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SCIENTIFIC ARTICLE

Pharmacokinetic and clinical effects of two bupivacaine concentrations on axillary brachial plexus block

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KEYWORDS
Bupivacaine;
Brachial plexus;
Pharmacokinetics;
Regional anesthesia

Abstract
Introduction: The risk of systemic bupivacaine toxicity is a persistent problem, which makes its pharmacokinetic study fundamental for regional anesthesia safety. There is little evidence of its influence on plasma peak at different concentrations. The present study compares two bupivacaine concentrations to establish how the concentration affects this drug plasma peak in axillary brachial plexus block. Postoperative latency and analgesia were also compared.
Methods: 30 patients were randomized. In the 0.25% Group, 0.25% bupivacaine (10 mL) was injected per nerve. In the 0.5% Group, 0.5% bupivacaine (5 mL) was injected per nerve. Peripheral blood samples were collected during the first 2 h after the blockade. For sample analyses, high performance liquid chromatography mass spectrometry was used.
Results: Plasma peak occurred 45 min after the blockade, with no difference between groups at the assessed time-points. Plasma peak was 933.97 ± 328.03 ng·mL^{-1} (mean ± SD) in 0.25% Group and 1022.79 ± 253.81 ng·mL^{-1} in 0.5% Group ($p = 0.414$). Latency was lower in 0.5% Group than in 0.25% Group ($10.67 \pm 3.71 \times 17.33$ min ± 5.30, respectively, $p = 0.004$). No patient had pain within the first 4 h after the blockade.
Conclusion: For axillary brachial plexus block, there was no difference in bupivacaine plasma peak despite the use of different concentrations with the same local anesthetic mass. The concentration inversely influenced latency.

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PALAVRAS-CHAVE
Bupivacaína;
Plexo braquial;
Farmacocinética;
Anestesia regional

Efeitos farmacocinéticos e clínicos de duas concentrações de bupivacaína no bloqueio do plexo braquial via axilar

Resumo
Introdução: O risco de intoxicação sistêmica pelo uso da bupivacaína é um problema persistentee torna seu estudo farmacocinético fundamental para a segurança da anestesia regional. São escassas as evidências sobre a influência de diferentes concentrações no pico plasmático desse fármaco. O presente estudo compara duas concentrações de bupivacaína para estabelecer como a concentração afeta o pico plasmático desse fármaco no bloqueio do plexo braquial via axilar. Também se compararam latência e analgesia pós-operatória.
Métodos: Foram randomizados 30 pacientes. No Grupo 0,25%, injetaram-se 10 mL de bupivacaína 0,25% por nervo. No Grupo 0,5%, injetaram-se 5 mL de bupivacaína 0,5% por nervo. Amostras de sangue periférico foram colhidas durante as duas primeiras horas após o bloqueio. Para análise das amostras, usou-se a cromatografia líquida de alta frequência acoplada ao espectrômetro de massas.
Resultados: O pico plasmático ocorreu 45 minutos após o bloqueio, sem diferença entre os grupos nos tempos avaliados. O pico plasmático (média $\pm$ DP) foi 933,97 $\pm$ 328,03 ng.mL^{-1} no Grupo 0,25% e 1.022,79 $\pm$ 253,81 ng.mL^{-1} no Grupo 0,5% (p = 0,414). O Grupo 0,5% apresentou menor latência com relação ao Grupo 0,25% (10,67 $\pm$ 3,71 $\times$ 17,33 min $\pm$ 5,30; respectivamente; p = 0,004). Nenhum paciente apresentou dor nas primeiras quatro horas após o bloqueio.
Conclusão: Para o bloqueio do plexo braquial via axilar, não foi detectada diferença no pico plasmático de bupivacaína apesar do uso de diferentes concentrações, com a mesma massa de anestésico local. A concentração influenciou inversamente a latência.

Introduction

The success of regional anesthesia (RA) is directly related to the evolution of knowledge and the development of local anesthetics (LA). Despite efforts to increase its safety, a persistent problem in clinical practice is local anesthetic systemic toxicity (LAST).[1,2] The rapid increase in LA plasma levels leads to devastating neurological and cardiac complications; LA systemic toxicity accounts for one-third of deaths or brain damage during regional anesthesia.[3,4] Regarding RA type, peripheral nerve block may require a greater LA volume, with a higher risk of LAST compared to epidural block.[1,5,6]

The increased use of ultrasound in clinical practice has reduced the occurrence of complications related to peripheral block, mainly due to the reduction of inadvertent vascular puncture.[7,8] Moreover, in order to improve the safety of regional anesthesia, anesthesia societies around the world recommend using the minimum dose required and stipulate the maximum LA dose to be used in peripheral blocks.[9] However, there is no consensus among the different societies about the maximum recommended dose of LA, which reveals a gap in understanding the pharmacokinetics of these drugs.[9] Furthermore, there are several factors that may influence LA plasma peak such as the infusion site vascularization and the tissue binding ability.[9]

Surprisingly, data on the effect of different LA concentrations on plasma levels are scarce and conflicting so far. However, understanding the pharmacokinetics of these chemical compounds is essential to prevent complications.[10–12]

This study was performed to evaluate this relationship, particularly regarding axillary brachial plexus block. Thus, the present study provides an analysis of the pharmacokinetic profiles of two bupivacaine concentrations obtained after axillary brachial plexus block. Despite the different concentrations used, the total mass of local anesthetic was maintained to evaluate the effect of these different concentrations on this drug plasma peak. As a secondary objective, latency and postoperative analgesia were evaluated in both groups.

Material and method

A prospective and randomized clinical trial was performed at the operating room of the Hand and Upper Limb Surgery Department at a quaternary University Hospital. The anesthetic procedures were initiated in January 2014, after approval by the Ethics and Institutional Research Committee approval number 288,461. Inclusion criteria were: candidates for elective distal forearm and hand surgery, with brachial plexus block indication for anesthesia and analgesia, aged between 18 and 65 years, with physical status (ASA I or II) according to the American Society of Anesthesiologists, body mass index (BMI) less than 35 kg m^{-2}, and a signed written informed consent. Exclusion criteria were: cognitive impairment, infection at the puncture site, coagulopathy, history of bupivacaine allergy.

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