SAFE USE OF PROPOFOL IN A PATIENT WITH ACUTE INTERMITTENT PORPHYRIA

G. MITTERSCHIFFTHALER, A. THEINER, H. HETZEL AND L. C. FUITH

The porphyrias are a group of diseases characterized by defects in porphyrin metabolism. Only acute intermittent porphyria (AIP), variegate porphyria (VP) and hereditary copro-porphyria can lead to acute attacks. These may be caused by drugs, especially barbiturates. Other anaesthetic agents such as Althesin, diazepam and ketamine may also induce life threatening porphyrinic attacks [1]. This case report describes the safe use of propofol on two occasions during the anaesthetic management of a patient suffering from acute intermittent porphyria.

CASE HISTORY

A 43-yr-old female (weight 52 kg, height 1.65 m) was admitted to hospital with a stage IIb cervical carcinoma (parametrial infiltration [2]). The patient had previously undergone surgery for appendectomy and tonsillectomy at 8 and 11 yr respectively, without major anaesthetic complications. In 1967 she delivered a son who died after 6 months.

In 1969 a live, healthy female infant was delivered by Caesarean section, for which anaesthesia had been induced with thiopentone. The patient remembers muscle weakness in her right arm, which persisted for several days.

Her first acute porphyric attack occurred in 1974. No precipitating factor was identified. In the following 10 years three further acute episodes occurred, each necessitating admission to hospital. Two of these attacks followed influenzal illnesses.

SUMMARY

On two occasions a patient suffering from acute intermittent porphyria (AIP) was anaesthetized with propofol as the sole agent. The concentrations of urinary porphobilinogen, porphyrins and porphyrin precursors did not exceed preoperative values, and no exacerbation of the disease was noted.

Each attack was characterized by abdominal pain, general muscle weakness, and increases in the concentrations of urinary porphyrins and porphyrin precursors. A positive diagnosis was based on the porphyrin chromatogram, which was typical for AIP [3].

On this admission the patient had no clinical symptoms of porphyria, but did have signs of a chronic distal neuropathy; the concentrations of urinary porphobilinogen, porphyrins and porphyrin precursors were increased (table I). All other laboratory findings, including tests of hepatic function, were normal.

Combined percutaneous and high-dose rate afterloading radiation (HDR) therapy using an afterloading machine (Selectron type with cobalt 60, 500 mCi/pellet) was planned. In order to position the radiation applicator it was necessary to dilate the cervical os under general anaesthesia. The patient was not premedicated. Anaesthesia was induced with propofol 100 mg i.v. using a forearm vein. After 20 s the patient lost consciousness, and ventilation was assisted with 100 % oxygen. The gynaecological procedure lasted 7 min. Eleven minutes after the injection of propofol the patient was completely responsive, fully orientated and co-operative. The subsequent postoperative period was uneventful. The 24-h
TABLE I. Twenty-four-hour urinary excretion of porphyrins and precursors

<table>
<thead>
<tr>
<th>Anaesthetic</th>
<th>Before operation</th>
<th>After operation</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Delta-aminolevulinate (mg)</td>
<td>1</td>
<td>31.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Porphobilinogen (mg)</td>
<td>1</td>
<td>36.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>32.6</td>
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<tr>
<td></td>
<td>Uroporphyrin (µg)</td>
<td>1</td>
<td>14.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>12.2</td>
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<tr>
<td></td>
<td>Total porphyrins (mg)</td>
<td>1</td>
<td>611.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>655.6</td>
</tr>
</tbody>
</table>

Urinary excretion of porphobilinogen and precursors remained close to the preoperative values (table I).

Two weeks later a further radiation treatment was planned. As before, anaesthesia was induced using propofol 100 mg i.v. An increment of 60 mg was necessary as the positioning of the radiation applicator proved to be more difficult than on the first occasion. Recovery was complete and no porphyric symptoms appeared. Once again, porphyrin excretion remained unchanged.

DISCUSSION

Acute intermittent porphyria is characterized by a decrease in the activity of uroporphyrinogen-synthase (UPG-S) [4]. As a result, haem production decreases. Reduced haem enhances the activity of delta-aminolaevulinate synthase (ALA-S) by negative feedback. Increased amounts of delta-aminolaevulinic acid, porphobilinogen and porphyrins are produced. Porphyrinogenic drugs act by further enhancing ALA-S activity by a variety of mechanisms [5]. Clinical symptoms of the acute attack are closely related to the nervous system. Abdominal pain, constipation, muscle weakness, ascending paralysis, encephalopathy, psychosis, tachycardia and hypertensive crisis are most common.

For positioning of the radiotherapy applicator a short-acting anaesthetic with rapid recovery is necessary, so that treatment can begin at once. During the following radiation time (generally about 5 min) the patient must be awake and fully responsive, since she is monitored indirectly by closed-circuit television.

Spinal anaesthesia is usually used for this purpose. However, little guidance is available on the application of regional anaesthesia to patients with porphyria, and general anaesthesia was considered safer in this subject. Furthermore, the patient suffered from chronic distal neuropathy and this provided a further contraindication to regional anaesthesia [6, 7].

The porphyrinogenicity of propofol has been compared with that of phenobarbitone, which is a powerful porphyrin inducer [8]. The effects of both drugs upon delta-aminolaevulinate synthase activity were measured quantitatively in rat liver. Propofol did not enhance activity of this enzyme and the authors concluded that it would probably be a safe drug for patients with porphyria. The results of that study led to the choice of propofol in our patient.

Although two administrations of propofol to this patient were entirely uneventful, recommendations for using propofol in AIP patients must be very guarded until further successful administrations are reported.

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REFERENCES

