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Use of gabapentin and pregabalin for pruritus and neuropathic pain associated with major burn injury: A retrospective chart review

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ABSTRACT

Introduction: Pruritis after burn is one of the most common chronic complaints in burn survivors. Pruritus is often indistinguishable from neuropathic pain. There is a paucity of studies reporting the use of gabapentin and pregabalin to treat both pruritus and neuropathic pain. The purpose of this current study is to explore and document the effect of gabapentin and pregabalin in children and adolescent burn survivors.

Methods: A retrospective review of charts and pharmacy records of gabapentin and pregabalin dispensed to control pruritus and/or pain was conducted for burn survivors up to 20 years of age. Data collected included medication doses, age and weight of patients, presence of neuropathic pain and pruritus, reported response to medication, and side effects of these medications. 136 individuals who received gabapentin, pregabalin, or both medications are included in the study. 112 received only gabapentin, none received only pregabalin, and 24 received both. All results are documented in mean ± standard deviation (s.d.) dose/kg/day. 104 individuals experienced pruritus exclusively, two experienced neuropathic pain exclusively, and 30 experienced both. Use of medications was considered effective if the individuals reported pruritus or pain relief from the medication. The medication was considered safe if the individuals did not experience adverse side effects warranting discontinuation of the drugs. Medications were continued with dose adjustments if an individual reported minor side effects such as sedation or hyperactivity.

Results: The average effective dose mg/kg/day for gabapentin and pregabalin was calculated for each of the three age groups (≤5 years, 6–12 years, and >12 years). The average effective dose of gabapentin was 23.9 ± 10.3 mg/kg/day for children ≤5 years, 27.0 ± 15.3 mg/kg/day for children 6–12 years, and 34.1 ± 15.7 mg/kg/day for children >12 years. The average effective dose of pregabalin was 6.5 ± 3.5 mg/kg/day for children 6–12 years and 4.7 ± 1.6 mg/kg/day for children >12 years. One 5-year-old child received 3.7 mg/kg/day of pregabalin. Note that for all patients in this study, pregabalin was added after an inadequate response to gabapentin. For individuals receiving both gabapentin and pregabalin, the maximum gabapentin failure dose for pruritus was 32.8 ± 18.0 mg/kg/day and for both pain and pruritus was 28.1 ± 18.3 mg/

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kg/day. For individuals treated with only gabapentin, 91.4% had an adequate response for pruritus, 100% for neuropathic pain, and 43.3% for both pruritus and pain. 100% of individuals treated with both gabapentin and pregabalin had an adequate response for pruritus and 88.2% had an adequate response for both pruritus and pain. Gabapentin was associated with hyperactivity in two individuals, and sedation in one individual. One individual reported nausea, vomiting, and headaches when taking both medications; this resolved when gabapentin was discontinued. One individual reported sedation while taking both medications.

Conclusion: Gabapentin and pregabalin are effective in relieving pruritus and neuropathic pain in most burn survivors. In some instances, these medications can be given together. Few individuals reported side effects.

1. Introduction

Children recovering from major burn injury often have a long-term complaint of itching, particularly during the wound healing process 80–100% of the time [1]. Itching, in these cases, has been described as "persistent, relentless, [and] distressing [2]." Thus, this itching can greatly diminish a patient's quality of life by negatively impacting not only the sleep patterns but also the overall emotional well-being of the patients.

The pathophysiology of pruritus is complex and not yet fully explained. While the physical sensation of itch and pain can be different, they do share many similar neuronal pathways [3]. Mechanical, thermal, chemical, and electrical stimuli can affect both pain and itch. At lower intensity stimulation, itching may be perceived, while at higher intensity stimulation, pain may be perceived. Neuropathic pain is frequently accompanied with and indistinguishable from pruritus. C-fibers collect the stimulatory information of itch and pain and run through the spinal-thalamic tract. Some research also suggests that there may be specialized itch pathways; it has been found that epidermal C-fibers transmit itch sensations, while dermal C-fibers transmit pain sensations. The current study examines gabapentin and pregabalin therapy for itch and neuropathic pain in pediatric burn survivors.

Gabapentin is an amino acid, structurally resembling GABA, a neurotransmitter [4]. It has been used primarily as an anti-epileptic medication and neuropathic pain medication. Its mechanism of action is not completely known. The most common hypothesis suggests that the drug molecule binds to the alpha-2-delta subunit of voltage-gated calcium channels in the central nervous system and causes reduced calcium influx, thereby limiting release of the excitatory neurotransmitter glutamate. By inhibiting these calcium channels, both anti-seizure activity and analgesic effects by gabapentin for neuropathic pain may be explained. Chang et al. also discusses the pharmacokinetics of gabapentin. It has been known that gabapentin is not metabolized in humans, undergoes first order kinetic elimination, and is excreted by the kidneys. They further report that most common side effects of gabapentin, regardless of dosage, are dizziness and somnolence [4]. The side effect profile of gabapentin also includes shaking, blurred vision, anxiety and memory problems.

Pregabalin is similar in structure to the neurotransmitter GABA, and has been used for treatment of seizures, neuropathic pain, fibromyalgia, and anxiety [5]. Like gabapentin, pregabalin binds to alpha-2-delta subunit of voltage-gated calcium channels. It also reduces the influx of calcium at neuronal terminals. It has been discovered that pregabalin has six times higher efficacy of binding to the voltage-gated calcium channels than gabapentin. It is known as the more potent drug. Pregabalin is also, for the most part, not metabolized, and is excreted by the kidneys unchanged [5]. Pregabalin's side effect profile includes tiredness, dizziness, headache, dry mouth, nausea, vomiting, and constipation. Serious side effects may be blurred vision, hives, rash, and itching.

Traditionally, itch has been treated by massage emollients, antihistamines, and in some cases, tricyclic antidepressants such as doxepin [6,7]. The use of antihistamines is generally considered to be safe. Gabapentin has been used in treatment for uraemic pruritus [8]. More recently, gabapentin's effectiveness for pruritus associated with major burn injuries was reported for a small series of patients [2]. It was also effective in patients who failed traditional treatment methods such as the use of antihistamines. Ahuja et al. showed that gabapentin alone was more effective than both cetirizine and cetirizine in combination with gabapentin for the treatment of pruritis after burn.

Pregabalin has recently been used for itch relief [9]. It has typically been limited to nerve and muscle pain management, seizures, and chronic uremic pruritus. A study published in 2013 in Burns, by Ahuja and Gupta, called "A four arm, double blind, randomized and placebo controlled study of pregabalin in the management of pruritis after burn," showed that pregabalin could treat pruritis after burn and produced a "quicker, predictable and complete response" when compared to treatment with antihistamines and coconut massage oils. Nevertheless, the lack of extensive research and evidence on the pregabalin's comparability to gabapentin and overall effectiveness of pregabalin for pruritis after burn stimulates interest in this topic. Studies have shown that pregabalin has a better pharmacodynamics and pharmacokinetics outlook than gabapentin [10]. Pregabalin is considered more potent and causes fewer side effects than gabapentin in treatment of pain. In some cases, it is even considered a more cost-effective option [9].

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