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REVIEW ARTICLE

Pain Management in Burn Patients

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Abstract
Background and objectives: Despite advances, inappropriate analgesic treatment for burn patients is still seen. The objective of this review was to collect data on pain management in burn patients.
Content: We reviewed the mechanisms of pain, burn patient assessment, as well as pharmacological and non-pharmacological treatment.
Conclusion: Pain management in burn patients is still a challenge for the multidisciplinary team. Frequent and continuous evaluation of the patient's response is very important due to the various stages that the hospitalized burn patient goes through, as well as a combination therapy with analgesic and non-pharmacological measures. Understanding the complexity of the pathophysiological, psychological, and biochemical changes a burn patient presents is the first step to achieve success in analgesic management.

Introduction

Despite significant recent advances regarding treatment for burn victims, the inappropriate analgesic management is still seen [1]. This is due to both the complex nature of pain presented by these patients and insufficient training of the professionals involved [2-4].

The inadequate control of pain may diminish trust within the medical team, which may negatively affect the treatment outcome [5]. Moreover, it may contribute to the development of chronic pain, paresthesia, and dysesthesia [6-11]. There is an association between insufficient pain relief and the onset of some psychiatric disorders, such as depression and post-traumatic stress disorder [12].

A successful treatment requires careful assessment of its nature, understanding the different types and patterns of pain and knowing the best treatment. A good initial assessment serves as a baseline to evaluate the results of subsequent interventions [13].

A multidisciplinary approach to these patients is critical, due to the complexity of factors involved in pain. During hospitalization, analgesia requirements vary because of the numerous procedures that patients undergo as well as their evolving condition. This makes it difficult to predict the amount of analgesic to be administered at a given time.

This review aims to present the main forms of pharmacological and non-pharmacological management of pain available in the literature.

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Mechanisms of pain

The pain soon after the burn is due to direct stimulation and injury of the nociceptors present in the epidermis and dermis, which leads to the transmission of nerve impulses by A-delta and C fibers to the spinal cord dorsal horn. The impulse magnitude is modulated by both the peripheral stimuli and descending influences from the brain [14].

The inflammatory response is initiated minutes after injury and leads to the release of numerous chemical irritants that for several days sensitize and stimulate the nociceptors at the site. The site remains painful and sensitive to mechanical and thermal stimuli, with primary hyperalgesia. The change in sensitivity to mechanical stimuli seen in the injury adjacent tissues is referred to as secondary hyperalgesia. The quality of pain changes, as the inflammatory response subsides. Pain intensity varies, but it is typically at its maximum in places of skin loss and tissue donor areas. In case of severe burns, the initial destruction of nerve endings leads to local insensitivity to pain. In these areas, there may be a disorderly regeneration of nerve tissue, which will predispose to neuropathic pain. It is estimated that up to 52% of burn patients have chronic pain [15].

Evaluation

It is extremely important to evaluate constantly the burn victim for pain in order to guide the analgesic management and response to drug [7]. Characteristics, such as pain location, pain improvement or worsening, and type and intensity of pain are essential for management.

Pain intensity in this group of patients is usually assessed using a numerical scale (0-10). However, the visual analogue scale, verbal descriptive scale, and faces and colors scales are used [16]. There are also behavioral observational scales validated for use in patients who are unable to express themselves effectively. The Abbey pain scale (for elderly with cognitive disorders) [17] and FLACC score (for young children) [18] are reported.

Four patterns of pain have been observed in burn patients. There may be constant pain at rest and in motion (background pain), aggravated by episodes of intense and sudden pain (breakthrough pain), pain during procedures [16], and pain in the postoperative period.

Pharmacological treatment

Drug administration is the primary and most effective way of treating pain in burn patients because of its nature and intensity [19]. As mentioned previously, the inadequate management of analgesia is still very common and it is extremely important to continually reassess the effectiveness of therapy, as well as the use of more aggressive methods [20-23].

Some changes in drug pharmacokinetics are seen in burn patients. During the initial phase, when an inflammatory response develops, there is decreased blood flow to the organs, with a consequent drug clearance decrease. After this phase, there is an overall increase of metabolism with a subsequent clearance increase. In burn injuries with a body surface area greater than 20%, there is a widespread capillary leakage, with loss of interstitial proteins. Therefore, the effect of drugs with high protein binding is difficult to control [24]. One should also be cautious with increased total body water commonly seen during treatment.

Opioids

Among the most commonly used drugs, opioids play a key role in pain management in burn patients. The variety of options available in the market allows good flexibility regarding potency, route of administration, and duration of action tailored to each patient. Its adverse effects are well-known, particularly itching, respiratory depression, and nausea. Due to the risk of tolerance or opioid-induced hyperalgesia, its use should always be incorporated into a multimodal treatment approach [25].

The pain at rest (background pain) present in burn patients is moderate and should be treated more appropriately with moderate potency drugs, whose plasma concentration remains relatively constant throughout the day. The most common examples are: intravenous opioid infusion, with or without patient-controlled analgesia, long-term opioids (methadone) administered orally, or prolonged enteral absorption opioids (controlled-release morphine or oxycodone). Tramadol and opioids also promote a beneficial effect in neuropathic pain [26,27]. There is no evidence in literature regarding the superiority of a particular opioid for neuropathic pain treatment [24]. Remifentanil, an opioid with ultra rapid onset of action and plasma metabolism, is an important option for analgesia during procedures when delivered by continuous infusion. Fentanyl and alfentanil may also be used, with the advantage of promoting residual analgesia.

Anti-inflammatory drugs, paracetamol and dipyrone

These medications may reduce the amount of opioid needed by up to 20-30%. %. Nonsteroidal anti-inflammatory drugs (NSAIDs) may also reduce the adverse effects of opioids significantly [28]. The most appropriate drugs for patients with burns are paracetamol, dipyrone, and selective cyclooxygenase-2 inhibitors. Although these drugs are weak when used alone, they act synergistically with opioids [29]. Due to the inhibition of platelet aggregation, the use of NSAIDs should be avoided in situations in which risk of bleeding is a concern (such as severe burn) [30]. Its use also requires caution in patients with cardiovascular and gastrointestinal diseases [31].

Anticonvulsants

Gabapentin and pregabalin are often used for treating neuropathic pain in burn patients. Directly, these drugs diminish the central sensitization of pain by binding to calcium channels; indirectly, they inhibit presynaptic N-methyl-D-aspartate (NMDA) receptors [32]. In a small study of burn patients, pain intensity and opioid consumption were significantly reduced in patients taking gabapentin. Between 3 to 24 days after the accident, patients received 2,400 mg of it, divided into three doses [33]. In another study, pregabalin was evaluated and well-tolerated, significantly reducing several components of neuropathic pain in burn patients. Additionally, there were fewer pain complaints during procedures [34].

Antidepressants

Antidepressants are effective drugs and therefore play an important role in the concept of multimodal treatment of pain associated with burns [35]. Amitriptyline, used in low doses, has an established role in the management of neuropathic pain. It acts by activating the descending inhibitory pathways in the spinal cord. The required dose is usually not more than 75 mg per day. Selective serotonin reuptake inhibitors may also be used in case of intolerance to side effects of tricyclics.

The analgesic effect of antidepressants usually occurs within days or weeks. There are no studies regarding the analgesic effect and time to start analgesic therapy in burn patients [24].

Ketamine

Ketamine is a non-competitive antagonist of NMDA receptors and may be used for conscious sedation during dressing changes in burn patients [36]. It induces a state of dissociative anesthesia with intravenous doses of 1 $mg.kg^{-1}$. As an advantage, it maintains the airway reflexes, blood pressure, and heart rate by indirect release of norepinephrine. The occurrence of hallucinations, a significant adverse effect, may be attenuated by concomitant administration of benzodiazepines or propofol [37,38]. In a meta-analysis of ketamine at low doses and postoperative consumption of opioids, the authors concluded that there is a reduction of up to one-third in total dose administered. Furthermore, ketamine was effective as rescue medication in case of pain less responsive to opioids [39]. Ketamine appears to promote some action in reducing hyperalgesia [59].

Benzodiazepines

Because anxiety disorders may exacerbate pain complaints, the use of anxiolytics associated with analgesic drugs is a common practice in many centers [40,41]. Fear and tension cause decreased pain tolerance [42]. The burn patients who benefited most from therapy with benzodiazepines were those extremely anxious and with severe pain [43]. When there is need for rapid onset of action, midazolam may be used. Lorazepam is more suitable than diazepam for this group of patients because of the decreased hepatic metabolism often present, which may prolong the half-life of the latter [44].

Lidocaine

Therapy with intravenous lidocaine was effective in reducing neuropathic pain scores, mainly associated with nerve injury [45]. A clinical study, however, showed only a small difference in pain scores, requiring opioid maintenance doses during burn patients' dressing changes [46].

Alpha-2 agonist

Alpha-2 agonists have interesting properties that facilitate their use in analgesic management of burn patients. Besides stimulating the descending inhibitory pain pathways, they have sedative and antihypertensive effects. Clonidine may be used safely in analgesic management of child burn victims [47,48]. In some burn centers, it is routinely prescribed for children and adults. Dexmedetomidine has a shorter duration of action than clonidine and its action is more selective for alpha-2 receptors. One study reported positive results in the association between ketamine and dexmedetomidine compared to ketamine alone or in combination with midazolam during dressing changes in burn patients [49].

Non-pharmacological treatment

Non-pharmacological therapy is an important measure complementary to medication to manage pain and anxiety in burn patients. It should be initiated as early as possible in order to prevent the development of anxiety, which can perpetuate the cycle of pain [16]. The approach should be multidisciplinary, involving psychologists, psychotherapists, physiotherapists and pain specialists.

Psychology techniques such as relaxation, distraction, and cognitive-behavioral therapy, are beneficial for relieving anxiety and pain during rehabilitation [50-52].

Hypnosis is an altered state of consciousness characterized by increased receptivity to suggestion, ability to change perceptions and sensations, and increased capacity for dissociation [53]. It has been used in pain management in burn patients during procedures and to control anxiety. Neurophysiological studies support this therapy [54].

Another approach used successfully is virtual reality. It consists of a technology that isolates the patient from the real world, letting his vision only in contact with a three-dimensional virtual environment. In the context of burn patients, this virtual world is called SnowWorld, specially created to counter sensations most commonly caused by a burn injury. In some studies, virtual reality used as a technique of distraction during procedures was effective in reducing the intensity of pain in burn patients [55,56].

Conclusion

Pain management in burn patients is still a challenge for the multidisciplinary team. Frequent and continuous evaluation of the patient's response is very important, due to the various stages that the hospitalized burn patient goes through, as well as a combination therapy with analgesic and non-pharmacological measures. Understanding the complexity of the pathophysiological, psychological, and biochemical changes presented by a burn patient is the first step to achieve success in analgesic management.

References

1. McCaffrey M, Pasero C – Pain management: problems and progress. In: McCaffrey M, Pasero C (ed.). Pain: clinical manual. 2nd ed., St. Louis: Mosby, 1999, pp. 712-713.
2. Patterson D, Sharar S – Burn pain. Em: Loeser J (ed.). Bonica's management of pain. 3rd ed. Philadelphia: Lippincot, Williams & Wilkins, 2001, pp. 780-787.
3. Schafheutle EI, Cantrill JA, Noyce PR – Why is pain management suboptimal on surgical wards? J Adv Nurs, 2001;33(6):728-737.
4. Twycross A – Educating nurses about pain management: the way forward. J Clin Nurs, 2002;11(6):705-714.
5. Weissman DE, Haddox JD – Opioid pseudo-addiction, an iatrogenic syndrome. Pain, 1989;36: 363-366.

6. Brenner GJ, Ji RR, Shaffer S, Woolf CJ – Peripheral noxious stimulation induces phosphorylation of the NMDA receptor NR1 subunit at the PKC-dependent site, serine-896, in spinal cord dorsal horn neurons. Eur J Neurosci, 2004;20:375-384.
7. Dworkin RH – An overview of neuropathic pain: syndromes, symptoms, signs, and several mechanisms. Clin J Pain, 2002;18:343-349.
8. Ikeda H, Stark J, Fischer H et al. – Synaptic amplifier of inflammatory pain in the spinal dorsal horn. Science, 2006;312:1659-1662.
9. Kawasaki Y, Kohno T, Zhuang ZY et al. – Ionotropic and metabotropic receptors, protein kinase A, protein kinase C, and Src contribute to C-fiber-induced ERK activation and camp response element-binding protein phosphorylation in dorsal horn neurons, leading to central sensitization. J Neurosci, 2004;24:8310-8321.
10. Olgart L – Breakthrough in pain research. Charting of the synaptic network may lead to new analgesics. Nord Med, 1998;113:6-12.
11. Woolf CJ, Manion RJ – Pain: aetiology, symptoms, mechanisms, and management. Lancet, 1999;353:1959-1964.
12. Courtemanche DJ, Robinow O – Recognition and treatment of the post-traumatic stress disorder in the burn victim. Burn CareRehabil, 1989;10:247-250.
13. Sousa FAEF – Dor: o quinto sinal vital. Rev. Latino-Am. Enfermagem, 2002;10:446-447.
14. Richardson P, Mustard L – The management of pain in the burns unit. Burns, 2009;35(7):921-936
15. Dauber A, Osgood PF, Breslau AJ et al. – Chronic persistent pain after severe burns: a survey of 358 burn survivors. Pain Med, 2002;3:6-17.
16. Mahar PD, Wasiak J, O'Loughlin CJ et al. – Frequency and use of pain assessment tools implemented in randomized controlled trials in the adult burns population: a systematic review. Burn, 2012;38:147-154.
17. Abbey J, Piller N, De Bellis A et al. – The Abbey Pain Scale: a 1-minute numerical indicator for people with end-stage dementia. Int J Palliative Nurs, 2004;10(1):6-13.
18. Merkel SI, Voepel-Lewis T, Shayevitz JR et al. – The FLACC: a behavioral scale for scoring post-operative pain in young children. Paediatr Nurs, 1997;23(3):293-297.
19. Latarjet J, Choinère M – Pain in burn patients. Burns, 1995:21:344-48.
20. Atchison NE, Osgood PF, Carr DB – Pain during burn dressing changes in children: relationship to burn area, depth, and analgesis regimen. Pain, 1991;47:41-47.
21. Perry S, Heidrich G, Ramos E – Assessment of pain in burned patients. Burn Cure Rehabil, 1981;2: 322-326.
22. Latarjet J – La douleur de l'enfant brûlé. Bilan des pratiques. In: Comm. 16e Réunion Annuelle de la Societe Française de la Douleur, Paris, 26-28 Novembre 1992.
23. Choinikre M – The pain of burns. Em: Wall P, Melzack R (ed.). Textbook of pain. Edinburgh: Churchill Livingstone, 1988, pp. 402-408.
24. Girtler R, Gustorff B – Pain management in burn injuries. Anaesthesist, 2011;60(3):243-250.
25. Wiechman SA, Sharar SR, Patterson DR – Burn pain. In: Waldman, SD. Pain management. 2nd ed. Philadelphia: Elsevier Saunders, 2011, pp. 228-242.
26. Duhmke RM, Cornblath DD, Hollingshead JR – Tramadol for neuropathic pain. Cochrane Database Syst Rev, 2004(2):CD003726.
27. Gatti A, Sabato AF, Occhioni R et al – Controlled-release oxycodone and pregabalin in the treatment of neuropathic pain: results of a multicenter Italian study. Eur Neurol, 2009;61(3):129-137.
28. Malenfant A, Forget R, Papillon J et al. – Prevalence and characteristics of chronic sensory problems in burn patients. Pain, 1996;67(2-3):493-500.
29. Marret E, Kurdi O, Zufferey P et al. – Effects of nonsteroidal antiinflammatory drugs on patientcontrolled analgesia morphine side effects: meta-analysis of randomized controlled trials. Anesthesiology, 2005;102:1249-1260.
30. Giessler GA, Mayer T, Trupkovic T – Das Verbrennungstrauma. Anaesthesist, 2009;58:474-448.
31. Amer M, Bead VR, Bathon J et al. – Use of nonsteroidal anti-inflammatory drugs in patients with cardiovascular disease: a cautionary tale. Cardiol Rev, 2010;18(4):204-212.
32. Simonnet G – Preemptive antihyperalgesia to improve preemptive analgesia. Anesthesiology, 2008;108:352-354.
33. Cuignet O, Pirson J, Soudon O et al. – Effects of gabapentin on morphine consumption and pain in severely burned patients. Burns, 2007;33(1):81-86
34. Gray P, Kirby J, Smith MT et al. – Pregabalin in severe burn injury pain: a double-blind, randomised placebo-controlled trial. Pain, 2011;152(6):1279-1288.
35. Pal SK, Cortiella J, Herndon D – Adjunctive methods of pain control in burns. Burns, 1997;23(5):404-412.
36. MacPherson RD, Woods D, Penfold J – Ketamine and midazolam delivered by patient-controlled analgesia in relieving pain associated with burns dressings. Clin J Pain, 2008;24(7)568-571.
37. Lilburn J, Dundee J, Nair S et al. – Ketamine sequalae evaluation of the ability of various premedicants to attenuate its psychic actions. Anaesthesia, 1978;33:307-311.
38. Tosun Z, Esmaoglu A, Coruh A – Propofol-ketamine vs propofol-fentanyl combinations for deep sedation and analgesia in pediatric patients undergoing burn dressing changes. Pediatr Anesth, 2008;18:43-47.
39. Visser E, Schug S – The role of ketamine in pain management. Biomed Pharmacother, 2006;60:341-348.
40. Perry S, Heidrich G – Management of pain during debribement: a survey of U.S. burn units. Pain, 1982;13:267.
41. Martin-Herz SP, Patterson DR, Honari S et al. – Pediatric pain control practices of North American Burn Centers. J Burn Care Rehabil, 2003;24:26.
42. Edwards RR, Smith MT, Klick B et al. – Symptoms of depression and anxiety as unique predictors of pain-related outcomes following burn injury. Ann Behav Med, 2007;34(3):313-322.
43. Patterson DR, Ptacek JT, Carrougher GJ et al. – Lorazepam as an adjunct to opioid analgesics in the treatment of burn pain. Pain, 1997;72:367.
44. Martyn JAJ, Greenblatt DS, Quinby WC – Diazepam pharmacokinetics following burns. Anesth Analg, 1983;62:293-297.
45. Kalso E, Tramer MR, Moore RA et al. – Systemic local anaesthetic type drugs in chronic pain: a qualitative systematic review. Eur J Pain, 1998;2:3-14.
46. Wasiak J, Spinks A, Costello V et al. – Adjuvant use of intravenous lidocaine for procedural burn pain relief: a randomized double-blind, placebo-controlled, cross-over trial. Burns, 2011;37(6):951-957.
47. Ambrose C, Sale S, Howells R et al. – Intravenous clonidine infusion in critically ill children: dose dependent sedative effects and cardiovascular stability. BJA, 2000;84:794-796.
48. Lyons B, Casey W, Doherty P et al. – Pain relief with low-dose intravenous clonidine in a child with severe burns. Intens Care Med, 1996;22:249-251.
49. Gündüz M, Sakalli S, Güneş Y et al. – Comparison of effects of ketamine, ketamine-dexmedetomidine, and ketamine-midazolam on dressing changes of burn patients. J Anaesthesiol Clin Pharmacol. 2011;27(2):220-224.

50. Turk DC, Salavoy P – Managing chronic illness. In: Nicassio PM, Smith TW (ed.). Cognitive behavioural treatment of illness behaviour. 1996, pp. 245-285 [chapter 7].
51. Fernandez E, Turk DC – The utility of cognitive coping strategies for altering pain perception: a meta-analysis. Pain, 1989;38:123-135.
52. Eccleston C, Yorke L, Morley S et al. – Psychological therapies for the management of chronic and recurrent pain in children. Cochrane Database Syst Rev, 2009;(2):CD003968.
53. Patterson DR – Clinical hypnosis for pain control. Washington: American Psychological Association, 2010.
54. Crawford HJ, Knebel T, Vendemia JMC – The nature of hypnotic analgesia: neurophysiological foundation and evidence. Contemp Hypn, 1998;15(1):22-33.
55. Hoffman HG, Patterson DR, Carrougher GJ et al. – Effectiveness of virtual reality-based pain control with multiple treatments. Clin J Pain, 2001;17:229.
56. Hoffman HG, Patterson DR, Carrougher GJ – Use of virtual reality for adjunctive treatment of adult burn pain during physical therapy: a controlled study. Clin J Pain, 2000;16:244.