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Successful Use of Gabapentin in Acute Pain Management Following Burn Injury: A Case Series

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ABSTRACT

Pain after burn injury has multiple qualities, including neuropathic and hyperalgesic elements. This element of the burn patients' pain experience is frequently difficult to manage and contributes significantly to their suffering. The onset may be either immediate or delayed. Gabapentin has established efficacy in the reduction of burn-induced hyperalgesia and allodynia in animal and human experimental burn models. This article reports a case series of six patients who, following admission to hospital with burn injury, described burning dysesthesia at either the injury or graft donor site. These patients were prescribed gabapentin in addition to standard analgesia. The use of gabapentin resulted in a rapid reduction in the severity of the neuropathic element of the pain. The medication was well tolerated, with no severe adverse reactions.

Conclusions. This case series introduces the use of gabapentin as a potentially important therapy in the management of neuropathic pain following burn injury. Further research is required to define the use of gabapentin in this specific setting.

Key Words. Burn Injury; Human; Gabapentin; Pain Management; Neuropathic Pain

Introduction

The pain following burn injury is a complex mixture of background and incident pain with inflammatory and neuropathic components. The description of the neuropathic pain may include burning dysesthesia, hyperalgesia, and lancinating neuralgic episodes. This pain experience is compounded by the psychological trauma of the original insult and subsequent treatment. It is this complexity that adds to the challenge of pain assessment and management in patients following burn injury.

Opioids combined with regular nonopioid analgesics (acetaminophen and/or nonsteroidal anti-inflammatory drugs) form the main treatment strategy in nociceptive pain after burn injury. The management of the neuropathic element is less well described. This article presents a case series of the successful use of gabapentin in the management of acute neuropathic symptoms in burn patients. To the authors' knowledge, this has not previously been reported. All patients were inpatients of the Professor Stuart Pegg Adult Burns Unit, Royal Brisbane and Women's Hospital, Australia.

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Case Series

Case 1

A 52-year-old man sustained 14% total body surface area (TBSA) mixed superficial and partial thickness burn following steam and hot water scald. Surgical debridement was not required. His initial pain was well controlled with regular acetaminophen 1,000 mg qid (four times per day). On day 5, the patient described an increasing pain and was prescribed oxycodone 5 mg qid prn. On day 7, he described an intense burning pain at the injury site, with a numerical rating scale (NRS) of

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7/10. This pain was resistant to the oxycodone and was exacerbated by exposure of the wound to air. Gabapentin was prescribed at 300 mg tds (three times per day), with symptom resolution within 24 hours. The NRS was 0/10 on day 13. The gabapentin was slowly weaned, and he was discharged well on day 14.

Case 2

A 39-year-old man suffered 8% TBSA flame burn to hands, arms, and face while attempting to rescue his nephew from a burning house. This burn resulted in a mixed superficial and partial thickness injury, with some areas requiring surgical debridement and skin grafting. Initial analgesia consisted of oral regular acetaminophen 1,000 mg qid, regular ibuprofen 400 tds, oxycodone 5 mg prn, and subcutaneous morphine 10 mg prn. The day following the injury, he described a burning and knife-like pain. Treatment with gabapentin 300 mg tds was commenced, with titration to 600 mg tds by day 4. The neuropathic pain was controlled, and he was discharged on day 12.

Case 3

A 24-year-old woman was scalded by hot wax, resulting in 5% TBSA partial thickness burn. This did not require surgical debridement or skin grafting. She was discharged well from the Burns Unit on day 4 following the injury. However, on day 6, she was readmitted with a new "stinging" pain that was only partially responsive to regular oral oxycodone at 10 mg tds and acetaminophen at 1,000 mg tds. Gabapentin was added at 300 mg tds, with good response and no side effects. She was again discharged on day 9 following the original accident, with weaning schedules of gabapentin and oxycodone.

Case 4

A 28-year-old woman sustained an 18% TBSA partial thickness burn following a butane gas flame exposure. Analgesia was initially attained, with regular acetaminophen 1,000 mg qid, oral oxycodone 5 mg tds, and parenteral morphine 5 mg for breakthrough. On day 3 following the injury, she described a deep throbbing pain, with a burning element that was not responding to current therapy. Gabapentin 300 mg tds was prescribed. The morphine was ceased and replaced with regular sustained release oxycodone at 10 mg bid and oxycodone 5 mg for breakthrough. Pain relief was reported to be "greatly improved." No surgical debridement was required, and she was discharged well on day 7, with a weaning schedule of gabapentin.

Case 5

A 23-year-old man was involved in a work-related injury where equipment exploded causing a 40% TBSA burn, of which 22% TBSA was a deep injury. He required three episodes of surgical debridement and skin grafting. Analgesia was initially provided, with regular acetaminophen 1,000 mg tds and a continuous morphine infusion of 80 mg over 24 hours with breakthrough when required. On day 4, he described a severe burning pain in the injured hands and also at the donor sites that was not responding to morphine. Gabapentin was prescribed initially at a dose of 300 mg tds and increased to 600 mg tds on day 7. There was no further reference to burning pain during his admission. The gabapentin was weaned and ceased prior to discharge on day 21.

Case 6

This 35-year-old woman received a scald from hot cooking oil, resulting in a 30% TBSA mixed depth injury. Four visits to the operating theater were required for surgical debridement, grafting, and dressing changes. Analgesia initially consisted of oral regular acetaminophen 1,000 mg tds, ibuprofen 400 mg tds, oxycodone 5 mg tds, and subcutaneous morphine 7.5 mg for breakthrough pain. On day 2, she described a severe stinging burning pain that was not responsive to current analgesia. She was prescribed gabapentin 300 mg tds, which was further titrated to 400 mg tds on day 4. A background level of opioid analgesia was established with regular sustained release oxycodone at 20 mg bd. There was no subsequent reference to burning pain, although she required regular and breakthrough opioid for the management of background and procedural nociceptive pain. She was discharged on day 30 on gabapentin 300 mg tds, oxycodone sustained release 10 mg bd, and oxycodone immediate release 5 mg for breakthrough analgesia. The gabapentin was ceased at an outpatient review on day 52 after the original burn injury.

Discussion

Pain following burn injury has diverse pathology with peripheral and central processes [1,2], and

has been the subject of many reviews [3–10]. The features are:

1. Inflammatory nociceptive pain due to the burn injury and tissue trauma.
2. Procedural pain related to the treatment of the burn injury, including surgical debridement, skin grafting, staple removal, physiotherapy, dressing changes, and baths. Unless preemptive analgesia is prescribed, procedural pain can be intense although of limited duration.
3. Neuropathic pain often characterized by a constant burning or spontaneous stabbing pain.

The focus of this case series has been to present six cases where gabapentin was effective for the relief of the neuropathic element of the burn pain experience.

The neuropathic element is a less well-understood aspect of burn pain with limited research. It is often poorly responsive to opioid analgesia as described by the patient in Case 3. The burning dysesthesia described may occur soon after the injury as seen in Case 2 or delayed by several days as in Cases 1, 3, 4, and 5. It may occur at the site of the burn or at the donor site as described in Case 5. Also, the presence and intensity of burning dysesthesia appears independent of the mechanism of burn injury, and the pain may continue beyond the healing of the burn injury [11–15].

In an animal model, a superficial burn injury results in a surrounding area of secondary tactile allodynia in the normal skin [16,17]. This model has been used extensively in the research of peripheral and central sensitization [16–24]. The burn-induced hyperalgesia is blocked by both intraperitoneal gabapentin and pregabalin (a structurally related agent with alike mechanism of action) [25].

Human burn models [26–28] also result in an area of surrounding hyperalgesia and allodynia that can be suppressed with oral gabapentin but not placebo [29].

Both the animal and human experimental burn models confirm that following a burn injury, there is a resultant development of secondary tactile allodynia and hyperalgesia—qualities often attributed to neuropathic pain.

Previous drug therapy for the management of neuropathic pain following burn injury includes intravenous lignocaine [30] and mexiletine (authors' personal experience). Systemic lignocaine has been used successfully in the treatment of neuropathic pain resulting from a range of conditions [31]. Its reported efficacy in the burn population is further evidence that there is an underlying neuropathic element of the burn patients' pain experience. Sodium valproate has been considered, but may cause fatal hepatic toxicity [32] and a rare but serious effect on platelet function [33] with a subsequent bleeding risk. Complex regional pain syndrome has been reported following burn injury on several occasions [34–37], and gabapentin has been used as part of multimodal therapy in this setting [34].

Based on this evidence and our own experience in the management of neuropathic pain, the authors initiated treatment with gabapentin immediately after the patient complained of any of the characteristic symptoms of neuropathic pain.

Gabapentin and pregabalin, often referred to collectively as the gabapentinoids, have found a role in several clinical settings. These agents were originally designed as anticonvulsants and are currently recommended as add-on therapy for partial epilepsy [38,39]. Several clinical trials have also demonstrated their efficacy in the management of anxiety disorders [40–44]. Furthermore, the gabapentinoids have established a clear role in the management of neuropathic pain from various pathological causes, including painful diabetic peripheral neuropathy [45,46], postherpetic neuralgia [47–49], phantom limb pain [50], and trigeminal neuralgia [51]. There is also evidence that they have an opioid-sparing and antihyperalgesic effect when given postoperatively after breast surgery [52] and dental extraction [53], and may improve outcome when given preoperatively in hysterectomy [54] and knee surgery [55]. However, the burn pain experience differs significantly from the postsurgical model due to the widespread nature of cutaneous injury with extensive nerve ending damage and exposure. The effect of these agents on neuropathic pain and hyperalgesia has resulted in the gabapentinoids being grouped with other agents as "antihyperalgesics" [56]. Both gabapentin and pregabalin are generally well tolerated, with the most common adverse effects being dizziness and drowsiness.

The mechanism of action of the gabapentinoids is not entirely established, but, it is known that they have a high affinity for the $\alpha_2\delta$-1 subunit of the neuronal voltage-gated calcium channel in the dorsal horn of the spinal cord and dorsal root ganglia [57,58]. It is believed that binding to this subunit results in reduced calcium influx, with a subsequent reduction in neurotransmitter release [57,59].

It has been demonstrated in animal studies that the expression of the $\alpha_2\delta$-1 subunit is up-regulated in several neuropathic pain models [60,61]. Also, when these animals are treated with the gabapentinoids, there is a correlation between their effectiveness in reducing allodynia and hyperalgesia and the expression of the $\alpha_2\delta$-1 subunit [60]. This suggests a mechanistic relationship.

Conclusion

Pain management of burn patients is a challenging and important part of their recovery. It is essential to care for the patient using a biopsychosocial approach that includes pharmacotherapy, physical measures, and psychological support. A pharmacological strategy of regular acetaminophen and opioids is usually required with the use of adjuvant agents for any neuropathic element. In addition, an analgesic plan for procedural pain is also required.

This case series of six patients reports the successful use of gabapentin in the acute setting following a major burn injury. All patients described a rapid resolution of their neuropathic symptoms with good tolerability. This treatment may provide an important means of reducing suffering and improving outcome for this patient group. The apparent efficacy of gabapentin in this setting warrants further investigation. To this end, the authors have initiated a randomized placebo-controlled trial of pregabalin in the management of pain in patients with a severe burn injury.

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