FACTORS AFFECTING PLASMA CONCENTRATIONS OF LOCAL ANALGESIC DRUGS

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Little of a quantitative nature is known about the factors which influence the absorption of local analgesic drugs from the site of injection or application into the blood stream. The present work is an attempt to elucidate the relative importance of some of these factors.

Patients were anaesthetized with a light general anaesthetic and one of two local techniques—either epidural block or intercostal regional block (Farman, Gool and Scott, 1962) depending upon the intended operative procedure. Lignocaine was the first drug investigated and the various series repeated using prilocaine. The dose of analgesic drug was 400 mg in every patient and the injections were made over a period of one minute. In certain groups, adrenaline in a concentration of 1/200,000 or 1/80,000 was added to the analgesic solution used. Venous blood samples were withdrawn at 5, 10, 15, 20, 30 and 60 minutes from the end of injection and analyzed for concentration of drug in the plasma.

Choice of drug. When used in plain solution, lignocaine gives mean values some 40–50 per cent greater than prilocaine (Citanest).

Possible reasons for the lower levels with prilocaine are slower absorption (lignocaine has greater vasodilator power), different distribution in blood (partition between cells/plasma) and more rapid degradation.

Site of injection. Differences here presumably reflect the varying vascularity of the tissues at site of block. Significantly lower plasma concentrations are found after epidural block compared with intercostal regional block when similar analgesic solutions are used.

Adrenaline. The plasma concentrations obtained with plain lignocaine are reduced by approximately 25 per cent if adrenaline 1/80,000 is added to the solution. This effect is not seen with prilocaine.

Concentration of solution. Provided the total dose of the drug remains the same (400 mg in present series), altering the concentration of the analgesic solution in the range 1–2 per cent makes no difference to plasma concentrations. High concentrations (4 per cent) do give increased plasma levels when a total dose of 400 mg is maintained.

REFERENCE

SOME CIRCULATORY EFFECTS OF ATROPINE IN ANAESTHETIZED PATIENTS

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Observations were made on twenty-six patients during operations involving minimal blood loss. None was suffering from circulatory disease. After routine premedication anaesthesia was induced with thiopentone and maintained either with nitrous oxide, oxygen and halothane (0.5–2 per cent) with the patient breathing spontaneously, or else with a relaxant (gallamine or tubocurarine) and artificial ventilation with nitrous oxide, oxygen and occasionally halothane 0.5 per cent. After about 30 minutes, when the blood pressure and heart rate were stable, measurements were made before and after the intravenous injection of atropine (mean dosage 0.01 mg/kg).

Cardiac output was measured with a Cambridge Mk II recorder and earpiece. The method of Gabe, Tuckman and Shillingford (1962) was employed to detect changes in output from serial
non-calibrated dye-dilution curves. 20 mg doses of Coomassie Blue were flushed into the patient through a large-bore polythene catheter inserted into an antecubital vein (Bousvaros et al. 1963). Blood pressure was measured by sphygmomanometry and the mean arterial pressure derived from the formula

\[ MAP = \text{diastolic pressure} + \frac{\text{Pulse pressure}}{3} \]

The heart rate was taken from the pulse wave on the recorder tracing. Peripheral resistance was obtained from the formula

\[ \text{Peripheral resistance} = \frac{MAP}{\text{cardiac output}} \]

There was an almost immediate rise in cardiac output, reaching a maximum 2–5 minutes after the injection of atropine. The twelve patients who breathed spontaneously had initial heart rates between 52 and 86 (mean 62) beats/min and mean arterial pressures between 58 and 95 (mean 77) mm Hg. In this group atropine caused the greatest increases of rate and output; MAP rose while stroke volume and peripheral resistance fell. Seven patients who received tubocurarine had initial rates between 62 and 80 (mean 70) per minute and mean arterial pressures between 83 and 100 (mean 90) mm Hg. They showed similar but less marked circulatory changes. The seven in whom gallamine was used had initial rates between 70 and 120 (mean 99) per minute and mean arterial pressures between 73 and 126 (mean 97) mm Hg. Atropine caused only small rises in output and rate and little fall in peripheral resistance. There were no significant changes in stroke volume or MAP.

The dose of atropine ranged from 0.006–0.022 (mean 0.01) mg/kg but there was no relation between dose and response within this range. There was a relationship between initial heart rate and the increase in rate. This was greatest in patients receiving halothane, whose rates were originally low and least in those having gallamine whose rates were already high. This suggests the possibility of an upper limit for tachycardia induced by atropine. The increase in output was much less than the increase in rate in the patients who were breathing spontaneously, suggesting that other factors were involved in the response to vagal block.

REFERENCES


FACTORS INFLUENCING THE ARTERIAL PO2 DURING ANAESTHESIA WITH ARTIFICIAL VENTILATION

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Factors influencing arterial PO2 have been studied in anaesthetized surgical patients, ventilated artificially at a minute volume of about 10 L/min. Inspired oxygen concentration varied between 94 and 99 per cent in eight patients and between 21 and 32 per cent in eighteen patients. Observations were repeated at intervals during anaesthesia and attempts were made to re-expand atelectatic lung by passive hyperinflation of the lung. Analytical methods were those previously described (Nunn, 1964) except that analysis of oxygen in the gas phase was carried out with a Servomex paramagnetic oxygen analyzer (Nunn, Bergman, Coleman and Casselle, 1964).

Mean oxygen consumption was 98 per cent of basal in the patients breathing less than 32 per cent oxygen. Initial values of RQ were high but fell towards a mean value of 0.75 after 1 hour of anaesthesia. Mean arterial Pco2 was 26.2 mm Hg. The mean physiological deadspace/tidal volume ratio was 32 per cent, showing no change with duration of anaesthesia. Ideal alveolar PO2 was principally a function of inspired oxygen concentration since the Pco2 did not vary widely from one patient to another. At high Po2, the mean alveolar-arterial PO2 gradient (AaD) was 145 mm Hg corresponding to a calculated shunt of 11 per cent, not significantly greater than the values found during spontaneous respiration (Nunn, 1964). For the patients breathing less than