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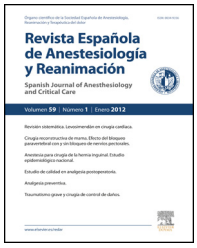

ORIGINAL ARTICLE

Comparison of the hemodynamic response to induction and intubation during a target-controlled infusion of propofol with 2 different pharmacokinetic models. A prospective randomized trial☆

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KEYWORDS
Intravenous anaesthesia;
Propofol;
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Drug delivery systems;
Consciousness monitors;
Haemodynamics/drugs effects

Abstract
Objective: To determine the best propofol pharmacokinetic model that meets patient requirements and is devoid of major haemodynamic side effects.
Material and methods: Prospective, randomised, open-label, clinical trial was performed on an intention to treat basis. It included 280 patients with ASA physical status I–III, aged 18–80 years and a weight range between 45 and 100 kg, scheduled for surgery under general anaesthesia. They were randomised into two groups according to the pharmacokinetic model: Modified Marsh group and Schnider group. The haemodynamic changes that occurred during the induction and intubation were analysed. A propofol target-controlled infusion was started to achieve and maintain a bispectral index value between 35 and 55. At minute 6, orotracheal intubation was performed and the study finished at minute 11.

Heart rate, mean arterial pressure and their product (HR × MAP) were measured and recorded every minute throughout the study. Every HR × MAP value was compared to its baseline value to determine the minimum value before intubation, the maximum value after intubation, the maximum variation after intubation, and its final value. The GRADIENTE (MIN, MAX) variable (primary endpoint of this study) analyses the difference between maximal and minimal values related to intubation. Propofol doses and calculated concentrations and any hypotensive events were also recorded.

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Results: No differences were found between groups regarding haemodynamic performance. GRADIENTE (MIN, MAX) values and the percentage of hypotensive events were: Modified Marsh group median 77.41% vs. Schnider group 84.86% ($p = 0.821$) and 17.3% vs. 12.8% ($p = 0.292$), respectively.
Conclusion: The study failed to demonstrate any haemodynamic difference between the two groups, even though the Modified Marsh group received a larger dose of propofol.

PALABRAS CLAVE
Anestesia intravenosa;
Propofol;
Farmacocinética;
Sistemas de liberación de medicamentos;
Monitores de conciencia;
Hemodinámica/efectos de fármacos

Comparación de la respuesta hemodinámica durante la inducción y la intubación con 2 modelos de infusión controlada por objetivo en el sitio de efecto para propofol: estudio prospectivo y aleatorizado

Resumen
Objetivo: Determinar qué modelo farmacocinético para propofol proporciona una mayor estabilidad hemodinámica durante la inducción anestésica.
Material y métodos: Ensayo clínico prospectivo, aleatorizado, no ciego y por intención de tratar donde se incluyeron 280 pacientes ASA I–III, 18–80 años de edad y 45–100 kg de peso, programados para cirugía bajo anestesia general. Los pacientes se distribuyeron aleatoriamente en 2 grupos, dependiendo del modelo farmacodinámico para propofol empleado (Marsh Modificado o Schnider), para analizar el comportamiento hemodinámico durante la inducción y la intubación. Se administró una infusión controlada por objetivo de propofol para mantener un índice biespectral de 35–55. En el minuto 6 se realizó la intubación orotraqueal, finalizando el estudio a los 11 min del comienzo.

Fueron recogidos cada minuto la frecuencia cardiaca, la tensión arterial media, las dosis, las concentraciones de propofol y la aparición de hipotensión. El producto de la frecuencia cardiaca y la tensión arterial media (FC × TAM) fue calculado cada minuto y analizado pormenorizadamente, determinando, entre otros, el valor mínimo antes de la intubación, el máximo tras ella, y la relación entre estos 2 valores (GRADIENTE [MÍN, MÁX], variable principal del estudio).
Resultados: No hubo diferencias significativas en el comportamiento hemodinámico entre los grupos del estudio. GRADIENTE (MÍN, MÁX): 77,41 vs. 84,86% (p = 0,821); hipotensión: 17,3 vs. 12,8% (p = 0,292); Marsh Modificado y Schnider, respectivamente.
Conclusión: No se han podido demostrar diferencias en el comportamiento hemodinámico, a pesar de que el grupo del Marsh Modificado recibió una dosis mayor de propofol.

Introduction

Haemodynamic changes during general anaesthesia have a poor prognosis, and should be avoided. Most variations are secondary to anaesthesia induction and orotrachael intubation (OTI).[1,2]

The decline in heart rate (HR) and blood pressure (BP) during anaesthesia induction is dependent on a variety of factors, including the anaesthetic dose used, high ASA (American Society of Anaesthesia) physical status, and certain diseases (anaemia, hypovolaemia, or ventricular dysfunction).[3–7] OTI, however, is accompanied by an increase in these haemodynamic parameters.[3,8,9] Correct analgesic management can minimise this response.

The decline in blood pressure during anaesthesia induction with propofol is due to a loss of systemic vascular resistance[10,11] or a decline in cardiac output, which can be aggravated by the addition of other drugs, such as fentanyl.[12,13] However, the haemodynamic response to intubation is milder with propofol than with other hypnotic agents.[8,14] Correct analgesic management can minimise this response.

Target-controlled infusion (TCI) and the use of parameters such as the bispectral index (BIS) to measure depth of anaesthesia can help anaesthesiologists adjust the dosage to the needs of each patient over time, thus giving better control over haemodynamic changes.[15]

Different TCI models for propofol have previously been compared to evaluate pharmacological aspects such as the accuracy of the calculated concentration, the pharmacokinetic and pharmacodynamic properties, and the safety of the drug.[16,17] Different forms of administration (manual infusion), different types of general anaesthetic,[18–21] and even different effect-site concentration (Ec) TCI models have been compared.[22] In all these studies, the most predominant side effect was haemodynamic compromise.