

**Target Controlled Infusion as a New Mode  
For Total Intravenous Anesthesia**

*Essay*

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## **ABSTRACT**

Target controlled infusion is a new mode for total intravenous anesthesia, the rationale for TCI is based on setting a desired “target” concentration which the device achieves and maintains in plasma. Continuous infusions of intravenous anesthetics and analgesics are now commonly used to induce and maintain sedation and general anesthesia. Any drug can be used in total intravenous anesthesia but drug with more rapid onset and recovery profile is preferred.

### **Key words**

Target controlled infusion \_ Total intravenous anesthesia\_ Awareness under anesthesia.

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## *List of Abbreviations*

1. AEP: Auditory evoked potential.
2. BIS: Bispectral index.
3. CBF: Cerebral blood flow.
4.  $C_{et}$ : Target effect site concentration.
5.  $C_{pt}$ : Target plasma concentration.
6. CFM: Cerebral function monitor.
7. CFAM: Cerebral function analysing monitor.
8. CL: Clearance.
9. CNS: Central nervous system.
10. CSA: Compressed spectral array.
11. DOA: Depth of anesthesia.
12. ECG: Electrocardiography.



13. EEG: Electroencephalography.
14. EP<sub>s</sub>: Evoked potentials.
15. FDA: Food and Drug Administration.
16. FEMG: Frontalis electromyogram.
17. FFT: Fast fourier transform.
18. GABA: Gamma aminobutyric acid.
19. HRV: Heart rate variability.
20. ICP: Intracranial pressure.
21. ICU: Intensive care unit.
22. IFT: Isolated forearm technique.
23. LBM: Lean body mass.
24. LOC: Lower oesophageal contractility.
25. MCI: Manually controlled infusion.
26. MF: Median frequency.
27. NMDA: N-methyl-D-aspartate.
28. PACU: Post anesthesia care unit.
29. PONV: Postoperative nausea and vomiting.
30. PRIS: Propofol infusion syndrome.

31. PRST: Patient response to surgical stimulus.
32. RSA: Respiratory sinus arrhythmia.
33. SEF: Spectral edge frequency.
34. SEMG: Spontaneous surface electromyogram.
35. SEP: Somatosensory evoked potentials.
36. SLOC: Spontaneous lower oesophageal contractility.
37. TIVA: Total intravenous anesthesia.
38. TCI: Target controlled infusion.
39.  $t_{1/2}$ : Half life.
40. VEP: Visual evoked potentials.
41.  $V_d$  : Volume of distribution.

# INTRODUCTION

Modern anesthesia is still mostly administered by the inhalational route and there is increasing concern over its potential for pollution, such contamination could be avoided with the use of total intravenous anesthesia (TIVA).<sup>(1)</sup> TIVA is defined as a method of producing general anesthesia by injecting intravenous drugs excluding simultaneous administration of any inhalational agent. Any drug can be used in total intravenous anesthesia but drug with more rapid onset and recovery profile is preferred.

Target controlled infusion (TCI) is a way of delivering intravenous anesthesia and specifically anesthetic drugs. The rationale for TCI is based on setting a desired “target” concentration which the device achieves and maintains in plasma.<sup>(2, 3)</sup>

Since first described by schottler and colleagues in 1983, target controlled infusion (TCI) delivering systems have become widespread.<sup>(4)</sup> This technique allows more precise titration to a given clinical effect, as it makes it easier to achieve steady-state drug-blood concentrations. By contrast, manual adjustment of the drug continuous-infusion rates result in more unstable drug concentrations<sup>(5)</sup>, also the use of TCI take into account the interindividual pharmacokinetic and pharmacodynamic patient’s variability.<sup>(6)</sup>

Despite the very low incidence of awareness during the use of target controlled infusion, the bispectral index (BIS) developed from a processed electroencephalogram is reported to decrease the incidence of awareness under anesthesia.<sup>(7)</sup>

The use of simplified neuromonitors using processed EEG (e.g Bispectral index) has become widespread in recent years, improving individualized titration of anesthetic depth, electroencephalographic monitoring has been shown to reduce drug consumption, thus causing less hemodynamic instability and faster arousal, while reducing perioperative awareness.<sup>(8,9)</sup>

# **DRUGS USED IN TOTAL INTRAVENOUS ANESTHESIA**

## **Sedatives/ Hypnotics:**

### **PROPOFOL:**

**Propofol** is a short acting intravenous anesthetic and hypnotic agent, which has a rapid onset of action, short half life and very favourable recovery characteristics.<sup>(10)</sup>

### **Indications, Dosage and Routes of administration:**

#### 1. Induction of Anesthesia:

- IV 1-2.5 mg/kg (given as 40 mg every 10 seconds) until adequate anesthesia achieved.<sup>(11)</sup>

The onset of hypnosis after a dose of 2.5 mg/kg is rapid (one arm brain circulation), with a peak effect seen at 90 to 100 seconds. The duration of hypnosis is dose dependent, being 5 to 10 minutes after 2 to 2.5 mg/kg.<sup>(12)</sup>

#### 2. Maintenance of Anesthesia:

- Continuous IV Infusion
  - 100-200 mcg/kg/min started immediately following the induction dose lower infusion rates (50-100 mcg/kg/min) after 30 to 60 minutes should be used to optimize recovery time.

- Intermittent IV
  - 20-50 mg when anesthesia lightening.<sup>(13)</sup>

Maintenance anesthesia should be titrated to individual requirements.

Elderly and debilitated patients may require up to 50% lower induction and maintenance doses.<sup>(14)</sup>

### 3. Refractory agitation in ICU patients:

- Initial dose of 5 mcg/kg/minute, increase by 5-10 mcg/kg/minute q5minutes until desired level of sedation is achieved (usual dosage range 5-80 mcg/kg/minute). Daily assessment of minimum effective dose to maintain goal level of sedation is required.<sup>(15)</sup>

### 4. Procedural Sedation during surgical procedures:

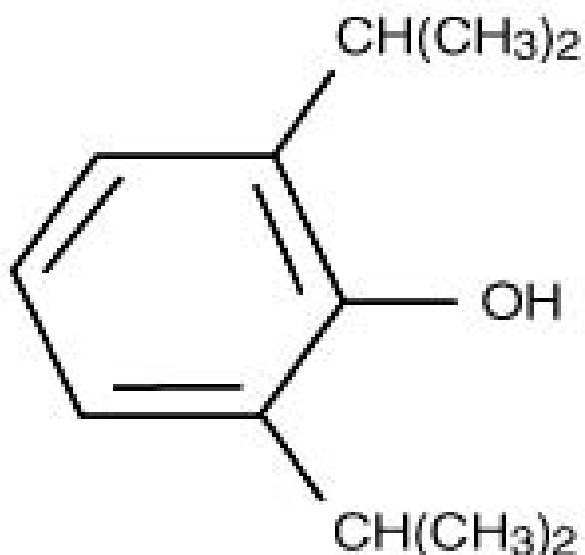
- 0.25-0.5 mg/kg IV over 1 minute, then 10-20 mg slow IV Q1-2 minutes PRN until patient is sedated.<sup>(16)</sup>

Propofol is known as a dose dependent potent inhibitor of airway reflexes in hypnotic concentrations.<sup>(17)</sup> Even subhypnotic doses are effective in preventing laryngospasm on tracheal extubation in children.<sup>(18)</sup>

The occurrence of adverse events such as postoperative nausea and vomiting (PONV) has a major influence on the quality of recovery and on the duration of postoperative stay. Importantly, there is a low incidence of PONV associated with Propofol anesthesia.<sup>(19)</sup>

## Chemistry:

Propofol (Fig. 1) is one of a group of alkylphenols.<sup>(20)</sup> The alkylphenols are oils at room temperature and insoluble in aqueous solution, but they are highly lipid soluble. Today, several formulations are presently marketed, and several others are in development. The formulation that followed the removal of Cremophor consists of 1% (weight/volume) propofol, 10% soybean oil, 2.25% glycerol and 1.2% purified egg phosphatide. Because of concern regarding microbial growth in the emulsion, disodium edetate (0.005%) was added as a retardant of bacterial growth. This formulation has a pH of 7 and appears as a slightly viscous, milky white substance. A second formulation changes in the diluent may result in slight changes in pharmacokinetics, cracking of the emulsion, spontaneous degradation of propofol, and possibly changes in pharmacologic effect. If a dilute solution of propofol is required, it is compatible with 5% dextrose in water.<sup>(21)</sup>



**Figure 1: Structure of propofol, an alkylphenol derivative**