Rev Bras Anestesiol. 2015;65(1):1–6

REVISTA BRASILEIRA DE ANESTESIOLOGIA

Official Publication of the Brazilian Society of Anesthesiology
www.sba.com.br

SCIENTIFIC ARTICLE

Rectal dexmedetomidine in rats: evaluation of sedative and mucosal effects

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Received 1 July 2013; accepted 9 September 2013
Available online 5 November 2013

KEYWORDS
Dexmedetomidine;
Rectum;
Rat;
Anesthesia;
Mucosa

Abstract
Background and objectives: In this study, we investigated the anesthetic and mucosal effects of the rectal application of dexmedetomidine to rats.
Methods: Male Wistar albino rats weighing 250–300 g were divided into four groups: Group S ($n = 8$) was a sham group that served as a baseline for the normal basal values; Group C ($n = 8$) consisted of rats that received the rectal application of saline alone; Group IPDex ($n = 8$) included rats that received the intraperitoneal application of dexmedetomidine (100 $\mu g\,kg^{-1}$); and Group RecDex ($n = 8$) included rats that received the rectal application of dexmedetomidine (100 $\mu g\,kg^{-1}$). For the rectal drug administration, we used 22 G intravenous cannulas with the stylets removed. We administered the drugs by advancing the cannula 1 cm into the rectum, and the rectal administration volume was 1 mL for all the rats. The latency and anesthesia time (min) were measured. Two hours after rectal administration, 75 $mg\,kg^{-1}$ ketamine was administered for intraperitoneal anesthesia in all the groups, followed by the removal of the rats' rectums to a distal distance of 3 cm via an abdominoperineal surgical procedure. We histopathologically examined and scored the rectums.
Results: Anesthesia was achieved in all the rats in the Group RecDex following the administration of dexmedetomidine. The onset of anesthesia in the Group RecDex was significantly later and of a shorter duration than in the Group IPDEx ($p < 0.05$). In the Group RecDex, the administration of dexmedetomidine induced mild–moderate losses of mucosal architecture in the colon and rectum, 2 h after rectal inoculation.
Conclusion: Although 100 $\mu g\,kg^{-1}$ dexmedetomidine administered rectally to rats achieved a significantly longer duration of anesthesia compared with the rectal administration of saline, our

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http://dx.doi.org/10.1016/j.bjane.2013.09.005

histopathological evaluations showed that the rectal administration of 100 μg kg^{-1} dexmedetomidine led to mild–moderate damage to the mucosal structure of the rectum.

PALAVRAS-CHAVE
Dexmedetomidina;
Reto;
Rato;
Anestesia;
Mucosa

Dexmedetomidina retal em ratos: avaliação dos efeitos sedativos e sobre a mucosa

Resumo
Justificativa e objetivos: Neste estudo nós investigamos os efeitos anestésicos e sobre a mucosa da aplicação retal de dexmedetomidina a ratos.
Métodos: Ratos machos albinos Wistar, pesando 250-300 g, foram divididos em quatro grupos: Grupo S ($n = 8$) foi um grupo sham que serviu de base para os valores basais normais; Grupo C ($n = 8$) consistiu em ratos que receberam a aplicação retal apenas de soro fisiológico; Grupo IPDex ($n = 8$) consistiu em ratos que receberam aplicação intraperitoneal de dexmedetomidina (100 μg kg^{-1}) e Grupo RecDex ($n = 8$) consistiu em ratos que receberam a aplicação retal de dexmedetomidina (100 μg kg^{-1}). Para a administração dos fármacos por via retal, usamos cânulas intravenosas de calibre 22, com os estiletes removidos. A administração consistiu em avançar a cânula 1 cm no reto, e o volume de administração retal foi de 1 mL para todos os ratos. Os tempos (min) de latência e de anestesia foram registrados. Duas horas após a administração por via retal, 75 mg kg^{-1} de cetamina foram administrados a todos os grupos para anestesia intraperitoneal, seguido por remoção dos retos dos ratos a uma distância 3 cm distal por meio de procedimento cirúrgico abdominoperineal. Os retos foram histopatologicamente examinados e classificados.
Resultados: A anestesia foi realizada em todos os ratos do grupo RecDex após a administração de dexmedetomidina. O tempo de início da anestesia no Grupo RecDex foi significativamente mais longo e com uma duração mais curta que no Grupo IPDEx ($p < 0,05$). No Grupo RecDex, a administração de dexmedetomidina induziu perdas leves a moderadas da arquitetura da mucosa do cólon e reto 2 h após a inoculação retal.
Conclusão: Embora a administração de 100 μg kg^{-1} de dexmedetomidina por via retal em ratos tenha resultado em uma duração significativamente maior da anestesia, em comparação com a administração retal de soro fisiológico, nossas avaliações histopatológicas mostraram que a administração retal de 100 μg kg^{-1} de dexmedetomidina ocasionou danos leves a moderados à estrutura da mucosa retal.

Introduction

Premedication is the preoperative nasal, oral, rectal, intramuscular or intravenous administration of sedative drugs to lower the patient's fear of surgical intervention, achieve sedation and anxiolysis, and decrease the amount of anesthetics needed.[1–6] In addition to benzodiazepines such as midazolam, which are commonly used for this purpose, the use of alpha 2 agonists such as clonidine and dexmedetomidine is becoming popular.[3–8] For pediatric patients, it is essential that premedication agents are administered non-invasively, i.e., transmucosally, nasally or orally.[3–5,7,8] Rectal administration is also preferred, particularly for the premedication of young children.[2,3,9–11] Previous studies have shown that, similar to midazolam and ketamine, clonidine can be administered rectally for premedication.[2,9–14]

Dexmedetomidine is an alpha adrenergic agonist with high levels of specificity and selectivity to alpha 2 receptors. Dexmedetomidine can be used for sedation, analgesia and anesthesia in intensive care settings, as well as for local and regional anesthesia applications.[8,15–17] Research has also shown that dexmedetomidine can be administered orally, nasally, transmucosally or intramuscularly for premedication.[4,8,18–24] However, there are no published studies concerning the rectal application of dexmedetomidine for premedication.

Our hypothesis was that dexmedetomidine administered rectally to rats would produce a sedative effect with no damage to the rectal mucosa.

To test this hypothesis, we compared the anesthetic effects of equal doses of dexmedetomidine administered rectally or intraperitoneally to rats. In addition, we compared the histopathological effects on rectal mucosa of rectally administered dexmedetomidine.

Materials and methods

This study was approved by the Animal Ethics Committee of the Bulent Ecevit University (formerly Zonguldak Karaelmas University) Medical School. All the animals were treated humanely and in compliance with the recommendations of