INTRAVENOUS OCTAPRESSIN DURING HALOTHANE ANAESTHESIA: A PILOT STUDY

BY

C. A. SHANKS

Department of Anaesthesia, Christchurch Hospital, Christchurch, New Zealand

SUMMARY

Octapressin was injected during halothane anaesthesia in fifty patients. Divided doses of up to 10 pressor units were used. Skin and mucous membrane pallor were usual, and at times associated with cyanosis around the neck. Systolic blood pressure elevations were usually of the order of 10 mm Hg and lasted for less than 10 minutes. Moderate elevations of diastolic blood pressure were observed. It is suggested that if, during halothane anaesthesia, inadvertent intravenous injection occurs while infiltrating vasoconstrictor agents for local haemostasis, Octapressin is less likely to be followed by dangerous complications than are the catechol amines.

If a solution containing a drug used for haemostatic purposes is infiltrated or applied during surgery, it may enter the general circulation with possibly adverse results. Animal studies with the catechol amines during halothane anaesthesia show the development of cardiac arrhythmias and arrest, particularly if administered intravenously (Raventós, 1956; Hall and Norris, 1958; Rogoman, Johnston and Conn, 1963). The danger of the concurrent use of adrenaline and halothane is recognized by most of those who employ this procedure, but they consider the risks involved to be negligible. When the catechol amines are infiltrated in man during halothane anaesthesia, cardiac arrhythmias can occur (Brindle, Gilbert and Millar, 1957; Millar, Gilbert and Brindle, 1958). They cause an increase in the incidence and severity of the arrhythmias when infused intravenously at a rate of about 10 µg/min, or less in some circumstances (Anderson and Johansen, 1963). More disastrous proofs of the danger are given in reports of cardiac arrest under these conditions (Mushin and Rosen, 1962; Rosen and Roe, 1963).

Octapressin (Sandoz) is a polypeptide which differs from lysine-vasopressin by the substitution of phenylalanine for tyrosine in the 2 position (Boissonnas and Guttman, 1960). One of its actions is vasoconstriction, influencing "the contractile elements of the small vessels and capillaries" (Triangle, 1962). Its use as a local haemostatic agent has given promising results in tonsillectomies (Missura and Weder, 1962), and obstetrics and gynaecology (Hochuli and Käser, 1962). The manufacturers recommend 5 to 10 pressor units for most purposes, in amounts of local anaesthetic, or of physiological saline solution, varying between 20 and 100 ml.

It was therefore decided to investigate some of the systemic effects of this drug during halothane anaesthesia, by injecting doses intravenously up to a total of 10 pressor units.

METHOD

In this series of fifty patients undergoing relatively minor surgery, the ages ranged between 9 and 83 years, and they weighed 28 to 108 kg. None had overt cardiac disease, although two were hypertensive, with casual blood pressures of 200/110 mm Hg and 210/130 mm Hg.

Premedication generally consisted of papaveretum and hyoscine but five patients were given papaveretum and atropine, and a further four had atropine with pethidine and levallorphan. All patients received a sleep dose of thiopentone 2.5 per cent, usually 200 to 300 mg, and if intubation was to be performed, suxamethonium 40 to 100 mg was given, and the patient oxygenated. Anaesthesia was then maintained using a mixture of nitrous oxide and at least 35 per cent oxygen, administered through a Magill circuit at 8 to 10 l./min. Halothane was delivered by a Mark II Fluotec vaporizer, often set at 1.5 to 2 per cent initially, then turned...
to 1 per cent within 10 minutes, where it remained until the operation was almost completed. A further 10 minutes or more then elapsed, during which halothane was continued while baseline recordings were obtained. Observations on the skin circulation, pulse and blood pressure were made, and electrocardiographic recordings (mainly the standard limb leads) taken, usually twice every 5 minutes.

After the recordings had reached a stable level for 5 minutes or more, a test dose of 0.5 pressor units of Octapressin was injected intravenously, followed at 10-minute intervals by increasing doses. This was continued until either a total of 10 units had been reached or time would not permit further injections, it being felt that at least 10 minutes of observations during 1 per cent halothane administration were required after the last injection. Early in the series, the incremental increases were small, but latterly injections of 0.5, 3 and 6.5 units were usually given. Thirty-four of the fifty cases received a total of 8 to 10 pressor units of Octapressin.

RESULTS

Skin colour.

Even with the first injection of 0.5 unit, the skin and mucous membranes of the head and neck became pale, further doses causing an increasing pallor. This was enough to elicit remarks from uninitiated bystanders about the ill appearance of the patient, even when this effect was not irregular and blotchy, or with the cyanotic tinge which occasionally developed. This pallor usually spread later to the hands, arms and other portions of the body, and was noticeable for up to 2 hours postoperatively. The cyanotic tinge was usually confined to the neck and upper thorax, but elsewhere the rate of capillary refill was not excessively, if at all, slowed. The skin seldom became much cooler, and no sweating was observed.

Heart rate and blood pressure.

As anaesthesia progressed, the heart rate usually slowed to 50–80 per minute. In less than one-fifth of cases, Octapressin led to a further fall in rate of 10–20 beats per minute, this invariably occurring with the first injection only and independently of any blood pressure changes. However, further injections appeared to decrease the pulse amplitude, making palpation difficult at times.

In some patients the systolic blood pressure showed a steady background fall. Injections of Octapressin caused peak elevations of up to 40 mm Hg within 5 minutes. The rise was usually only about 10 mm Hg, lasting for less than 10 minutes, and often followed only the first one or two doses. Rarely, the pressure fell following the injection.
Once stabilized, the diastolic pressures did not vary a great deal until injections began, then most showed a more or less steady rise, increasing 5 to 20 mm Hg with each injection. Again further rises followed only the first one or two doses in almost half the cases, though not necessarily those in which the systolic pressure did not respond. When the halothane was discontinued, both systolic and diastolic pressures usually rapidly rose to, or slightly above, pre-operative levels. Figure 1 illustrates the blood pressure and heart rate changes in a typical case.

Electrocardiograms.
Five cases showed occasional supraventricular coupled beats; nodal extrasystoles were observed in three cases, and atrial in two. In all except one, these were present before the injections of Octapressin had begun. Another patient had occasional ventricular extrasystoles before and after injections.

There were no electrocardiographic changes to suggest myocardial ischaemia.

Other observations.
The pupils did not seem to be affected by Octapressin. There was no apparent alteration in respiration, except in one otherwise unremarkable case which showed Cheyne-Stokes breathing for about half a minute immediately following injections of both 3 and 6.5 units.

Several patients have been infiltrated with 0.5 per cent lignocaine containing Octapressin during halothane anaesthesia. There was an adequate haemostasis in most, and no adverse effects were seen except a tendency to produce rectal incontinence when the perineal region was infiltrated.

There were no postoperative sequelae attributable to Octapressin; however, the antidiuretic effects were not investigated.

DISCUSSION
In this clinical assessment of the cardiovascular effects of Octapressin a compromise had to be made between conditions prevailing during clinical anaesthesia with halothane and a standardized technique. The preponderant use of papaveretum and hyoscine as a premedication leads to a reduction of tidal volume in many patients (Bryce-Smith and O'Brien, 1957), but the circulatory adjustments to the resultant hypercapnia were preferred to those of assisted respiration. The period of not less than 10 minutes during which the patients became “settled” permitted the effects of intubation, etc., to disappear (King et al., 1951; Bullough, 1959).

Intervals of 10 minutes between injections of Octapressin were chosen, as a previous small study (Hugin, 1962) indicated that the blood pressure response lasted 20 to 30 minutes, and because Ruskin (1947) found that vasopressin caused changes in the electrocardiographic pattern within 6 to 10 minutes, returning to normal after 10 to 14 minutes.

The pulse rate often slows during halothane anaesthesia, and additional bradycardia due to Octapressin was neither frequent nor marked, being seen with the first injection only. Although it may be of value in other circumstances, the blood pressure responses would probably be too low and unreliable for the use of Octapressin as a pressor agent with halothane. However, halothane also reduces the effects of the catechol amines (Nayler, 1959; Price and Price, 1962). With the common lack of response to later doses, it would seem that tachyphylaxis can be rapidly established.

Vasopressin is well recognized to constrict vessels, including the coronary arteries, and may cause arrhythmias (Grollman and Geiling, 1932; Dearing, Barnes and Essex, 1944; Wakim, Denton and Essex, 1954). Its use has been associated with myocardial infarction and cardiac arrest (Mills et al., 1949; Slotnik and Tiegland, 1951). This happens not in response to the blood concentration of the drug, but “only in the event of prior sensitization, by one or more additional factors, of the myocardium and/or the coronary arteries” (Kramer et al., 1962). In the present study the “additional factors” of increased vagal tone and a respiratory acidosis were probably present in some patients, due to the combined effects of the premedication and halothane. If Octapressin also causes coronary artery constriction, there now must be the complication of an ischaemic and irritable myocardium, further depressed by halothane (Severinghaus and Cullen, 1958), this in the presence of a raised peripheral resistance together with an unaltered or slowed heart rate.

Although electrocardiography showed no changes which could be attributed to Octapressin, this is not necessarily a reliable guide. Studies with Pitressin show variable results (Graybiel and
Glendy, 1941; Ruskin, 1947; Mills et al., 1949), but a partial answer to these variations may be found in the differences of dose, rate, frequency and method of administration. Similarly, electrocardiographic changes may have occurred had the 10 units of Octapressin been given as a single injection. As one-third of the patients in the series were over 50 years of age, it is likely that coronary artery disease affected some, in spite of the absence of clinical signs.

While it is realized that the results from such a small series merely indicate that adverse reactions to Octapressin should not be common during halothane anaesthesia, the fact that 20 to 100 per cent of the maximum recommended haemostatic dose can be given intravenously must place it in a more favourable light than the catechol amines when used in comparable circumstances.

ACKNOWLEDGMENTS

Thanks are due to the surgical and theatre staffs for their co-operation during these investigations, and I am most grateful to my senior anaesthetic colleagues for their helpful advice and encouragement. Dr. P. Sheppard kindly interpreted the electrocardiographic recordings. Sandoz Pharma Ltd. generously provided supplies of Octapressin.

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