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SCIENTIFIC ARTICLE

Comparative study between fast and slow induction of propofol given by target-controlled infusion: expected propofol concentration at the effect site. Randomized controlled trial☆

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Abstract
Background and objective: Studies have shown that the rate of propofol infusion may influence the predicted propofol concentration at the effect site (Es). The aim of this study was to evaluate the Es predicted by the Marsh pharmacokinetic model (ke0 0.26 min^{-1}) in loss of consciousness during fast or slow induction.
Method: The study included 28 patients randomly divided into two equal groups. In slow induction group (S), target-controlled infusion (TCI) of propofol with plasma, Marsh pharmacokinetic model (ke0 0.26 min^{-1}) with target concentration (Tc) at 2.0-$\mu g\ mL^{-1}$ were administered. When the predicted propofol concentration at the effect site (Es) reached half of Es value, Es was increased to previous Es + 1 $\mu g\ mL^{-1}$, successively, until loss of consciousness. In rapid induction group (R), patients were induced with TCI of propofol with plasma (6.0 $\mu g\ mL^{-1}$) at effect site, and waited until loss of consciousness.

☆ Study developed at CET/SBA of Instituto Penido Burnier e Centro Médico de Campinas.
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Results: In rapid induction group, Tc for loss of consciousness was significantly lower compared to slow induction group (1.67 ± 0.76 and 2.50 ± 0.56 μg mL^{-1}, respectively, $p = 0.004$).
Conclusion: The predicted propofol concentration at the effect site for loss of consciousness is different for rapid induction and slow induction, even with the same pharmacokinetic model of propofol and the same balance constant between plasma and effect site.

PALAVRAS-CHAVE
Anestésicos;
Venoso;
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Geral;
Venosa

Estudo comparativo entre indução rápida e lenta de propofol em infusão alvo-controlada: concentração de propofol prevista no local de ação. Ensaio clínico aleatório

Resumo
Justificativa e objetivo: Estudos mostraram que a taxa de infusão de propofol pode influenciar na concentração prevista de propofol no local de ação (Ce). O objetivo deste estudo foi avaliar a Ce prevista pelo modelo farmacocinético de Marsh (ke0 0,26 min^{-1}) na perda da consciência durante indução rápida ou lenta.
Método: Participaram deste estudo 28 pacientes, divididos aleatoriamente em dois grupos iguais. No grupo indução lenta (L), foram induzidos com propofol em infusão alvo-controlada (IAC) plasmática, modelo farmacocinético de Marsh (ke0 0,26 min^{-1}), com concentração alvo (Ca) em 2,0 μg.ml^{-1}. Quando a concentração de propofol prevista no local de ação (Ce) atingia metade do valor da Ca, aumentava-se a Ca para Ca anterior + 1 μg.ml^{-1}. Assim sucessivamente até o momento da perda da consciência do paciente. No grupo indução rápida (R), os pacientes foram induzidos com propofol em IAC plasmática com Ca em 6,0 μg.ml^{-1} e aguardava-se a perda da consciência do paciente.
Resultados: No grupo indução rápida, a Ce na perda da consciência foi significativamente mais baixa em relação ao grupo de indução lenta (1,67 ± 0,76 e 2,50 ± 0,56 μg.ml^{-1}, respectivamente, p = 0,004).
Conclusão: A concentração prevista de propofol no local de ação durante a perda da consciência é diferente numa indução rápida e numa indução lenta, até com o mesmo modelo farmacocinético de propofol e a mesma constante de equilíbrio entre o plasma e o local de ação.

Introduction

Recently several studies have shown a good correlation between the predicted propofol concentration at the effect site (Es) by Marsh pharmacokinetic model (ke0 0.26 min^{-1}) and sedation degree, bispectral index (BIS) values, entropy, evoked potential index, and loss and recovery of consciousness.[1–5]

Because of this good correlation with pharmacodynamics, some authors suggested that the target concentration of propofol should be titrated during maintenance of anesthesia based on Es reached in loss of consciousness.[3,4,6]

However, other studies show that the rate of infusion of propofol may influence the balance between the plasma concentration and the concentration at the effect site; that is, in the first-order mathematical constant called Ke0.[7,8]

The main objective of this study was to evaluate the Es predicted by the Marsh pharmacokinetic model (ke0 0.26 min^{-1}) on loss of consciousness during rapid or slow induction of patients undergoing laparoscopic cholecystectomy under total intravenous anesthesia with propofol and remifentanil. Es was also evaluated during anesthesia maintenance and recovery.

The hypothesis to be tested is that, even using the same pharmacokinetic model and the same equilibrium constant between plasma and effect site, the effect site in rapid induction is different from that in slow induction during loss of consciousnesses.

Method

After approval by the Research Ethics Committee and receiving the written informed consent, 28 patients, aged between 18 and 65 years, of both sexes, ASA physical status 1 and 2, and undergoing laparoscopic cholecystectomy under total intravenous anesthesia with propofol and remifentanil, were enrolled in this randomized clinical trial.

The sample size was based on a previous pilot study. Taking into account that the difference of proportionality