ISOFLURANE DOES NOT REDUCE AORTIC PEAK FLOW VELOCITY IN CHILDREN

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Inhalation agents form the basis of the vast majority of anaesthetics given to children. Halothane is currently the most popular but enflurane and, more recently, isoflurane are being used with increasing frequency. Nicodemus and colleagues (1969) have suggested that children may be particularly susceptible to the cardiovascular depressant effects of volatile anaesthetics, but haemodynamic studies in children have been limited by the invasive nature of the available techniques. However, with the development of pulsed Doppler echocardiography, which is a safe, reliable and non-invasive technique, such investigations are now feasible (Alverson et al., 1982). The present study was undertaken to evaluate the haemodynamic effects of halothane, enflurane and isoflurane in children, using this method.

PATIENTS AND METHODS

The technique of pulsed Doppler echocardiography enables two-dimensional imaging and recording of blood flow velocity to be carried out simultaneously. Blood flow velocity is related to the measured Doppler frequency shift in accordance with the Doppler equation:

\[ V = \frac{\Delta f c}{2FC\cos\sigma} \]

where \( V \) = mean velocity; \( \Delta f \) = frequency shift; \( c \) = speed of sound in tissue; \( \sigma \) = angle of incidence of the ultrasonic beam. In the case of pulsed Doppler echocardiographic measurement of cardiac output, the velocity of blood flow in the ascending aorta is measured. Cardiac output is determined in accordance with the principles of fluid dynamics of pulsatile flow (Caro et al., 1978), flow through a cylinder being equal to the product of mean velocity of flow and the cross sectional area (c.s.a.) through which it passes. Thus cardiac output is equal to the product of the mean velocity of flow in the ascending aorta and the cross sectional area of the aorta. An ATL MARK 600 Duplex scanner was used and ultrasound was transmitted and received by a transducer placed in the suprasternal notch. The beam of ultrasound was directed at the ascending aorta and its position delineated by the cursor line with 2-dimensional imaging (fig. 1). Frequency shift signals from red blood cells undergo spectral analysis and the final outline shown on the oscilloscope represents velocity of blood flow in the ascending aorta in \( \text{m s}^{-1} \) (fig. 1).

The diameter of the aorta was obtained from the two-dimensional image and the c.s.a. of aorta estimated: \((\pi D^2)/4. Mean velocity was determined by measuring the area between the curve and the zero velocity line and dividing by the distance along the \( x \) axis. Measurements were carried out on a Kontron Cardio 80 digitizing board, the mean

SUMMARY

Haemodynamic effects of 1 MAC halothane, enflurane and isoflurane were studied in 15 healthy children using pulsed Doppler echocardiography. Heart rate was significantly increased with isoflurane, but not with the other two agents. All three caused comparable decreases in arterial pressure. Cardiac output was increased with isoflurane, but remained unchanged with halothane and enflurane. Aortic peak flow velocity, a sensitive index of myocardial contractility, was decreased with halothane and enflurane, but not with isoflurane. These findings indicate that isoflurane causes less myocardial depression than halothane or enflurane in children.
velocity of five beats being averaged to eliminate the effects of respiration or rhythm changes. Stroke volume was derived by dividing cardiac output by heart rate. Control measurements were made when the children had become accustomed to the technique. In order to eliminate bias, calculations were made without the operator knowing which anaesthetic was being administered. Heart rate and rhythm were monitored continuously with the electrocardiogram, indirect arterial pressure with a Dinamap 845 oscillometer, temperature with an oesophageal thermistor probe and end-tidal carbon dioxide and anaesthetic concentrations with Datex infra-red analysers (Normocap and Normac).

Approval of the Research Ethical Committee and parental consent were obtained for the study. Fifteen healthy (ASA I) children were given halothane, enflurane or isoflurane on the basis of computer-generated random numbers. The children receiving the different anaesthetics were of comparable age and weight (table I). Control data were obtained with the child awake and after 30 min of 1 MAC anaesthesia. All measurements were made before surgery. Pre-anaesthetic medication was omitted, anaesthesia was induced with sodium thiopentone 5 mg kg\(^{-1}\), neuromuscular blockade with suxamethonium 1 mg kg\(^{-1}\) and the trachea was intubated with a Portex gas sampling tracheal tube. When spontaneous breathing had returned, the volatile agent under study was administered in 100% oxygen using a Bain breathing system and the inspired concentration adjusted to maintain an alveolar concentration of 1 MAC for 30 min. The MAC values for the age groups studied were 0.9% halothane (Gregory, Eger and Munson, 1969), 1.8% enflurane and 1.5% isoflurane (Cameron, Robinson and Gregory, 1984). The data were analysed using the “Statistical Package For Social Sciences” (Nie et al., 1975). The effects of each agent were analysed with a paired \(t\) test and the differences between agents using the Neumann–Keuls test. Analyses were based on percentage alterations from control values.

### RESULTS

Heart rate was significantly increased with isoflurane \((P < 0.05)\), but there was little alteration with either enflurane or halothane (table II, fig. 2). Systolic, diastolic and mean arterial pressures

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**Fig. 1.** Two-dimensional image of ascending aorta and typical tracing of aortic blood flow velocity \((m \text{s}^{-1})\).
were significantly decreased by all three agents, the reductions being largely comparable (tables II and III; fig. 2). Stroke volume was not significantly altered by any of the three agents (table IV). Cardiac output was increased significantly with isoflurane (P < 0.05), but remained unchanged with halothane and enflurane (table IV). Aortic peak flow velocity was significantly decreased with halothane (P < 0.001) and with enflurane (P < 0.01) (table V, figs 3 and 4) and, although it tended to increase with isoflurane, the increases were not significant. End-tidal carbon dioxide concentrations were comparable in all three groups at 30 min (6.4% halothane, 6.7% enflurane and 6.7% isoflurane).

**DISCUSSION**

The main finding of this study is that low concentrations of halothane and enflurane, but not of isoflurane, decreased aortic peak flow velocity in children. Rushmer (1966) has suggested that aortic peak flow velocity is a sensitive index of myocardial contractility. It reflects the magnitude of the impulse generated by the contracting left ventricle during the initial stage of ejection (Rushmer, 1964) and is particularly sensitive to...
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1.4-
1.3-
1.2-
1.1-
1.0-

\( \frac{P}{\text{MAC}} \)

- Halothane
- Enflurane
- Isoflurane

Fig. 3. The effects of halothane, enflurane, and isoflurane on aortic peak flow velocity.

-10-
0-
+10-
+20-

Halothane
Enflurane
Isoflurane

Fig. 4. Percentage alterations in aortic peak flow velocity.

changes in the inotropic state of the myocardium (Nutter, Nobel and Hurst, 1971). Thus it may be concluded that 1 MAC isoflurane causes less myocardial depression than 1 MAC halothane or enflurane. Comparable findings have been reported in adults by Stevens and his colleagues (1971) using the technique of ballistocardiography, which also measures the initial ventricular impulse. Recent investigations in children using M mode echocardiography provide further evidence that low concentrations of isoflurane do not adversely affect left ventricular function (McNeill, Lerman and Gregory, 1984; Neal et al., 1984).

It has been suggested that the difference in myocardial contractility between isoflurane and the other two anaesthetics may be caused by increased beta sympathomimetic activity (Stevens, Cromwell and Halsey, 1971; Balasaraswathi et al., 1982). It seems reasonable to assume that this may account for the increases in heart rate, cardiac output and aortic peak flow velocity found in the present study. Also, Hirshleifer and his colleagues (1975) have shown that acute increases in heart rate per se may augment myocardial contractility. All three agents produced comparable reductions in systolic, diastolic and mean arterial pressures. It is generally accepted that the hypotensive effects of halothane and enflurane are mainly caused by a decrease in cardiac output, while isoflurane causes substantial reductions in systemic vascular resistance (Jones, 1984). In the present investigation, only low alveolar vapour concentrations were studied and this may explain why neither halothane nor enflurane reduced cardiac output. Also, it is known that measurements of cardiac output based on pulsed Doppler echocardiography may be overestimated (Ihlen, Amlie and Dale, 1984), a common source of error being the measurement of aortic diameter and the calculation of aortic c.s.a. Although cardiac output determinations using pulsed Doppler echocardiography have been found to correlate favourably with those obtained by invasive methods (Darsee et al., 1980; Huntsman et al., 1983), it has been suggested that the technique may be more useful for comparing relative rather than absolute changes in cardiac output (Schuster et al., 1985).

Although it has been shown that spontaneous respiration may influence the cardiovascular effects of volatile anaesthetics (Cullen and Eger, 1974), only moderate increases in end-tidal carbon dioxide concentration were noted in the present study. Horan and colleagues (1977a, b) have reported that, in animal studies, minimum equipotent concentrations of halothane, enflurane and isoflurane have broadly comparable effects on conventional cardiovascular variables including arterial pressure, heart rate and cardiac output. However, they found that differences between the three agents became apparent when more sophisticated indices of myocardial contractility were studied.

Increases in heart rate were observed in children receiving isoflurane, a finding which has been reported in adults (Shimosato et al., 1982; Cahalan et al., 1983). This may be caused by increased sympathomimetic activity (Stevens, Cromwell and Halsey, 1971) and by preservation of baroreceptor responsiveness (Kotrly et al.,
Increases in heart rate may be associated with greater myocardial oxygen consumption (Braunwald, 1971). Although this may be of critical importance in the adult, especially in the presence of ischaemic heart disease, it is unlikely to be of clinical significance in the normal healthy child in whom increases in heart rate are well tolerated (Wetzel and Rodgers, 1981). It has been suggested (Brandom, Brandom and Cook, 1983; Boudreaux, Schieber and Cook, 1984) that the rapid body uptake of halothane may result in the development of high myocardial concentrations. This may account for the greater incidence of bradycardia, hypotension and cardiac arrest reported in children (Diaz and Lockhart, 1979). It is of interest that, although the uptake of isoflurane is more rapid in children than that of enflurane or halothane (Gallagher and Black, 1985), the findings of the present study indicate that it causes less myocardial depression than the other two agents. This suggests that, in children, there is a greater margin of safety with isoflurane than with other volatile anaesthetics.

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