Hemodynamic Effects of Gallamine during Halothane–Nitrous Oxide Anesthesia

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Halothane anesthesia may result in decreased cardiac output and hypotension.[1-2] Gallamine (Flaxedil) should be an ideal neuromuscular blocking agent during halothane anesthesia because of its profound anticholinergic effect on the heart.[3] The resulting tachycardia could attenuate the hemodynamic depression produced by halothane. This study reports the degree and duration of hemodynamic changes following gallamine during operation with halothane–nitrous oxide anesthesia and controlled ventilation.

METHODS

Nineteen patients without cardiac disease undergoing peripheral or abdominal operations not associated with significant blood loss and not requiring prior neuromuscular blockade were studied. All were premedicated with morphine (8–15 mg) and scopolamine (0.4 mg) 90 minutes before operation. Anesthesia was induced with thiamylal (Surital), 150–300 mg, followed by succinylcholine to facilitate tracheal intubation. Anesthesia was maintained with 0.5 to 1.0 per cent delivered halothane and 60 per cent nitrous oxide in oxygen using a semiclosed circle absorption anesthesia system. Ventilation was controlled with a volume ventilator to maintain P_{aCO_2} near 30 torr. Catheters were placed percutaneously in a radial or ulnar artery and external or internal jugular vein and connected to appropriate transducers.

After at least an hour of anesthesia, 1.0 mg/kg (nine patients) or 2.0 mg/kg (ten patients) of gallamine was rapidly injected intravenously. Mean arterial pressure and mean central venous pressure were recorded continuously for 3 minutes before and 20 minutes after administration of the neuromuscular blocker. Cardiac output was measured by the dye-dilution method with indocyanine green dye and a Beckman cardiodensitometer immediately before and 3, 10, and 20 minutes after gallamine administration. Heart rate was counted from the blood pressure record. Cardiac index, stroke volume index, and systemic vascular resistance were calculated.

Data were analyzed for significance with Student's t test ($P < 0.05$ was considered significant).

RESULTS

Hemodynamic changes following both doses of gallamine are summarized in figure 1.

Three minutes after 1 mg/kg of gallamine (73.3 ± 4.6 mg), heart rate increased 33 beats/min ($P < 0.05$) and cardiac index 0.7 l/min/m² ($P < 0.05$). No other measurement was significantly different at this time. After 10 and 20 minutes, cardiac index was no longer significantly different from control, but the sustained elevation in heart rate resulted in a decreased stroke volume index ($P < 0.05$).

Significant changes 3 minutes after 2 mg/kg of gallamine (130 ± 5.1 mg) were increased heart rate (43 beats/min) and cardiac index (1.1 l/min/m²) and decreased systemic vascular resistance (44 to 31 torr/l/min/m²). Cardiac index decreased after 3 minutes but remained significantly above control after 10 and 20 minutes. Heart rate remained elevated ($P < 0.05$) and stroke volume index was decreased ($P < 0.05$) at these times.

Mean arterial pressure increased about 10 torr and central venous pressure decreased 2–3 torr in both groups ($P < 0.05$). There was no significant difference between the two groups with respect to control values or degree of change in any measurement after gallamine administration.

DISCUSSION

Gallamine (1 and 2 mg/kg) produced sustained increases in heart rate for at least 20 minutes. The maximum increases were nearly the same after 1 and 2 mg/kg of gallamine, suggesting that the degree of tachy-

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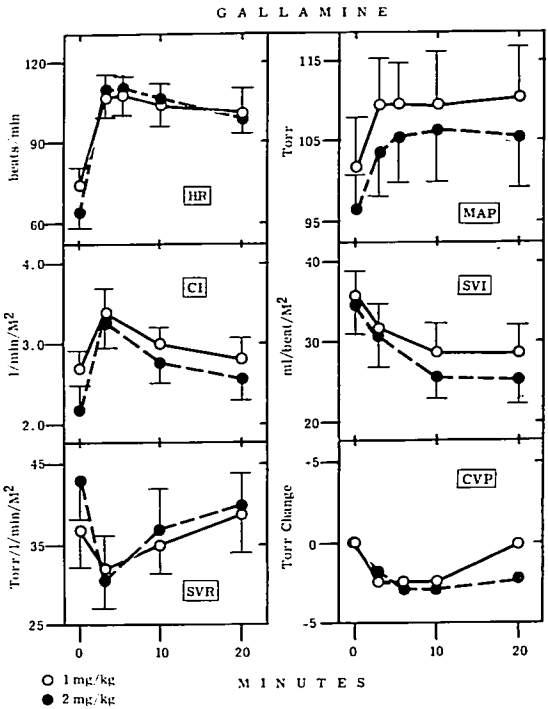

FIG. 1. Hemodynamic changes (mean ± SE) following 1 mg/kg (clear symbols) or 2 mg/kg (solid symbols) of gallamine. HR, heart rate; MAP, mean arterial pressure; CI, cardiac index; SVI, stroke volume index; SVR, systemic vascular resistance; CVP, central venous pressure.

cardia was independent of the dose used. This agrees with the study of Eisele *et al.*,[4] who reported maximum tachycardia after 80–100 mg of gallamine. Larger doses, even to 400 mg, did not further increase the heart rate.[4]

Increased heart rate was primarily responsible for the initial elevation in cardiac index, but with time the cardiac output and stroke volume decreased. A sympathomimetic action of gallamine on the heart has been demonstrated with *in-vitro* animal atrial preparations and proposed as a possible explanation for the immediate elevation in heart rate, cardiac output, and occasional cardiac dysrhythmias that follow gallamine administration.[5] Our high dose was near the concentration of gallamine used for the *in-vitro* studies (3 mg/kg) and might be expected to produce a more prolonged sympathomimetic effect than seen after our low dose. Indeed, cardiac index remained significantly above control after 10 and 20 minutes only in those receiving 2 mg/kg of gallamine. In contrast, heart contractile force was not changed after 2.6 mg/kg gallamine administered to patients during cardiopulmonary bypass.[6]

Mean arterial pressure increased only slightly after 1 or 2 mg/kg of gallamine despite the increased cardiac output. Kennedy and Farman[7] observed similar blood pressure changes with equivalent alterations in cardiac

output and heart rate following 0.5–1.0 mg/kg of gallamine. They also measured a decreased systemic vascular resistance after gallamine and attributed this to passive arteriolar distention secondary to the increased cardiac output.

Central venous pressure has now been demonstrated to decrease after gallamine, *d*-tubocurarine,[8] and pancuronium.[8] It is conceivable that loss of muscle tone with muscle paralysis could reduce tissue pressure around veins and allow venodilation, with subsequent decreased intravascular pressure. However, we have observed a decrease even when neuromuscular blockers were injected during succinylcholine-induced paralysis. In addition, this decreased central venous pressure has not been correlated with changes in cardiac output.

Anesthetic depth and surgical stimulation may alter hemodynamic responses to neuromuscular blockers. Although end-tidal halothane concentrations were not determined, the gas flows in all studies were similar. All measurements were made during a time when surgical stimulation was not judged to be changing.

Summary

The cardiac anticholinergic effect of gallamine should make this drug an ideal neuromuscular blocker during halothane anesthesia. The resulting tachycardia could attenuate decreased blood pressure and cardiac output during halothane administration. We found that 1–2 mg/kg of gallamine produced sustained increases in mean arterial pressure and heart rate for at least 20 minutes. However, cardiac index was elevated only transiently, and 3 minutes after gallamine administration decreased towards values present during nitrous oxide–halothane anesthesia alone. Stroke volume decreased as heart rate remained elevated. Therefore, the sustained elevation in heart rate and mean arterial pressure may not always reflect a less depressed circulation as reflected by cardiac output several minutes after gallamine administration. These data do not support a positive inotropic action of gallamine in anesthetized patients.

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