Intravenous General Anesthesia for Patients with Neurological Disorders

Intravenous general anesthesia protocol

Oxygen supplied through nasal cannula. Nitrous oxide (approximate concentration, 20%) can also be used together for oxygen supplementation. Intravenous general anesthesia was induced and maintained with continuous infusion of propofol. Using a propofol TCI pump (Graseby Medical Ltd., Hertfordshire, UK, or Terumo Co., Tokyo, Japan) with a built-in TCI system (Diprifusor, Astrazeneca Plc., London, UK) and according to the parameters reported by Marsh [4], continuous intravenous infusion of propofol was initiated using the TCI method. The dose of propofol was titrated to achieve a BIS of 50 and achieve an adequate level of anesthesia: asleep but not responding to stimulation. Endotracheal intubation was not performed, and spontaneous breathing was maintained. The level of anesthesia was maintained at BIS 30-50 by adjusting the target propofol level using TCI (Figure 1). Without BIS, The dose of propofol was titrated to achieve a Mackenzie Grant score of 5 and to achieve an adequate level of anesthesia: asleep, but not responding to stimulation. The level of anesthesia was maintained at a Mackenzie and Grant score of 5 by adjusting the target propofol level using the propofol TCI (Figure 2). If respiratory depression was observed or BIS value was less than 30, the target blood concentration of propofol was decreased by 0.2 μg/ml. If the anesthesia level was deemed inadequate BIS value was more than 50, the target blood level of propofol was increased by 0.2 μg/ml. The dental procedure was started after the anesthesia level became stable without respiratory depression. A local anesthetic was used appropriately by the operating dentist. Administration of propofol was discontinued at the end of the dental procedure. Patients were monitored until recovery from anesthesia, when they were fully awake and had stable respiration.

Antiepileptics affect for anesthesia

Patients with intellectual disabilities need higher doses of sedatives than those without intellectual disabilities to obtain an adequate level of anesthesia [5]. Among patients with neurological disorders, those with intellectual disabilities suffice with lower doses of sedatives to obtain an adequate level of anesthesia compared to patients with autism [6]. Many of neurological disorders patients

**Figure 1:** Intravenous general anesthesia protocol with BIS. TCI: target-controlled infusion. BIS: Bispectral index.
have epilepsy and are medicated with antiepileptic drugs. In these reports, the group with lower doses of sedatives to obtain an adequate level included those who were given an antiepileptic. In patients not given an antiepileptic, there were no differences in the required dose of propofol and emergence among patients with autism, cerebral palsy, and intellectual disability [7]. It reported that propofol dose required for anesthesia and the emergence time from anesthesia are affected by antiepileptic use [7].

Metabolic reactions are catalyzed by cytochrome P450 (CYP) and uridine diphosphate glucosyltransferase (UGT) enzymes. CYP2B6, CYP2C9, and CYP2C19 contribute to the metabolism of propofol [8-10]. Certain antiepileptic drugs increase the blood concentration of propofol by inhibiting the action of CYP and UGT [7].

Hepatic enzyme inhibition usually occurs because of competition at the enzyme site and results in a decrease in the rate of metabolism of the affected drug [11,12]. Thus, certain antiepileptic drugs have been increased the blood concentration of propofol by inhibiting the action of CYP and UGT. Carbamazepine contributes to the competitive inhibition of hepatic CYP2C9, because metabolism CYP is the same as propofol (7). In addition, carbamazepine inhibits 2C19 [13]. Topiramate inhibits CYP2C9, in clinical study [14]. Valproate contributes to the competitive inhibition of CYP2B6, because metabolism CYP is the same as propofol [7]. In addition, valproate inhibits CYP2C9 in vitro [15]. And valproate inhibits UGT 1A9, which mediates glucuronic acid conjugation, the main metabolic pathway of propofol [16,17]. Phenytoin contributes to the competitive inhibition of hepatic CYP2C9, because metabolism CYP is the same as propofol. In addition, phenytoin inhibits CYP2C9, clinically [14,18]. And, in vitro, phenytoin, phenobarbital, and valproate inhibit UGT 1A9, which mediates glucuronic acid conjugation, the main metabolic pathway of propofol [16,17]. Benzodiazepine as clonazepam contributes to the competitive inhibition of hepatic CYP3A4 and CYP2C19, because metabolism CYP is the same as propofol [19]. In addition, benzodiazepines such as diazepam and clonazepam have sedative effect through GABA-A receptor [20,21]. Therefore, by these mechanisms, antiepileptic drugs such as carbamazepine, valproate, phenytoin, benzodiazepine and topiramate reduce the required dose of propofol and extend the time needed for emergence from anesthesia.

In contrast, the propofol metabolism may be no affected by the use of phenobarbital and zonisamide. Phenobarbital inhibits UGT 1A9, in vitro [17,22]. But, phenobarbital induces CYP2C19 [23]. Thus, phenobarbital induces and inhibits the metabolism of propofol. Consequently, because inducement and inhibition compete, phenobarbital may not affect the metabolism of propofol. Hepatic enzyme inhibition usually occurs because of the enzyme site and results in a decrease metabolism of the affected drug [11,12]. Thus, it may suppose that zonisamide contribute to the competitive inhibition of hepatic CYP3A4 that is the same as propofol, because principal inactivation pathways of zonisamide is CYP3A4, CYP2C19 and CYP3A5 [24]. But, it is reported that zonisamide does not induce or inhibit the metabolism of other drugs that included drugs metabolize by CYP3A4 or CYP2C19 [25]. Therefore, zonisamide may not affect the metabolism of propofol.

References


