

SCIENTIFIC ARTICLE

Comparative immunohistochemical assessment of the effect of repetitive anesthesia with isoflurane and sevoflurane on rat liver[☆]



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KEYWORDS

Anesthesia;
Caspase-3;
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Abstract

Background and objectives: Inhalation anesthetics are used in human, as well as veterinary medical practice. In the present study we investigated the effect of isoflurane and sevoflurane on rat hepatocytes.

Methods: A total of 40 Wistar female rats were used in this study. Animals were divided in groups of 5 rats. Groups IM, SM served as control groups. Groups I1, I2, I3 were used to study isoflurane and S1, S2, S3 for sevoflurane study. They were anesthetized 3 times, for 2 h long, at 2 days interval with a concentration of: 1.5% isoflurane (I1, I2, I3) and 2% sevoflurane (S1, S2, S3). The oxygen supply throughout the anesthesia was 1 L O₂/min. Groups IM, IS, I1, S1 were sacrificed immediately after the last anesthesia. Groups I2, S2 were sacrificed 6 h after the last anesthesia, and groups I3, S3, 24 h post-anesthesia. Liver samples were harvested to highlight caspase-3 in apoptotic hepatocytes.

Results: Following isoflurane administration, there were less than 1% cells in apoptosis highlighted in rat livers from groups IM, I1 and I2. At 24 h post-anesthesia (group I3), a small number of apoptotic hepatocytes was highlighted (around 3.23% cells in apoptosis), with a strictly periacinar disposition, randomly distributed in a small number of hepatic lobules. After sevoflurane administration, less than 1% apoptotic hepatocytes were identified at all control moments throughout the study.

[☆] The study was carried out at the Department of Anesthesiology and Surgical Propedeutics, University of Agricultural Sciences and Veterinary Medicine, Cluj-Napoca, Romania.

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Conclusions: The results suggest that the anesthetics do not present a considerable hepatotoxicity. The comparative assessment of the two anesthetics shows that sevoflurane is superior to isoflurane.

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PALAVRAS-CHAVE

Anestesia;
Caspase-3;
Isoflurano;
Fígado;
Sevoflurano

Avaliação imuno-histoquímica comparativa do efeito da anestesia repetitiva com isoflurano e sevoflurano sobre o fígado de rato

Resumo

Justificativa e objetivos: Anestésicos inalatórios são usados em humanos e também na prática médica veterinária. No presente estudo investigamos o efeito de isoflurano e sevoflurano em hepatócitos de rato.

Métodos: No total, 40 ratos Wistar fêmeas foram usados neste estudo. Os animais foram divididos em grupos de cinco ratos cada. Os grupos IM e SM serviram como grupos controle. Os grupos I1, I2 e I3 foram usados para o estudo de isoflurano e os grupos S1, S2 e S3 para o estudo de sevoflurano. Os ratos foram anestesiados três vezes, durante o período de 2 horas em intervalos de dois dias, com uma concentração de 1,5% de isoflurano (I1, I2, I3) e 2% de sevoflurano (S1, S2, S3). O fornecimento de oxigênio durante a anestesia foi de 1 L O₂/min. Os grupos IM, IS, I1 e S1 foram sacrificados imediatamente após a última anestesia. Os grupos I2 e S2 foram sacrificados 6 horas após a última anestesia e os grupos I3 e S3 foram sacrificados 24 horas após a anestesia. Amostras dos fígados foram colhidas para ressaltar a caspase-3 em hepatócitos apoptóticos.

Resultados: Após a administração de isoflurano, havia menos de 1% das células em apoptose em destaque nos fígados dos ratos dos grupos IM, I1 e I2. Às 24 horas após a anestesia (grupo I3), um pequeno número de hepatócitos apoptóticos foi destacado (cerca de 3,23% de células em apoptose), com uma disposição estritamente periacinar, distribuídos aleatoriamente em um pequeno número de lóbulos hepáticos. Após a administração do sevoflurano, menos de 1% de hepatócitos apoptóticos foi identificado em todos os momentos de controle ao longo do estudo.

Conclusões: Os resultados sugerem que os anestésicos não apresentam uma hepatotoxicidade considerável. A avaliação comparativa dos dois anestésicos mostra que sevoflurano é superior ao isoflurano.

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Introduction

Inhalational anesthetics are widely used in both human and veterinary medicine. They can be utilized in anesthetic management in a large number of species, including reptiles, birds and wild animals.¹⁻⁵ The primary site for metabolism of inhalational anesthetics is represented by the liver.^{6,7} Under these circumstances, it is possible that some physiological or morphological changes appear in the liver, due to either the direct action of these anesthetics or some intermediary metabolites resulted during their degradation. These aspects have made the object of numerous studies which brought much useful information, but there are still controversies surrounding the inhalational anesthetics' action on the liver. Thus, there are studies that report a minor liver enzymes elevation, while others report fulminant necrotic hepatitis, resulting even in patient's death.⁸⁻¹⁰

The great majority of the investigations have studied the inhalational anesthetic effects on liver function.¹¹ Macro and especially microscopic aspects were the object of study of

a relatively small number of investigations. Some authors sustain that prolonged anesthesia with isoflurane does not induce hepatic lesions in animals.¹²⁻¹⁴ Soubhia et al.¹⁰ evaluated the transaminase activity, and also the liver, histologically, after exposure to sevoflurane, recording slightly increased values for transaminase activity and no morphological change of the liver parenchyma in light microscopy. Honda et al.¹⁵ evaluated both liver function and morphology after exposure to isoflurane and sevoflurane. The conclusion of the study was that the degree of hepatic lesions induced by isoflurane exposure was higher than the one induced by sevoflurane. Elena et al.¹⁶ studied liver, kidney and spleen physiology and histology after repeated sevoflurane anesthesia. The authors did not detect an altered liver and renal function or changes in the architecture of these organs. Other authors report histopathological lesions varying from panlobular, to multifocal, even fulminant necrosis.¹⁷ A case of fulminant liver failure was reported after the third exposure to isoflurane, with submassive and massive necrosis at histopathological examination.⁸ Zizek et al.⁹ also report

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