Asian Journal of Surgery (2017) 40, 35–40

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-asianjournalsurgery.com

ORIGINAL ARTICLE

Dexmedetomidine reduces neuropathic pain in a rat model of skin/muscle incision and retraction

Xizhao Huang [a,b], Rongfang Deng [b], Weifeng Tu [b], Zurong Hu [a,*]

[a] *Department of Anesthesiology, Guangdong Women and Children's Hospital, Guangzhou, China*
[b] *Department of Anesthesiology, General Hospital of Guangzhou Military Region Affiliated to Southern Medical University, Southern Medical University, Guangzhou, China*

Received 24 January 2015; received in revised form 24 September 2015; accepted 12 October 2015
Available online 28 April 2016

KEYWORDS
dexmedetomidine;
dorsal root ganglion neuron;
postoperative pain;
ropivacaine;
skin/muscle incision and retraction

Summary *Background:* Dexmedetomidine has been proposed as a novel anesthetic adjuvant. However, it remains unclear whether peripheral administration of dexmedetomidine is safe and effective to reduce acute postoperative pain. This study aimed to examine the effects of dexmedetomidine on neuropathic pain.
Methods: Adult male Sprague-Dawley rats were anaesthetized and randomly allocated into four groups ($n = 8$): Groups S, R, RD_1, and RD_5 were injected with saline, 0.5% ropivacaine, 0.5% ropivacaine combined with 1 μg dexmedetomidine, and 0.5% ropivacaine combined with 5 μg dexmedetomidine, respectively, around the saphenous nerve. Then, the rats were subjected to skin/muscle incision and retraction (SMIR) surgery in the medial thigh. Mechanical and heat sensitivity was evaluated and morphology of the dorsal root ganglion (DRG) neurons was observed by electron microscopy.
Results: Some 62.5%, 50%, 12.5%, and 25% of rats developed mechanical hypersensitivity in Groups S, R, RD_1, and RD_5, respectively. The number of swollen mitochondria in DRG neurons was significantly more in Group S (257.2 ± 60.9) and Group R (291.6 ± 82.1) than in Group RD_1 (97.2 ± 33.3) and Group RD_5 (13.6 ± 17.9). In addition, the edema in endoplasmic reticulum and Golgi apparatus was decreased in Group RD_1 and Group RD_5 compared with Group S and Group R.
Conclusion: Peripheral administration of dexmedetomidine improves mechanical and heat hyperalgesia and mitigates postoperative pain.
Copyright © 2016, Asian Surgical Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Conflicts of interest: The authors declare no conflicts of interest.

* Corresponding author. Guangdong Women and Children's Hospital, Guangzhou, China.
E-mail address: hzrong136@163.com (Z. Hu).

http://dx.doi.org/10.1016/j.asjsur.2015.10.009
1015-9584/Copyright © 2016, Asian Surgical Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Open inguinal hernia repair is one of the most painful procedures in surgery because it involves essential prolonged tissue retraction and often causes persistent postoperative pain. Local anesthetic into the retraction site can reduce the postoperative pain and reduce the dosage of morphine, which can prolong the first usage of morphine.[1,2] Since the clinical introduction of ropivacaine, its safety in the central nervous and cardiovascular systems compared with bupivacaine has attracted attention.[3] Ropivacaine is also widely used for infiltration anesthesia in Europe.[4–6] However, the local pharmacokinetics of ropivacaine show that the effects of infiltration anesthesia with ropivacaine on the dental pulp are not as strong as expected, because it has a high affinity for soft tissue.[6] To compensate for this weakness, clinical practitioners favored adding some adjuvants to ropivacaine.

A recent study showed that local injection of a novel $\alpha 2$ receptor agonist dexmedetomidine enhanced the local anesthetic potency of lidocaine via the $\alpha 2A$ adrenoceptor subtype in guinea pigs; dexmedetomidine at a concentration of 1μM induced peripheral vasoconstriction without a systemic cardiovascular response via the peripheral $\alpha 2A$ adrenoceptor subtype.[7]

The nerve endings of dorsal root ganglion (DRG) neurons have a variety of sensory receptors that are activated by mechanical, thermal, chemical, and noxious stimuli. The changes in structure and gene expression in DRG neurons appear to contribute to the development of neuropathic pain. However, no study has shown whether the peripheral administration of dexmedetomidine is safe and effective for reducing acute postoperative pain. In addition, the effects of dexmedetomidine on substructural changes in DRG neurons remain unclear. This study aimed to investigate the effects of dexmedetomidine on neuropathic pain after inguinal hernia repair surgery. To mimic the clinical scenario, a model of skin/muscle incision and retraction (SMIR) in the medial thigh has been established to evoke persistent postoperative pain. In this study, we used the SMIR model to examine the effects of dexmedetomidine on neuropathic pain and substructures in DRG neurons.

2. Materials and methods

2.1. Animals

Adult male Sprague-Dawley rats (200–300 g) were housed in pairs in plastic cages. Artificial lighting was provided on a fixed 12:12 hour light/dark cycle (7:00 AM light on) with free access to food and water. This study was conducted based on the recommendations in the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health. Animal studies were approved by the Animal Care and Use Committee of Southern Medical University.

2.2. Surgery procedures

Rats were anaesthetized with i.p. 10% chloral hydrate (100 mg/mL) at dose of 400 mg/kg, laid on their back, and the medial thigh on one side was shaved. The shaved skin was then swabbed with sterile alcohol wipes for the sterilization and visualization of the saphenous vein. The rats were randomly allocated into four groups ($n = 8$): Group R was injected with 0.5% ropivacaine around the saphenous nerve; Group RD_1 was injected with 0.5% ropivacaine combined with 1 μg dexmedetomidine around the saphenous nerve; Group RD_5 was injected with 0.5% ropivacaine combined with 5 μg dexmedetomidine around the saphenous nerve; and Group S was injected with 0.9% saline around the saphenous nerve.

An incision of 1.5–2 cm was made in the skin of the medial thigh approximately 4 mm medial to the saphenous vein. An incision (7–10 mm long) was then made in the superficial (gracilis) muscle layer of the thigh, approximately 4 mm medial to the saphenous nerve. The superficial muscle was then parted further, by spreading blunt scissors within the muscle incision site, to allow the insertion of a micro dissecting retractor. The retractor had four prongs spaced over 8 mm and each prong was 4 mm deep (Cat. No. 13-1090, Biomedical Research Instruments Inc., Silver Spring, MD, USA). The retractor was inserted into the incision site, to position all prongs underneath the superficial layer of thigh muscle. The skin and superficial muscle of the thigh were then retracted by 2 cm and the retraction was maintained for 1 hour. During the retraction, the saphenous nerve was displaced and potentially stretched around the retractor. The animals were monitored during the retraction period and if required, additional anesthesia was provided using chloral hydrate. During the retraction period, animals were completely covered (apart from the top of the head) with a large absorbent bench underpad to minimize heat loss and prevent dehydration of the surgical site. Following the SMIR procedure, the muscle and skin of the surgical site was closed with silk 3.0 and 4.0 Vicryl sutures, respectively. Sham-operated rats underwent the same procedure with the exception of the skin/muscle retraction. Following recovery from anesthesia, all animals could rise up on their hindpaws to reach food and water.

2.3. Assessment of mechanical sensitivity

Mechanical sensitivity was assessed using the up-down method as described previously.[8] Briefly, rats were placed inside acrylic cages on a wire mesh grid floor. The probe was applied to the middle of the left hind paw to determine the stimulus intensity threshold stiffness. Quick withdrawal in response to the stimulus was considered to be a positive response.

2.4. Assessment of heat sensitivity

Animals were placed in individual Perspex boxes on a glass floor. Nociceptive responses to a noxious heat stimulus were examined by measuring the hindpaw withdrawal latency from a focused beam of radiant heat to the plantar surface (Ugo Basile plantar test apparatus, Monvalle, Italy). The withdrawal latency to this stimulus was measured in seconds and the apparatus had a build-in cut-off latency of 31.2 seconds. Both hindpaws of each rat were tested three

Download English Version:

https://daneshyari.com/en/article/5731482

Download Persian Version:

https://daneshyari.com/article/5731482

Daneshyari.com