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SCIENTIFIC ARTICLE

Evaluation of sciatic nerve damage following intraneural injection of bupivacaine, levobupivacaine and lidocaine in rats

Oznur Sen[a,*], Nevzat Cem Sayilgan[b], Ayse Cigdem Tutuncu[b], Mefkur Bakan[c], Guniz Meyanci Koksal[b], Huseyin Oz[d]

[a] *Department of Anesthesiology and Reanimation, Ministry of Health, Haseki Training and Research Hospital, Istanbul, Turkey*
[b] *Department of Anesthesiology and Reanimation, Istanbul University, Cerrahpasa Medical Faculty, Istanbul, Turkey*
[c] *Department of Anesthesiology and Reanimation, Bezmialem Vakif University, Faculty of Medicine, Istanbul, Turkey*
[d] *Department of Anesthesiology and Reanimation, Medipol University, Faculty of Medicine, Istanbul, Turkey*

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KEYWORDS
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Abstract
Objective: The local anesthetics may cause neurotoxicity. We aimed to compare the neurotoxic potential of different local anesthetics, local anesthetic induced nerve damage and pathological changes of a peripheral nerve.
Methods: Sixty Wistar rats weighing 200–350 g were studied. Rats were assigned into 3 groups and 26-gauge needle was inserted under magnification into the left sciatic nerve and 0.2 mL of 0.5% bupivacaine, 5% levobupivacaine, and 2% lidocaine were injected intraneurally. An individual who was blind to the specifics of the injection monitored the neurologic function on postoperative 1st day, and daily thereafter. Neurologic examination included assessment for the presence and severity of nociception and grasping reflexes. At the 7th day sciatic nerve specimen was taken for evaluation of histopathologic changes.
Results: There was no statistical difference detected among groups regarding grasping reflex and histopathologic evaluation. Two cases in bupivacaine group, 1 case in levobupivacaine group and 2 cases in lidocaine group had slight grasping, while 1 case in lidocaine group had no grasping reflex on the seventh day. Severe axonal degeneration was observed in all groups, respectively in bupivacaine group 4 (20%), levobupivacaine group 3 (15%), and lidocaine group 6 (30%).
Conclusion: In all groups, histopathological damage frequency and severity were more than the motor deficiency.

* Corresponding author.
E-mail: senoznur@gmail.com (O. Sen).

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PALAVRAS-CHAVE
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Levobupivacaína;
Neurotoxicidade

Avaliação da lesão do nervo ciático após injeção intraneural de bupivacaína, levobupivacaína e lidocaína em ratos

Resumo
Objetivo: Os anestésicos locais podem causar neurotoxicidade. Nosso objetivo foi comparar o potencial neurotóxico de diferentes anestésicos locais, os danos induzidos aos nervos e as alterações patológicas de um nervo periférico.
Métodos: Sessenta ratos Whistler pesando 200-350 g foram estudados. Os ratos foram divididos em três grupos, uma agulha de calibre 26 foi inserida no nervo ciático esquerdo, com o uso de ampliação, e 0,2 mL de bupivacaína a 0,5%, levobupivacaína a 5% e lidocaína a 2% foram injetados por via intraneural. Um colaborador, cego para os conteúdos das injeções, monitorou a função neurológica no primeiro dia de pós-operatório e depois diariamente. O exame neurológico incluiu a avaliação da presença e da gravidade da nocicepção e dos reflexos de agarrar. No sétimo dia, uma amostra do nervo ciático foi colhida para avaliar as alterações histopatológicas.
Resultados: Não houve diferença estatística entre os grupos em relação ao reflexo de agarrar e à avaliação histopatológica. Dois casos no grupo bupivacaína, um caso no grupo levobupivacaína e dois casos no grupo lidocaína apresentaram um leve reflexo de agarrar; também no grupo lidocaína, um caso não apresentou reflexo de agarrar no sétimo dia. Degeneração axonal grave foi observada em todos os grupos: quatro casos no grupo bupivacaína (20%), três casos no grupo levobupivacaína 3 (15%) e seis casos no grupo lidocaína (30%).
Conclusão: Em todos os grupos, a frequência de dano histopatológico e de gravidade foi maior que a deficiência motora.

Introduction

Effects of intraneural injection of local anesthetics and peripheral nerve injury are rare complications of regional anesthesia. Most of these are temporary, subclinical mononeuropathies.[1] Reversible axonal damage and injury progressing to myelin degeneration can be determined histopathologically after intraneuronal injections. In animal studies, retention of motor functions despite the damage has been observed.[2]

This study has aimed at investigation in the rat of motor dysfunction and the histopathological changes after a single dose injection intraneurally of bupivacaine, levobupivacaine and lidocaine.

Methods

Hospital Animal Ethics Council approval was obtained for this study. Sixty Wistar rats of 200–350 g weight were kept in the laboratory under conditions of 20–24 °C temperature, 65–70% humidity, 12 h light and 12 h dark with unrestricted feed and liquid requirements. Experimentally, the rats were anesthetized, after food withdrawal for 4 h, by intraperitoneal injection of 100 mg/kg ketamine hydrochloride (Ketalar®, Eczacıbaşı Warner Lambert, İstanbul, Turkey). Subsequently, the gluteal muscle area was cleaned with batticon antiseptic solution and the sciatic nerve was exposed through a limited transverse incision. Intraneural injections were made with the use of an automatic infusion pump through no 26 cannula entered at 45–60° angles.

The rats were subdivided into three groups as Group B (Bupivacaine) given 0.2 mL 0.5% bupivacaine; Group C (Chirocaine) given 0.2 mL 0.5% levobupivacaine, and Group L (Lidocaine) given 0.2 mL 2% lidocaine over 1 min infusions. The rats were woken up after closing the incisions.

Neurological functions of the rats were evaluated by three individuals, not informed of the applied local anesthetics, every day up to 7 days after the intraneural injections. For neurological assessment, nociception and the grasping reflex were evaluated. Nociception was triggered by pain on the first and the fifth phalanges and rated as 4/'normal withdrawal reflex', 3/'slower withdrawal'; 2/'slow withdrawal or sound; absence of movement'; 1/'very slight withdrawal'; 0/'no withdrawal'; and the grasping reflex was rated as 2/'normal grasping reflex; 1/'slow grasping'; 0/'absence of grasping'.

The rats were given ketamine hydrochloride, sacrificed by decapitation and the sciatic nerve was excised. The samples were routinely placed in 10% buffered formaldehyde, embedded in paraffin, dyed with haemotoxylin and eosin and examined under light microscopy for integrity of the neurological structure, mechanical damage, myelin damage and cellular infiltration.

Myelin damage was estimated using the Nerve Injury Scoring System (NISS), and the scoring was as 1 = 'normal, mild degeneration or demyelination', 2 = 'moderate level of degeneration' or (<50% damaged nerve tissue) and 3 = diffuse degeneration or demyelinization (>50% damaged nerve tissue).

The statistical evaluation of the neurological results was carried out by the Kruskal–Wallis and Mann–Whitney *U* tests.