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Topical analgesia is a viable option

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Commentary

e last 2 decades more and more attention has been given to topical analgesia. Peripheral nerves in the epidermis are in uenced by topical analgesics with the aim to reduce neuropathic pain. Systemic side e ects are rare, because the purpose of topical analgesics is not to penetrate deeper than the epidermis. us topical analgesics are particularly bene cial in the treatment of geriatric patients with high risk of undesirable side e ects, drug interactions and altered metabolization due to intake of multiple medications. Even high concentrations of active compounds in topical analgesics do not give rise to serious side e ects, such as ketamine cream up to 20% [1]. e absence of severe side e ects most probably resides in the fact that the skin has its own metabolism for xenobiotic molecules [2]. Metabolism of ketamine occurs through various cytochrome P450s enzymes (CYP2B6, 2C9, 2C19, 3A4, 2A6, and 3A5), which are present in the epidermis [2].

Ketamine is mainly an N-methyl-D-aspartate (NMDA) receptor antagonist. NMDA receptors are peripherally present on sensory axons and keratinocytes [1,3]. Activation of these receptors results in mechanical allodynia and hyperalgesia, and ketamine can dampen this overactivity [1]. A double-blinded cross-over randomized clinical trial showed this dampening e ect of topical ketamine in patients with complex regional pain syndrome (CRPS). In 18 CRPS type I and 2 CRPS type II patients topical ketamine 10% signi cantly reduced allodynia evoked by lightly brushing, as well as hyperalgesia evoked by skin prick [1,4].

An important factor to achieve an analgesic e ect through topical analgesics is probably the integrity of the sensory nerves, with the preservation of the signal transduction from the skin to the brain. An elegant double blind study made this idea compelling, in which the e ect of topical clonidine 0.1% compared to placebo in painful diabetic neuropathy (n=179) was examined [5]. A er 12 weeks of treatment there was no statistical di erence between the active and placebo group in pain scored on the 11-point numerical rating scale (NRS). But when the groups were strati ed according to the function of the nociceptors, tested before the treatment with capsaicin 0.1%, interesting results revealed. e more burning patients experienced a er capsaicin 0.1% application, the more statistically signi cant and clinical di erence between the groups was present.

Analgesic cream could be used directly for testing instead of capsaicin 0.1%. In our experience the onset of action of topical analgesics is within 30 minutes [6]. e patient can thus directly give notice whether a speci c topical analgesic has a pain reducing e ect or not.

Another important factor which might blur the e ect of a topical analgesic is the negative symptom of neuropathic pain: no signal transduction. is negative symptom is o en experienced as numbness, tightness, 'walking on clouds', or as 'a wooden shoe'. e positive symptoms of neuropathic pain are due to overactivity of the nerves are experienced as tingling, pins and needles, stabbing, burning, painful cold and itch. Topical analgesics can only reduce the positive symptoms. When a topical analgesic has reduced positive symptoms, negative symptoms usually become more pronounced. e feeling of numbness or tightness can be so disturbing, that patients still score high on the NRS when measuring pain. us distinction in measurement of negative and positive symptoms is essential. A double blind study (NCT00471445) to evaluate amitriptyline 4% and ketamine 2% in chemotherapy induced polyneuropathy patients (n=458) indicated this important distinction. A composite score of negative and positive symptoms, numbness and tingling, was used as the primary endpoint. A er 6 weeks no statistical di erence was seen between the active and placebo group. us, when tingling is reduced, numbness will be more pronounced and the composite score of these two symptoms will stay the same.

Characterizing neuropathic pain to evaluate the e ect of a topical analgesic can be done through questionnaires such as the neuropathic pain symptom inventory (several neuropathic pain symptoms scored on the NRS). Educating patients that topical analgesics can only reduce the positive symptoms, though not the negative symptoms is necessary for an optimal treatment.

References

1. Kopsky DJ, Hesselink JMK, Bhaskar A, Hariton G, Romanenko V, et al. (2015) Analgesic effects of topical ketamine. Minerva Anestesiol 81: 440-449.
2. Oesch F, Fabian E, Guth K, Landsiedel R (2014) Xenobiotic-metabolizing enzymes in the skin of rat, mouse, pig, guinea pig, man, and in human skin models. Arch Toxicol 88: 2135-2190.
3. Miller KE, Hoffman EM, Sutharshan M, Schechter R (2011) Glutamate pharmacology and metabolism in peripheral primary afferents: physiological and pathophysiological mechanisms. Pharmacol Ther 130: 283-309.
4. Finch PM, Knudsen L, Drummond PD (2009) Reduction of allodynia in patients with complex regional pain syndrome: A double-blind placebo-controlled trial of topical ketamine. Pain 146: 18-25.
5. Campbell CM, Kipnes MS, Stouch BC, Brady KL, Kelly M, et al. (2012) Randomized control trial of topical clonidine for treatment of painful diabetic neuropathy. Pain 153: 1815-1823.
6. Kopsky DJ, Hesselink JM (2012) High doses of topical amitriptyline in neuropathic pain: two cases and literature review. Pain Pract 12: 148-153.

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