

Effect of pancuronium and pethidine on heart rate and blood pressure in ventilated infants

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SUMMARY To investigate cardiovascular effects in 32 ventilated neonates, given either pancuronium or pethidine, computer based data were analysed for five minutes preceding and for 20 minutes after administration of the drugs. Heart rate and direct mean arterial pressure remained unchanged but arterial pressure variability decreased with each drug.

Pancuronium, a competitive, non-depolarising, neuromuscular blocking agent is often used in conjunction with mechanical ventilation in newborn infants. It may have atropine like side effects. Increases in heart rate and blood pressure in both children and adults have been reported.¹ As would be expected with less vagally modulated hearts, studies generally show no change in infants' blood pressure though tachycardia has been reported.² There has been one anecdotal report of hypotension in association with pancuronium³ but there is no pharmacological basis for this effect as ganglion blockade and histamine release are negligible.¹ Theoretically changes in intrathoracic pressure associated with removal of spontaneous breathing effort may, however, decrease venous return and cardiac output; these in turn may lead to hypotension if ventilator settings are not appropriately adjusted, particularly in the presence of hypovolaemia.

Opiates are also recommended to facilitate ventilation, and pethidine (a synthetic opiate) is extensively used in our unit. Though it may produce transient orthostatic hypotension, studies have shown no effect on heart rate or blood pressure in supine unanaesthetised adults,⁴ though a reduction in both was seen in anaesthetised patients.⁵ We know of no relevant published reports concerning neonates.

We have investigated the possible adverse cardiovascular effects of these commonly used drugs and their influence on blood pressure instability using data recorded on a microcomputer.

Patients and methods

Thirty two infants admitted to the neonatal unit at

this hospital were enrolled in the study. All were being ventilated for respiratory distress syndrome and had an umbilical artery catheter in the thoracic aorta (Neocath Biomedical Sensors Ltd, High Wycombe, Buckinghamshire). None had received any drug except vitamin K and no colloid had been given in the hour preceding the study; skin perfusion, capillary filling, and urine output indicated normovolaemia. Procedures likely to affect the measurements were not carried out in the 15 minutes before, or during the study time of 20 minutes. The infants were each given a first dose of either pancuronium (0.1 mg/kg) or pethidine (standard analgesic dose 1.0 mg/kg) to assist ventilation after independent assessment by house officers, the study being complete when there were 16 consecutive infants in each group. The mean weight of those receiving pancuronium was 1100 g (range 640–2500) and the mean gestational age was 28 weeks (range 25–33). In the group receiving pethidine the mean weight was 1000 g (range 480–1800) and mean gestational age 28 weeks (range 25–31).

Blood pressure signals from a transducer (Medex MX800, Medex Inc, Haslingden, Rossendale, Lancashire) coupled to the umbilical artery catheter of each infant were relayed to a neonatal monitor (Model 431A Tektronix Ltd, Harpenden, Hertfordshire) that was interfaced with an analog digital converter and Apple IIe microcomputer. This method was chosen in preference to intermittent recording to produce the detail and continuity of a chart recorder but with more flexibility for storage and analysis of the data. Machine code software was designed to collect waveforms over a 20 second period and derive the heart rate, systolic pressure by averaging the peaks, and true mean arterial pressure (MAP), by analysis of the waveforms (digitising rate 50/second). When considering the effect of the drugs, MAP values were compared, MAP representing the complete cardiac cycle and forming the basis of cerebral perfusion pressure calculation. As the waveforms were undamped, judged by the presence of a dicrotic notch, systolic pressure was accurate and used to derive the coefficient of variation as a measure of blood pressure instability based on the formula: coefficient of variation = [standard deviation/average systolic pressure]

$\times 100\%/20$ second collecting phase. This required less microprocessing time than making calculations based on MAP.

The records of heart rate, MAP, and coefficient of variation, together with a marker when the drug was administered, were stored (time intervals being indicated) on floppy discs, one to two records per minute being derived, 20 seconds sampling time/20 seconds processing time for each cycle.

Results

The records were averaged for the five minutes preceding then at 0 to 5, 5 to 10, 10 to 15, and 15 to 20 minute intervals after the drug had been given (figure). As there were one or two original data points a minute, each derived data point represented about seven values. Using the unpaired *t* test

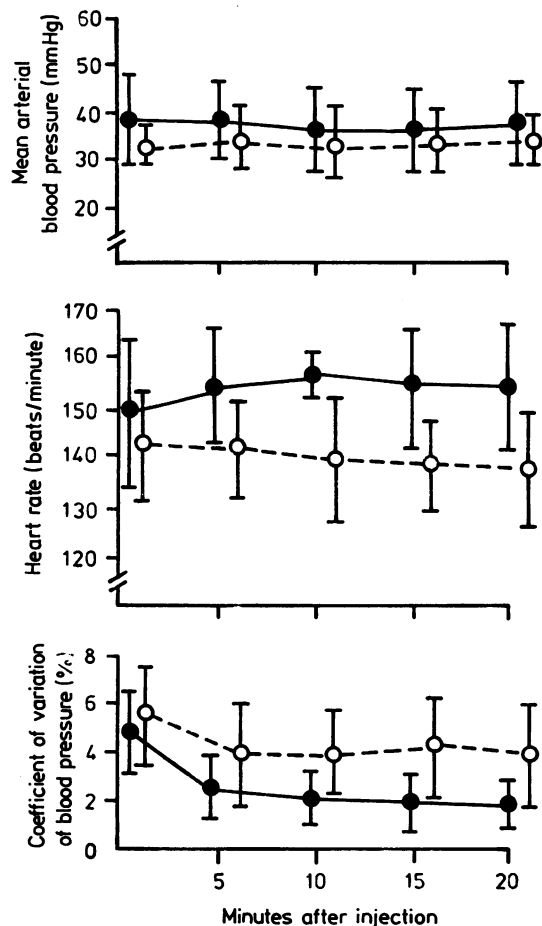


Figure Effects of pancuronium (—●—) and pethidine (---○---).

we found no significant differences between the pre-dose values of heart rate, MAP, or coefficient of variation between the groups. Analysis of variance showed no significant changes in heart rate or MAP after the dose of pancuronium or pethidine, though there was a tendency for heart rate to rise with pancuronium and fall with pethidine. A significant reduction ($p < 0.001$) was observed in the coefficient of variation of systolic arterial pressure at each time point after pancuronium (from 5.0% to between 1.9% and 2.6%) and after pethidine (from 5.8% to between 4.0% and 4.3%).

Discussion

Fluctuation of MAP and cerebral blood flow velocity may be associated with periventricular haemorrhage in preterm ventilated infants, and stabilisation may reduce the incidence.⁶ In this study both pethidine and pancuronium reduced fluctuation in MAP with no significant change in heart rate or MAP: thus they can both be used in ventilated infants without increasing the risk of cerebral ischaemia. After the administration of pancuronium the heart rate did not rise to the same extent as in children and adults, presumably because there is less vagal tone in neonates. There was a highly significant fall in coefficient of variation after the administration of both drugs (from 5.0% to an average of 2.1% after pancuronium and from 5.8% to an average of 4.1% after pethidine).

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