Automated Target Controlled Infusion Systems : The Future of Total Intravenous Anaesthesia

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Introduction

Propofol based total intravenous anaesthesia (TIVA) delivered by continuous manual infusion is associated with unsatisfactory perioperative conditions because of undulations in plasma concentration of anaesthetic drugs. Target Controlled Infusion (TCI) systems provide improved convenience and control during TIVA [1]. A TCI system utilizing pharmacokinetics of Propofol is now available in the armed forces hospitals. The present paper describes this new method of delivering anaesthetic medications.

Insights into a TCI System

In any TIVA technique, one has to ensure adequate concentration of a drug at the effect site. Thus a bolus of drug has to be given initially followed by an infusion rate which alters according to drug's elimination from body as well as two way transfers from central to multiple peripheral compartments. The TCI system which is essentially an infusion pump interfaced with a computer and is also known as computer assisted continuous infusion (CACI) device, is programmed to perform complex polyexponential pharmacokinetic calculations and infusion rate adjustments to achieve accurate plasma concentration.

The anaesthesiologist sets a predetermined target plasma concentration (Cp) of an agent known to be associated with a specific clinical effect and then the infusion rates are altered automatically according to a validated pharmacokinetic model. The computer periodically calculates or predicts Cp and matches it with desired target concentration and in case of a difference, alters the infusion rate of the pump.

Open Loop Control TCI systems depend upon the anaesthesiologist to modify the target concentration on the basis of clinical response. However Closed Loop

Control systems are programmed to alter the infusion rate on the basis of a measurable feedback signal till the desired target is achieved.

Clinical Applications and Limitations of TCI Systems

A TCI systems can rapidly achieve and maintain a desired concentration at the effect site making it as convenient as the use of a vaporizer. With TCI, induction and maintenance are a continuous process with a single agent and hence the ease of control of anaesthesia is improved as compared to conventional infusion techniques. Experienced as well as inexperienced anaesthetists prefer TCI methods to manual methods once exposed to both [2].

Infusions delivered by TCI system have been used in treatment of post-operative pain, sedation in intensive care units (ICU) and maintenance of anaesthesia. They are associated with fewer incidences of hypotension, bradycardia and lesser variation in plasma drug concentrations as compared to intermittent boluses. The target concentrations of various intravenous anaesthetic agents for specific clinical effects have been given in Table 1. Recently, TCI was described as technique which will optimize intraoperative conditions and recovery,

Table 1

Plasma concentrations of various intravenous anaesthetic agents for specific clinical effects

Drug	Skin incision	Major surgery	Analgesia/sedation
Propofol (µg/ml)	2-6	2.5-7.5	1-3
Midazolam (ng/ml)	-	150-300	40-100
Methohexital (µg/ml)	5-10	5-15	2-5
Etomidate (ng/ml)	400-600	500-1000	100-300
Sufentanil (µg/ml)	1-3	2-5	0.1-0.2
Alfentanil (µg/ml)	200-300	250-450	50-100
Remifentanil (µg/ml)	4-8	4-8	1-2

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Fig. 1

allowing faster home readiness in the ambulatory setting [3]. TCI was also found to be suitable in chronic alcoholic patients, children and in war scenario [4].

Performance of TCI system is judged by the difference between predicted plasma concentration and measured concentration of the drug. Inaccuracies can creep in because of hardware failure, incorrect pharmacokinetic modelling, inter-individual pharmacokinetics variability, and even the pharmacodynamic variations shown by the patient. Population pharmacokinetic modeling may broaden the application for TCIs [5].

Our Experience

In an ongoing clinical investigation (Fig.1), the suitability of the pharmacokinetic protocol to our population and comparison of manual infusion of propofol with propofol TCI were studied. The patients in TCI group were anaesthetized and maintained by TCI of propofol at a rate to achieve a target concentration of 3-5 $\mu\text{g/ml}$. In the other group, anaesthesia was induced with propofol in dosage of 2.5 mg/kg followed by manual infusion of propofol initially @ 10 mg/kg/hr and then @ 6 mg/kg/hr. Vecuronium was used as neuromuscular blocking agent.

Our early experience (data not statistically analysed) with 20 patients ranging in age from 18-60 years suggests that in the TCI group, an initial target of 4 $\mu\text{g/ml}$ was satisfactory. However, the target could be easily reduced to 3.5 or even 3 $\mu\text{g/ml}$ after 45-60 minutes of anaesthesia as guided by the clinical parameters. When compared with manual group, time to lose consciousness was longer and the amount of propofol resulting in loss of eye lash reflex was greater in TCI group. However, it was also evident that not only the degree of haemodynamic stability was greater but there were less frequent interventions in TCI group. Quality of anaesthesia as assessed by using Evan & Davies' 'pressure, rate, sweating and tears' scoring system was found to be better in TCI group. The total amount of propofol infused was higher in TCI group. During recovery, the time taken to open eyes was longer in TCI group though there was lesser incidence of post operative nausea vomiting. There were no instances of recall. While it would be premature to make any deductions now, it can be surmised that the Marsh's pharmacokinetic protocol overestimates the propofol infusion requirements for our study population (as delivered by the system used at our institute) and it could be possible to lower the target levels even further. A clearer picture is likely to emerge after the completion of study on a larger number of subjects.

Future Directions

With further refinement in pharmacokinetic modeling, devices predicting effect site concentration rather than plasma drug concentration are available. Anaesthesia work stations including TCI systems controlling a series of infusion pumps will be the norm of the day. Development of a true closed loop target delivery system where anaesthesia could be maintained solely on the basis of measurement of anaesthetic depth and analgesia is another exciting area.

Conflicts of Interest

None identified

References

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