A PREVIOUS HISTORY OF ACUTE INTERMITTENT PORPHYRIA AS A COMPLICATION OF OBSTETRIC ANAESTHESIA

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SUMMARY

The administration of general anaesthesia for Caesarean section is described in a patient with an established biochemical diagnosis of acute intermittent porphyria. The technique used did not precipitate an acute exacerbation of the disease. Drugs associated with obstetric care are considered in the context of their use in porphyria.

The problems of general anaesthesia associated with porphyria are well recognized, but the association of pregnancy and porphyria is rare. We describe the successful anaesthetic and analgesic management of a patient with acute intermittent porphyria who required Caesarean section.

Case history

Eight years before becoming pregnant, the patient, then aged 24 yr, was admitted to hospital with a history of prolonged intermittent abdominal pain. After initial conservative management, an exploratory laparotomy was performed with a presumptive clinical diagnosis of an appendix abscess. Thiopentone, suxamethonium, tubocurarine and halothane were used for anaesthesia. No problems were noted. Abdominal pain continued after the inconclusive laparotomy and narcotic analgesics were required. No organic cause for the pain was found and a psychiatrist’s opinion was sought. Symptoms subsided after 14 days and the patient was discharged from hospital.

A clinical and biochemical diagnosis of acute intermittent porphyria was not made until 2 months later when the patient was re-admitted with abdominal pain, tachycardia, neuropathy and severe myopathy involving the respiratory muscles. Two milder episodes occurred in the next 18 months. No precipitating factor was identified to account for each acute attack.

Eight years after her first attack, the patient presented in the antenatal clinic at 8 weeks gestation. She had remained well since her last acute attack 6 years previously. The arterial pressure was 120/80 mm Hg. The pregnancy was uneventful until 34 weeks when hypertension and proteinuria were noted. Arterial pressure was 150/90 mm Hg. Pre-eclampsia worsened despite hospital admission with a maximum arterial pressure of 170/120 mm Hg. An elective Caesarean section was planned at 37 weeks gestation because of the severe pre-eclampsia. Hypertension had remained at 160/110 mm Hg. Serial estimations of urinary porphobilinogen were performed before delivery.

No premedication was given other than oral magnesium trisilicate mixture. Arterial pressure on arrival in the anaesthetic room was 160/105 mm Hg. After pre-oxygenation, anaesthesia was induced by inhalation using a mixture of 50% cyclopropane and 50% oxygen. Cricoid pressure was firmly applied as the patient lost consciousness. Suxamethonium 100 mg was given to facilitate rapid tracheal intubation. Tubocurarine 25 mg was given i.v. and the lungs were ventilated artificially with 50% nitrous oxide in oxygen and by 0.3-0.5% methoxyflurane. Immediately after delivery, pethidine 100 mg was given i.v. and the ventilating mixture was changed to 70% nitrous oxide in oxygen. Syntocinon 5 i.u. was given i.v. Hartmann’s solution 500 ml followed by 5% dextrose 500 ml were given as i.v. fluid therapy. At the conclusion of the operation, residual neuromuscular block was antagonized with neostigmine 2.5 mg and atropine 1.2 mg. The anaesthetic was uneventful, although the pre-existing hypertension persisted during anaesthesia.

A live female infant was delivered weighing 2560 g. Apgar scores were 4, 7 and 10 at 1, 5 and 10 min respectively. The infant had made vigorous efforts at breathing during delivery, causing inhalation of liquor and this was thought to have produced
the low Apgar score at 1 min. Anaesthesia was thought not to be a contributory factor.

After operation, progress was uneventful except for persistent hypertension. There were no clinical signs of an acute attack of porphyria and urinary porphobilinogen excretion was unchanged from values before the operation. Glucose solutions 10% were used to maintain a minimum input of 1200 calories daily until normal oral intake was resumed. On direct questioning of the patient 24 h after operation, there was no evidence of awareness during anaesthesia. The patient was able to go home on the 14th day after operation.

**DISCUSSION**

The association of acute intermittent porphyria and pregnancy is known to produce a high risk of acute attacks, probably because of the increase in maternal oestrogen production.

One survey (Hunter, 1971) showed a high overall mortality rate of 27%. A later survey (Brodie et al., 1977) stated that 54% of women with the disease who become pregnant had an acute attack during pregnancy or the puerperium. Previous knowledge of the diagnosis did not alter the attack rate, but the maternal mortality rate was only 2%. That report did not give details of the use of analgesics or anaesthesia. The difference in mortality rates might be explained by the comparatively rare use of barbiturates as sedatives in the treatment of pre-eclampsia in recent years. Acute intermittent porphyria is clearly a serious, though uncommon, complication of pregnancy.

In order to establish a biochemical diagnosis of an acute attack in the period after operation baseline values of porphobilinogen excretion in the period before operation are required in patients with known porphyria. In normal pregnant women, porphobilinogen excretion increases to a small extent in late pregnancy, but does not become abnormal (Lyberatos et al., 1972).

**Problems of anaesthesia**

Of the induction agents, propanidid is known to be safe. Althesin is also recommended as a safe induction agent by one standard text (Churchill-Davidson, 1978) although another clinical report (Wetterberg, 1976) and animal studies (Parikh and Moore, 1975) suggest that it is unsafe. Ketamine has opposing evidence from two animal studies as to its safety in porphyria (Parikh and Moore, 1975; Kostrzewska and Gregor, 1978). Direct comparison of these results is not possible since a different species was used in each case, and therefore interpretation of the evidence is difficult. However, its safe use in clinical practice has been shown twice in the same patient (Rizk, Jacobson and Silvay, 1977).

There are conflicting reports as to the safety of the volatile anaesthetic agents in relation to porphyria. Halothane was successfully used twice (Rizk, Jacobson and Silvay, 1977) and is also considered safe from animal studies (Parikh and Moore, 1978), but has been reported as unsafe elsewhere (Wetterberg, 1976). Another authority (Vickers, 1977) considers both halothane and methoxyflurane to be safe, but again animal studies suggest that methoxyflurane is unsafe (Parikh and Moore, 1978). Enflurane has similarly conflicting reports (Parikh and Moore, 1978; Stone and Munson, 1979).

The choice of drug is not easy in the presence of such confusing evidence. Indeed, it is well recognized that an acute attack may not be precipitated even when known porphyrigenic drugs are administered to patients with porphyria (Ward, 1965). It is also difficult to extrapolate directly the results of animal studies to the clinical situation.

Our choice of technique was based on the current evidence available. The choice of an induction agent was a difficult problem. Barbiturates being excluded, propanidid appeared to be the drug of choice, but it has disadvantages when used for Caesarean section (Mahomedy et al., 1976). Ketamine may produce neonatal depression in larger doses (Downing et al., 1976) and there is conflicting evidence about its use in porphyria. Ketamine also causes an increase in arterial pressure and this would be undesirable in pre-eclampsia (Meer, Downing and Coleman, 1973). Inhalation induction of anaesthesia with cyclopropane combined with cricoid pressure provided the rapid, safe induction necessary for obstetric anaesthesia. This technique was discussed before operation with the patient, who found it acceptable.

It is common practice to use a small concentration of a volatile anaesthetic agent as an adjuvant to 50% nitrous oxide in oxygen to ensure freedom from awareness before delivery. Trichloroethylene is an agent widely used for this purpose, but no reference to its use in porphyria could be found. Methoxyflurane was used at that time since it was believed to be safe. However, Parikh and Moore (1978) later published evidence in animals suggesting that it may be unsafe.

Caesarean section normally demands the use of an oxytocic drug. Ergometrine is contraindicated in
porphyria (Wetterberg, 1976). Syntocinon is an acceptable alternative, particularly in a patient with hypertension, although there are no reports of its use in porphyria. Its use caused no problems in our patient.

Management after operation may require the use of analgesics and anti-emetics. I.m. pethidine (total dose 1200 mg over 72 h) was used for analgesia after operation. The safe use of metoclopramide in porphyria has been shown both by clinical use (Goldberg and McColl, 1978) and from studies in rats (K. McColl, personal communication). An anti-emetic was not necessary in our patient. Starvation is a known precipitating factor in porphyria. Dextrose solution 10% provided a suitable source of calories and fluid until oral intake was resumed.

The management of pre-eclampsia may require the use of sedatives. Barbiturates, although widely used in the past, are now contraindicated. Diazepam, given by bolus injection or as an infusion, is commonly used for sedation in pre-eclampsia. Animal studies (Parikh and Moore, 1978) suggest that it is safe, but there are two reports that its clinical use has precipitated an acute attack of porphyria (Wetterberg, 1976; Stone and Munson, 1979). Chlormethiazole infusion is increasingly used as i.v. sedation, but there are no reports in the literature as to its safety in porphyria. Hydralazine is used as a hypotensive agent in pre-eclampsia, often in combination with diazepam, but the safe use of hydralazine in porphyria has yet to be established. Pentolinium may be safely used as a hypotensive agent in porphyria (Katz and Kadis, 1973; Vickers, 1977). Chlorpromazine is known to be safe (Wetterberg, 1976; Vickers, 1977) and provides both sedation and hypotension and thus may be the drug of choice.

The use of local anaesthesia in porphyria is ill defined. Standard texts (Katz and Kadis, 1973; Atkinson and Rushman, 1977; Vickers, 1977; Churchill-Davidson, 1978) suggest that local anaesthesia should, for medico-legal reasons, be avoided in diseases where neurological symptoms may occur after operation and the local anaesthetic cannot be excluded as a causative factor. However, the safe use of extradural, caudal and pudendal blocks has been reported in porphyria (Tricomi and Baum, 1958; James, Rudolph and Abbott, 1961). If our patient had been allowed to deliver vaginally, we would have considered, if necessary, the use of extradural analgesia after consultation with the patient. General anaesthesia, however, was considered to be the most suitable technique for Caesarean section in this patient.

In the presence of conflicting reports on many drugs, it is not possible to make absolute statements on the safety of their use in porphyria. We would suggest, however, that the choice of drugs should be restricted to those indicated as being safe both by clinical case reports and by animal studies.

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REFERENCES


