Hemodynamic Effects of Pancuronium and Pancuronium Plus Metocurine in Patients Taking Propranolol

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An endotracheal intubating dose of pancuronium causes an increase in heart rate that could be detrimental to the balance between myocardial oxygen supply and demand.1,2 A combination of pancuronium plus metocurine (MP), however, is essentially free of significant changes in heart rate and blood pressure, implying that this combination may be better suited than pancuronium for patients with coronary artery disease.3 However, many patients with coronary artery disease are receiving β-adrenergic-blocking drugs. These drugs could alter the hemodynamic response to pancuronium or MP.

This study was performed to determine the cardiovascular response to endotracheal intubating dose of pancuronium and MP in patients taking propranolol.

MATERIALS AND METHODS

After Human Investigations Committee approval was obtained, 28 consenting patients scheduled for coronary bypass grafting were studied. All patients were taking propranolol and had normal left ventricular function (ejection fraction > 0.5, left ventricular end diastolic pressure < 15 mmHg). Preoperative medication consisted of diazepam (up to 0.15 mg/kg, orally), morphine (up to 0.15 mg/kg, im), scopolamine (0.2–0.4 mg, im), and nitroglycerin ointment (equivalent to 15 mg), and the morning dose of propranolol.

Monitoring included radial arterial and thermidilution, flow-directed pulmonary arterial catheters and an electrocardiogram. Neuromuscular blockade was monitored continuously by applying transcutaneous stimuli at a frequency of 0.2 Hz over the ulnar nerve at the wrist and recording the thumb adductor response with a force transducer. Time from onset of action to 95% twitch height depression was measured.

After preinduction hemodynamic measurements were obtained, morphine and diazepam were given iv in doses sufficient to abolish the lid reflex and the response to verbal stimuli. After the induction of anesthesia, measurements were performed when the acute hemodynamic response to the anesthetic drugs was completed and the blood pressure and filling pressures had remained stable for three min. After obtaining these postinduction measurements, the patients were distributed consecutively into one of four groups. One group received 0.07 mg/kg iv of pancuronium. A second group received an ED95 X 1 dose of MP (M = 0.072 mg/kg, P = 0.018 mg/kg, Group MP X 1), and a third group was given an ED95 X 2 dose of MP (M = 0.144 mg/kg, P = 0.036 mg/kg, Group MP X 2). The muscle relaxants were administered over a period of 30 s. The last group received no muscle relaxant and served as the control.

Measurements of heart rate (HR), mean arterial blood pressure (BP), mean pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP), central venous pressure (CVP), cardiac index (CI), and systemic vascular resistance (SVR) were made every 2.5 min for 10 min after administering the muscle relaxant. Patients in the control group had measurements made at similar time intervals.

Ventilation with an FiO2 of 1.0 was assisted or controlled throughout the study and monitored with a mass spectrometer to maintain the PaCO2 at 40 ± 5 mmHg and adequate oxygenation. Analyses of arterial blood gases were performed at the preinduction, postinduction, five- and ten-min measurements. The tracheas were intubated after completion of the study, and intubating conditions were noted.

Analysis of variance was used for statistical analysis of the hemodynamic variables of each group from the postinduction to the ten-min measurement, and paired Student’s t tests were used to compare hemodynamic changes associated with induction of anesthesia. Unpaired Student’s t test were used to evaluate for differences in neuromuscular blockade. Differences were considered statistically significant at P < 0.05. Data are reported as means ± SEM.

RESULTS

Patients in the four groups were alike in age, weight, number of coronary artery grafts, induction doses of
Only three of seven patients who received MP ED$_{95}$ \( \times 1 \) attained this level of neuromuscular blockade and coughed with endotracheal intubation. Endotracheal intubating conditions were good in all other patients.

**DISCUSSION**

In distinction to previous studies concerning cardiovascular effects of muscle relaxants,1–3 our patients preoperatively had received the \( \beta_1\)-\( \beta_2 \) receptor-blocking drug, propranolol, 1 to 4 hours prior to surgery. Although an isoproterenol challenge was not performed and the degree of \( \beta \) blockade not directly assessed in the present study, Pine et al.4 stated that \( \beta \) blockade remains for up to 8 hours after administration of an oral dose of propranolol. The patients in this study received propranolol within 4 hours of surgery.

In using the combination of metocurine and pancuronium in healthy patients not receiving \( \beta \) blockers, Lebowitz et al.5 showed potentiation of neuromuscular blockade without concomitant changes in heart rate and blood pressure. Pancuronium administered alone, however, produced an increase in heart rate. Therefore,

morphine and diazepam, and daily doses of propranolol (116 mg ± 61, mean ± SD). Arterial blood-gas values were in the normal ranges throughout the study.

The hemodynamic changes are summarized in figures 1 and 2. Induction of anesthesia was associated with significant decreases in SVR and BP (\( P < 0.05 \)) that were of the same magnitude in all groups. Induction of anesthesia did not significantly alter other hemodynamic variables.

Heart rate and CI increased from the postinduction value in all relaxant groups at 2.5 min, but the changes were not significant over 10 min (\( P > 0.05 \)). Significant hemodynamic changes did not occur in any other hemodynamic variable in any group.

The time from onset of action to 95% twitch height reduction showed significant differences among the groups. Group MP \( \times 2 \) had a significantly shorter time from onset to 95% twitch height reduction (171 ± 88 seconds, mean ± SD) than Group P (315 ± 157 s), and both produced a shorter time to 95% reduction compared with the group MP \( \times 1 \) (470 ± 185 s), \( t \) tests, \( P < 0.05 \)).

FIG. 1. Shown are the responses of heart rate and mean arterial blood pressure to the administration of morphine and diazepam, then the muscle relaxants. The values are means ± SEM. *Significant change related to preinduction in each group, \( t \) test, \( P < 0.05 \).

FIG. 2. The effects of the anesthetic induction then muscle relaxants on systemic vascular resistance and cardiac index are demonstrated. The values are means ± SEM. *Significant change related to preinduction in each group, \( t \) test, \( P < 0.05 \).
combining reduced doses of each agent minimized their individual hemodynamic effects while producing excellent neuromuscular blockade. The present study confirms the absence of clinically significant hemodynamic changes when MP is used in patients receiving β-blocking drugs.

The results of our study also reveal that an intubating dose of pancuronium did not increase heart rate. This finding conflicts with the study by Morris et al., who observed that while patients receiving propranolol generally had lower resting heart rates, they also had greater increases in heart rate after pancuronium than those patients who were not receiving propranolol. Although different anesthetics were used (narcotic vs. halothane), we believe the difference between Morris’ study and our study can be explained by the combined autonomic effects of a β-blocking agent, pancuronium, and a muscarinic-blocking drug. Pancuronium increases HR by two mechanisms. It releases norepinephrine and it also inhibits reuptake of norepinephrine. The second mechanism through which pancuronium causes an increased HR is vagal blockade. The patients in Morris’ study were not premedicated with an antimuscarinic drug, while all of the patients in this study received scopolamine. Pancuronium could release norepinephrine and block its reuptake; however, the hemodynamic effects of this norepinephrine would be blocked by propranolol. Pancuronium also could not act as a vagolytic agent in our study, because the muscarinic receptors probably were blocked by scopolamine. Therefore, both mechanisms through which pancuronium increases HR were blocked.

The situation is complicated further by applying the findings of Roizen et al. Serum norepinephrine decreased after the administration of pancuronium but did not decrease when pancuronium was preceded by an antimuscarinic drug. Roizen et al. suggested that vagal blockade increases HR and BP which, in turn, activates baroreceptors to reflexly decrease norepinephrine output. In our study, the combination of scopolamine followed by pancuronium could have helped maintain the norepinephrine levels that had been increased by pancuronium.

The β-receptor hemodynamic effects of norepinephrine are blocked by β-blocking drugs, however, since the α effects of norepinephrine are not blocked by propranolol, SVR may increase without an increase in heart rate after the administration of pancuronium. This change did not occur in our study.

The doses used in our study were those suggested by Lebowitz et al., and could have been the cause of only three patients attaining 95% twitch height reduction in the MP × 1 group. This study could have been strengthened by pre-determining the ED₉₅ of each relaxant.

The combination of metocurine and pancuronium has an advantage over pancuronium given alone. Because of its more rapid onset of action, MP × 2 is a better choice than 0.07 mg/kg of pancuronium if rapid endotracheal intubation is desired.

In summary, MP and pancuronium used in the presence of propranolol are not associated with significant hemodynamic changes. Significantly, pancuronium does not cause tachycardia in these patients.

REFERENCES