Propofol and electroconvulsive therapy in a patient at risk from acute intermittent porphyria

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Summary
A severely depressed 57-yr-old woman at risk from acute intermittent porphyria presented for a course of electroconvulsive therapy. With propofol as the induction agent the course of electroconvulsive therapy was both uneventful and successful. (Br. J. Anaesth. 1998; 80: 260–262)

Keywords: anaesthetics i.v., propofol; brain, electroconvulsive therapy; complications, porphyria

Acute intermittent porphyria (AIP) may be induced in susceptible patients by several commonly used anaesthetic drugs. Isolated case reports suggest that propofol may be a safe alternative in such patients. Propofol has also been reported to reduce the duration of seizure activity during electroconvulsive therapy (ECT) and as a consequence doubts have been expressed about the efficacy of ECT after anaesthesia with propofol.

Case report
A 57-yr-old woman suffering from Parkinson’s disease presented with a major depressive disorder as part of an organic affective syndrome. She had paranoid and nihilistic delusions and was refusing food and fluids. As these symptoms had failed to respond to drug therapy ECT was felt to be the only alternative. The patient was a member of a large family with a history of autosomally dominant AIP.

Her red blood cell porphobilinogen deaminase (PBG-D) activity was abnormally low (12.7 nmol porphyrin formed/ml erythrocytes/h; normal range 30–54) confirming that she too had AIP. Urinary porphyrins were normal. The patient gave no history of having suffered from a symptomatic episode of AIP.

At the preanaesthetic assessment the woman, who weighed 45 kg, was noted to be tremulous, bradykinetic and rigid, consistent with Parkinson’s disease. She was normotensive and no abnormality was found on cardiorespiratory examination, but the ECG indicated changes consistent with an old anteroseptal myocardial infarction. The patient denied having suffered from cardiorespiratory symptoms. Apart from borderline hypokalaemia, all routine laboratory investigations were normal. Her current medication was pergolide, cabeneldopa, benzhexol, thyroxine and lofepramine.

A total of seven ECT treatments were administered in the ECT suite over a period of 23 days. ECG, arterial pressure and oxygen saturation were monitored routinely. After 1 min of preoxygenation with 100% oxygen, anaesthesia was induced with propofol and neuromuscular block facilitated by succinylcholine. Bilateral ECT was administered after a brief period of hyperventilation with 100% oxygen and seizure duration was timed from application of the current (table 1).

In our patient mean seizure time was 31 (range 16–55) s and aggregate seizure duration was 218 s. The patient was monitored during recovery while breathing 35% oxygen. Administration and conduct of all seven treatments was uneventful. In total, the patient had received propofol 450 mg (mean induction dose 64 (range 60–80) mg) over a 23-day period.

No urinary porphyrins or blood porphobilinogen were detected when measured on day 14 after the fourth treatment. During the course of the ECT the patient remained an inpatient on a neurological ward where the staff were particularly vigilant for signs and symptoms of AIP. At no time did the patient’s neurological condition give cause for concern. At the end of treatment her mood had returned to normal with full remission of her psychotic symptoms.

Discussion
The porphyrias are a group of uncommon inherited metabolic disorders in which there is a disturbance of haem synthesis. In AIP a deficiency of porphobilinogen deaminase (PBG-D) results in the accumulation of the intermediate metabolites porphobilinogen (PBG) and animolaevulinic acid (ALA). AIP can be induced by many drugs familiar to the anaesthetist, in particular the barbiturate induction agents. Clinically, symptoms may be severe and of rapid onset. Abdominal pain, paralysis, mania, coma and death can ensue.

In recent years conflicting reports have appeared in the literature on the porphyrigenicity of propofol. Several reports have shown that a single induction dose had no adverse clinical effect. Mitterschiffthaler and colleagues reported the safe use of...
Table 1 Current applied, seizure duration and anaesthetic drugs administered during the course of ECT given to our patient with acute intermittent porphyria. *Porphobilinogen and urinary porphyrins were measured after treatment No. 4.

<table>
<thead>
<tr>
<th>Treatment No.</th>
<th>Day</th>
<th>Current administered (mA bilateral)</th>
<th>Seizure duration (s)</th>
<th>Propofol dose (mg)</th>
<th>Succinylcholine dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>400</td>
<td>55</td>
<td>80</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>400</td>
<td>20</td>
<td>70</td>
<td>40</td>
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<td>9</td>
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<td>16</td>
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<td>35</td>
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<tr>
<td>4*</td>
<td>12</td>
<td>500</td>
<td>45</td>
<td>60</td>
<td>35</td>
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<tr>
<td>5</td>
<td>18</td>
<td>500</td>
<td>25</td>
<td>60</td>
<td>35</td>
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<td>7</td>
<td>23</td>
<td>500</td>
<td>22</td>
<td>60</td>
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</tr>
</tbody>
</table>

Propofol on two occasions in a susceptible patient within a 2-week period, and Harrison and McAuley’s9 successfully sedated a patient with a symptomatic life-threatening AIP for 32 days in intensive care. An in vivo rat model failed to find any evidence of the porphyrogenicity of propofol.10 Increase in urinary porphyrins after propofol anaesthesia has been reported in susceptible patients.11,12 On one occasion this was only after a third propofol anaesthetic. In both reports patients remained asymptomatic and anaesthesia was otherwise uneventful. Kasraei and Cousins13 reported a patient who was readmitted with an acute symptomatic attack of coproporphyria 4 days after propofol anaesthesia. However, the patient had also been exposed to several other potentially porphyrogenic drugs, the significance of which is uncertain.

Our patient received seven propofol anaesthetics over a 23-day period without biochemical or clinical evidence of induced AIP. Of interest is Kauppinen and Mustajoki’s14 findings that patients with AIP who have never experienced any symptoms, particularly if they have low concentrations of urinary porphyrin precursors, appear to tolerate precipitating drugs well. The authors proposed a more permissive attitude to the administration of potentially porphyrogenic drugs in previously totally asymptomatic patients. In those patients known to have had a previous attack, the exclusion of such drugs was regarded as mandatory. Our patient had been asymptomatic all her life.

One concern expressed in previous isolated case reports is that not every administration of a porphyrogenic drug induces porphyria and consequently many reports have concluded with a warning about the use of propofol in patients at risk from acute porphyria.11,13 and that perioperative biochemical monitoring should always be carried out. For a detailed discussion of anaesthesia for the porphycritic patient the reader should consult the review by Harrison, Meissner and Hift.1

For a course of ECT to be effective a minimum aggregate seizure duration is thought to be necessary.15 Preoxygenation and ventilation with 100% oxygen during ECT has been shown to prolong seizure duration,16 as has hypocapnia induced by passive hyperventilation.17 Several reports have been published which show that propofol anaesthesia reduces seizure duration18–20 and as a consequence the manufacturers have recommended that propofol is unsuitable for use in ECT.

Avramov, Husain and White20 demonstrated a dose-dependent decrease in seizure duration with both methohexital and propofol. The authors concluded that induction doses of propofol in excess of 1.5 mg kg⁻¹ significantly reduced seizure duration. Smaller doses of propofol in the range 0.75–1.0 mg kg⁻¹ were similar to commonly used doses of methohexital. Our patient received propofol in the dose range 1.3–1.7 mg kg⁻¹. In another comparative study,21 seizure duration was also reduced after propofol. The efficacy of ECT was found to be unaffected by the choice of propofol as the anaesthetic induction agent compared with methohexital. This finding was also observed by Kirkby and colleagues.21

A seizure duration of more than 25 s is often quoted as being necessary for ECT.22 However, observed seizure duration is usually less than that demonstrated by simultaneous EEG recording. On this basis, with the exception of the third treatment, most of our patient’s seizure times could be regarded as adequate. The aggregate seizure duration over seven treatments was sufficient to bring about a beneficial clinical response. The crucial test as regards the efficacy of ECT is whether the patient responds to the treatment as expected.22

Our patient with AIP had an uneventful and successful course of ECT using propofol as the anaesthetic agent. The barbiturate anaesthetic methohexital is still regarded by many as the anaesthetic agent of choice for ECT. The known porphyrogenicity precluded its use in our patient. Ketamine, an anaesthetic known to be safe in porphyria, was felt to be particularly unsuitable for ECT in our patient because of its known hallucinogenic effects.

Unfortunately, approximately 9 months later the patient had a relapse of her depressive illness necessitating a further course of ECT. Again propofol was used as the induction agent with success and without ill effect.

References


