its joint inotropic and vasoconstrictor profile of action, is considered to be a suitable choice by several investigators during epidural blockade.[13] Ranner *et al.*[8] reported that the hemodynamic effects of an inhalational agent, isoflurane, combined with sympathetic blockade can be countered by dopamine. In this study, 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dopamine effectively counteracted cardiovascular suppression during thoracic epidural anesthesia. We confirmed that this concentration of dopamine when administered during the propofol-thoracic epidural anesthesia intervention also restores MAP to its baseline level.

Dobutamine, a synthetic analogue of dopamine, has predominately beta-1 effects although, at clinical doses, it can act on beta-2 and alpha-1receptors. Thoracic epidural anesthesia reduces arterial blood pressure by blocking cardiac sympathetic nerve activity. These findings support the hypothesis that, to restore the MAP and HR to preanesthetic levels, dobutamine beta-1 effects are desirable as pressor agents for use during combined thoracic epidural anesthesia and propofol. Dobutamine, 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$, is sufficient to restore MAP and HR. However, when widespread sympathetic block, including that of the splanchnic region, is present, blood pooling and decreases in venous return occur, and the use of an alpha-1 agonist, in addition to a beta-1 agonist, may be necessary.

Takasaki *et al.*[16] discussed cardiovascular support drugs during thoracic epidural analgesia: cardiac output was restored by the three drugs to the same degree. However, central venous pressure was increased more with dopamine or dobutamine than with ephedrine, and pulmonary capillary wedge pressure was increased more with dopamine than with ephedrine. Therefore, ephedrine is the best of these three drugs for the control of arterial pressure, and dobutamine is better than dopamine in improving cardiac function during thoracic epidural analgesia. When MAP and HR recovered to pre-anesthetic levels, they increased after tracheal intubation, because thoracic epidural anesthesia could not inhibit the stimulation of tracheal intubation.[17] During tracheal intubation, MAP increased considerably from baseline (20% in the ephedrine group, 34% in the dobutamine group, and only 11% in the dopamine group). Heart rate also increased (30% in the ephedrine group, 41% in the dobutamine group, and only 18% in the dopamine group from baseline values) in response to tracheal intubation. At a dose of 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dopamine increased MAP less than 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ dobutamine. Therefore, the countering effects of dopamine induced less hemodynamic change than ephedrine and dobutamine after tracheal intubation.

In summary, ephedrine, dopamine, and dobutamine prevented hypotension produced by administration of propofol during thoracic epidural anesthesia. Dopamine, 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, was superior because it also maintained hemodynamic stability of MAP and HR even after tracheal intubation.

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