Phenylketonuria (PKU) is an autosomal recessive disorder in which the synthesis of tyrosine from phenylalanine is impaired as the result of a deficiency of phenylalanine hydroxylase in the liver. The resulting accumulation of phenylalanine and its metabolites leads to central nervous system disorders, such as mental retardation, spastic paralysis and epilepsy, and a variety of biochemical disorders.1–3

This report describes the case of a 42-year-old Japanese woman with mental retardation and epilepsy associated with PKU, who underwent dental caries treatment under general anesthesia. She was diagnosed with PKU at 2 years old. Consequently, she underwent phenylalanine-restricted diet therapy, and yet she was diagnosed with sequelae of PKU and mental retardation at 14 years old. Oral administration of therapeutic phenylalanine-free milk, pantethine, and magnesium sulfate was restarted, but she did not respond well to the diet therapy. She was also prescribed carbamazepine for epileptic seizure but still developed seizures several times a year. In addition, bromperidol and piperiden were prescribed for psychiatric symptoms such as auditory hallucinations and obsessions.

For perioperative anesthetic management of patients with PKU, it is important to prevent increased activity of enzymes involved in amino acid metabolism and excessive increase in glycolysis or protein catabolism, all of which may be caused by preoperative restriction of oral intake and surgical stress.4 Therefore, arterial blood samples were collected before anesthesia induction, during surgery, and after extubation to measure plasma concentrations of cortisol, phenylalanine, and tyrosine based on the stress response during dental treatment and the effects of anesthetics that were evaluated (Table 1).

Anesthesia was induced with intravenous propofol, fentanyl, and rocuronium under inhaled oxygen and nitrous oxide. Anesthesia was maintained with oxygen, nitrous oxide, 1–2 μg/mL propofol with target controlled infusion (TCI), and 0.1 μg/kg/min remifentanil. Propofol and remifentanil have short durations of action and thus provide high controllability and early recovery. The use of these anesthetics was also effective for reducing the intra-operative stress response and for preventing an increase in plasma phenylalanine concentration, as shown by the decrease in plasma cortisol concentration. In addition, as the treatment procedures used in the present case were minimally invasive, the concomitant use of nitrous oxide reduced the doses of propofol and remifentanil and provided stable perioperative respiratory and hemodynamic status, suggesting the usefulness of the concomitant use of nitrous oxide in the anesthetic management of PKU patients. The patient was maintained in a stable condition with no occurrence of seizure, psychomotor excitement symptoms, or any other serious neurological symptoms in their perioperative care. We obtained patient consent the for publication of personal information.

Adult PKU patients are required to adhere to a therapeutic milk-based strict dietary restriction. The present patient had multiple dental caries despite oral hygienic management. Because patients with PKU who develop mental retardation and epilepsy as a result of inadequate phenylalanine-restricted diet therapy have a risk of cardiovascular or metabolic disorders associated with dental caries or periodontal disease, strict oral hygiene must be maintained.
## References


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**Table 1** Perioperative changes of serum amino acid concentration.

<table>
<thead>
<tr>
<th>Serum concentration</th>
<th>Preoperative</th>
<th>Intraoperative</th>
<th>Recovery room</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenylalanine (nmol/L) (42.6–75.7)</td>
<td>1485.4</td>
<td>1426.6</td>
<td>1431.3</td>
</tr>
<tr>
<td>Tyrosine (nmol/L) (40.4–90.3)</td>
<td>28.6</td>
<td>26.8</td>
<td>27.7</td>
</tr>
<tr>
<td>Cortisol (µg/dL) (4.0–18.3)</td>
<td>4.0</td>
<td>2.7</td>
<td>2.1</td>
</tr>
</tbody>
</table>

* Normal ranges are shown in parentheses.

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