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Lidocaine for pain relief in burn injured patients (Review)

Wasiak J, Cleland H

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Lidocaine for pain relief in burn injured patients.
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[Intervention Review]

Lidocaine for pain relief in burn injured patients

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ABSTRACT

Background

Pain is a major issue for patients suffering from many different types of wounds in particular those with burn injuries. Prompt, aggressive use of opioid analgesics such as morphine has been suggested as critical to avert the cycle of pain and anxiety, but side effects are encountered. It is proposed that newer agents such as lidocaine could be effective in reducing pain and alleviating the escalating opioid dosage requirements in patients with burn injury.

Objectives

To assess the safety and effectiveness of intravenous lidocaine as a means of pain relief versus no therapy, placebo, other drugs or two or more of the above therapies in combination in patients exposed to burn injury.

Search methods

We searched the Cochrane Central Register of Controlled Trials (*The Cochrane Library,* Issue 1, 2007), MEDLINE (1966 to March 2007), EMBASE (1980 to 2007), CINAHL (1982 to March 2007).

Selection criteria

Those trials that were considered were: randomised controlled trials (RCTs) and controlled clinical trials (CCTs), both published and unpublished studies, which assessed the efficacy of intravenous lidocaine varying doses as a single-agent therapy with no therapy, placebo, other analgesics such as opioids, lidocaine plus another drug, or two or more of the above therapies as a means of pain relief in patients exposed to burn injury.

Data collection and analysis

The two review authors applied the entry criteria to identified studies.

Main results

No clinically relevant RCTs or CCTs were identified through the above searches.

Authors' conclusions

No information is available from the published RCTs or CCTs on clinically relevant primary outcome measures which can influence current burns care practice and management. Therefore, since current clinical evidence is subject to the inherent weaknesses of case series or

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reports, intravenous lidocaine must be considered a pharmacological agent under investigation in burns care whose effectiveness is yet to be determined in well-designed and conducted clinical trials.

PLAIN LANGUAGE SUMMARY

Lidocaine for pain relief in burn injured patients

There are no clinically relevant randomised controlled trials showing that burns patients benefit from intravenous lidocaine for pain relief. Burns are very common, sometimes fatal, and the pain associated with such injury is one of the most difficult types of suffering to relieve. The use of high-dose opioid medications like morphine is common, but side effects are encountered. Alternative agents such as lidocaine, an anaesthetic, have been proposed. This review found no clinically relevant trials looking at the use of lidocaine to manage burn pain.

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BACKGROUND

Pain is a major factor for patients suffering from many different types of wounds in particular those with burn injuries (Briggs 1999). These patients can experience periods of intense and prolonged pain. This pain can be exacerbated by frequent dressing changes which are necessary to prevent infection and aid wound healing. In the long term, poorly managed pain in burn patients may lead to non-compliance with hospital treatment, a disruption in care (Andreasen 1972) and an increased risk of post traumatic stress disorders (Schneiber 1993; Taal 1997). Ultimately, the alleviation and prevention of pain is both a medical and nursing responsibility.

The aim of zero background pain (no pain at rest) in burn injuries is an achievable and perfectly realistic goal (Latarjet 2002). A study by Choiniere 1989 demonstrated that the time of greatest pain for a burn patient is usually during therapeutic procedures. This was also supported by Hollinworth 2000 who identified that pain could be evoked by the debridement of slough and necrotic tissue, the application of antiseptics and the use of wound cleansing procedures during dressing changes. This procedural related pain can be difficult to manage (Ulmer 1998) and may be under treated (Sheridan 1997; Ulmer 1998).

The severity of this pain has established the use of potent opioid analgesics such as morphine as a standardised means of pain control. A major side effect encountered in burn patients receiving high doses of opioids, however, is that of respiratory depression (Cassuto 2003) leading to the use of ventilatory support. Consequently the risk of nosocomial pneumonia increases and problems with gut motility and subsequent constipation secondary to the opiate use emerge.

Alternatively, agents such as lidocaine (also named lignocaine) - a local anaesthetic agent of the amide type that has been used for local anaesthesia and systemically as an antiarrythmic drug - have been proposed as a means to alleviate the debilitating effects of various types of pain (Edwards 1999; Ferrante 1996; McLeane 2001; Stark 2000). Systemic lidocaine has also been reported to be effective in treating the neuropathic pain of a burn injury (Cassuto 2003).

As systematic lidocaine has been shown to be effective in the reduction of neuropathic pain (Mao 2000) and has none of the side effects of high dose opioids, it is expected that we could establish that the administration of lidocaine may lead to a reduction in the procedural and background pain levels of burn patients, leading to less opiate requirements and consequently less associated complications.

OBJECTIVES

The objective of this review was to assess the safety and effectiveness of intravenous lidocaine as a means of pain relief versus no therapy, placebo, other drugs or two or more of the above therapies in combination in patients exposed to burn injury.

METHODS

Criteria for considering studies for this review

Types of studies

We sought to include all RCTs and CCTs, published and unpublished, which assessed the efficacy of intravenous lidocaine as a means of pain relief in patients exposed to burn injury.

Types of participants

We focused on adults over 18 years of age with any burn injury to the epidermis, subcutaneous tissues, vessels, nerve, tendons, or bone who may have required lidocaine as a means of pain relief. It was expected that studies would be included regardless of the method of burn injury. However, we excluded burn patients requiring pain relief measures for multiple treatment regimes such as skin-grafting procedures.

Types of interventions

We sought all studies that compared intravenous lidocaine of varying doses as a single-agent therapy with no therapy, placebo, other analgesics such as opioids, lidocaine plus another drug, or two or more of the above therapies in combination regardless of the duration of the treatment. If a second active ingredient was to be included during administration, only those studies that had a concurrent group on intravenous lidocaine would have been examined.

Types of outcome measures

Primary outcomes

Pain measured by a visual analogue scale (VAS), verbal or numerical rating scale, or other validated assessment tool, time to re-medication and requirements for rescue analgesia.

Secondary outcomes

Adverse effects, measures of satisfaction or patient preference and assessment of quality of life would not be included.

Search methods for identification of studies

We searched the Cochrane Central Register of Controlled Trials (*The Cochrane Library*, Issue 1, 2007), MEDLINE (1966 to March Week 2, 2007), EMBASE (1980 to 2007), CINAHL (1982 to March Week 3, 2007). In MEDLINE, a strategy was combined with the optimum trial search strategy described in the Cochrane Handbook (Higgins 2006).

No language restrictions were applied. The search strategy was adapted for other databases. Please see Appendix 1 for the MEDLINE search strategy.

Data collection and analysis

Trial identification

Both review authors reviewed titles and abstracts to identify potentially relevant trials using the selection criteria. Studies that clearly failed to meet the inclusion criteria were not reviewed. Those that could not be excluded were retrieved and reviewed in full-text independently by both review authors. In all instances, differences of opinion were resolved by discussion among the review authors.

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Data extraction

There were no data to extract, however, data from the eligible studies would have been extracted independently by two review authors using standardised forms developed for this review. Data extracted would have included: study characteristics, participant demographics, intervention and comparison details plus outcome measures and results. Primary authors would have been contacted to provide missing data. In all instances, differences of opinion would have been resolved by discussion among the review authors.

Quality assessment

The methodological quality of any included trials would have been assessed independently by both review authors, with discrepancies resolved by discussion, however, there were no included trials to be assessed. Quality assessment was to be based on the method described by Schulz 1995. The Schulz 1995 method involved assessment of the following criteria: adequacy of the randomisation process, adequacy of the allocation concealment process, the inclusion in the analysis of randomised participants (intention-to-treat) and blinding.

Data analysis

In the event of published trials having been identified, the data would have been analysed in the following way: a statistical summary of treatment effects would proceed only in the absence of significant clinical or statistical heterogeneity. Heterogeneity would have been tested using the I^2 statistic (Higgins 2003). Dichotomous data would have been expressed as relative risk (RR). Continuous data would have been converted to the weighted mean difference (WMD) and an overall WMD would then be calculated. Overall estimates would be based on the random effects model (DerSimonian 1986).

Publication bias would have been tested using funnel plots or other corrective analytical methods, depending on the number of clinical trials included in the systematic review. We would have performed subgroup analysis where appropriate by calculation of RR or WMD in each subgroup and examination of the 95% confidence intervals. We would have taken non-overlap in intervals to indicate a statistically significant difference between subgroups. We would have made all analyses on an intention-to-treat basis where possible, and where not possible we would have stated this clearly.

RESULTS

Description of studies

A total of 25 references were identified from searching the literature. Independent scrutiny of the titles and abstracts identified five potentially relevant studies. Of the five potentially relevant studies, all were excluded because they did not report on primary clinical outcome measures (Holthsuen 2000; Koppert 2004; Mattsson 2000); or used an alternative study design such as a case report (Cassuto 2003) or a case series (Jönsson 1991).

Risk of bias in included studies

There are currently no relevant primary outcome measures to report from the published RCTs or CCTs investigating the use of intravenous lidocaine of varying doses as a single-agent therapy with no therapy, placebo, other analgesics such as opioids, lidocaine plus another drug, or two or more of the above therapies in this review.

Effects of interventions

There are as yet no relevant primary outcome measures to report from the published RCTs or CCTs investigating the use of intravenous lidocaine of varying doses as a single-agent therapy with no therapy, placebo, other analgesics such as opioids, lidocaine plus another drug, or two or more of the above therapies in those with burn injury.

DISCUSSION

There are currently no relevant primary outcome measures to report from the published RCTs investigating the use of intravenous lidocaine as a means of pain relief versus no therapy, placebo, other drugs or two or more of the above therapies in combination in patients exposed to burn injury.

Intravenous lidocaine has been a well documented treatment for other clinical conditions such as cardiac arrhythmias and neuropathic pain (Cassuto 2003). In recent times and in the setting of burns pain, there has been growing evidence in the form of case reports or case series to suggest that lidocaine can improve the analgesic efficacy, alleviate the deleterious effect of opioid administration, and minimise the necessity of escalating opioid dosage in patients with thermal injury (Cassuto 2003; Edwards 1999; Jönsson 1991), although these were excluded from our search.

Several mechanisms have been proposed for this action, namely that systemic lidocaine can depress conduction in afferent nerves, inhibit dorsal horn neural transmission, and modify the cerebral perception of pain (Abelson 2002; Attal 2000). More so, it has been postulated that burn injury is likely to trigger the release of inflammatory agents such as histamine, serotonin, and prostaglandins which in turn could trigger nociceptive impulses, making lidocaine's potent anti-inflammatory properties integral to the suppression of pain (Edwards 1999).

Given that a number of RCTs and case series (Cassuto 2003; Jönsson 1991) highlight that intravenous lidocaine may lead to a reduction in the procedural and background pain levels of burn patients and lead to less opiate requirements and consequently less associated complications, there is a need for ongoing support and funding of RCTs and CCTs in this area.

AUTHORS' CONCLUSIONS

Implications for practice

No information is available from the published RCTs or CCTs on clinically relevant primary outcome measures which can influence current burns care practice and management. Therefore, since current clinical evidence is subject to the inherent weaknesses of case series or reports, intravenous lidocaine must be considered a pharmacological agent under investigation in burns care whose effectiveness is yet to be determined in randomised, well-designed and conducted clinical trials.

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Implications for research

The evaluation of the clinical effectiveness and relevance of intravenous lidocaine can only be carried out, where possible, in the context of a RCT. A number of RCTs have been published in this area, although they do not appear clinically relevant to a modern day burns unit. Any future trials would need to consider, in particular appropriate sample sizes with power to detect clinically important differences, careful definition and selection of target patients, appropriate lidocaine doses, appropriate and carefully defined comparator therapies. The review authors would welcome any correspondence regarding published trials that we've not identified in this review, or about any possible trials underway.

ACKNOWLEDGEMENTS

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References to studies excluded from this review

Cassuto 2003 *{published data only}*

Cassuto J, Tarnow P. Potent inhibition of burn pain without use of opiates. *Burns* 2003;**29**:163-6.

Holthsuen 2000 *{published data only}*

Holthusen H, Irsfeld S, Lipfert P. Effect of pre- or post-traumatically applied i.v. lidocaine on primary and secondary hyperalgesia after experimental heat trauma in humans. *Pain* 2000;**88**(3):295-302.

Jönsson 1991 *{published data only}*

Jönsson A, Cassuto J, Hanson B. Inhibition of burn pain by intravenous lignocaine infusion. *The Lancet* 1991;**338**(8760):151-2.

Koppert 2004 *{published data only}*

Koppert W, Brueckl V, Weidner C, Schmelz M. Mechanically induced axon reflex and hyperalgesia in human UV-B burn are reduced by systemic lidocaine. *European Journal of Pain* 2004;**8**(3):237-44.

Mattsson 2000 *{published data only}*

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Abelson KS, Hoglund AU. Intravenous administered lidocaine in therapeutic doses increases the intraspinal release of acetylcholine in rats. *Neuroscience Letter* 2002;**317**(2):93-6.

Andreasen 1972

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Attal 2000

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Briggs M, Hofman D. Pain Management. 9th European Conference in Advances in Wound Management. 1999.

Choiniere 1989

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Hollinworth H. Pain and wound care. Wound Care Society Educational Leaflet. Huntingdon, UK: Wound Care Society 2000; Vol. 7:2.

Latarjet 2002

Latarjet J. The management of pain associated with dressing changes in patients with burns. *EWMA journal* 2002;**2**(2):5-9.

Mao 2000

Mao J, Chen LL. Systemic lidocaine for neuropathic pain relief. *Pain* 2000;**87**:7-17.

McLeane 2001

McLeane G. Intravenous infusion of Lidocaine is not associated with changes in cardiovascular parameters: a study of 15 patients. *The Pain Clinic* 2001;**13**(1):83-6.

Schneiber 1993

Schneiber S, Galai-Gat T. Uncontrolled pain following physical injury as the core trauma in post-traumatic stress disorder. *Pain* 1993;**54**:107-10.

Schulz 1995

Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;**273**(5):408-12.

Sheridan 1997

Sheridan RL, Hinson M, Nackel A. Development of a burn pain and anxiety management program. *Journal of Burn Care and Rehabilitation* 1997;**18**:455-9.

Stark 2000

Stark RJ, Hand PJ. Intravenous lignocaine infusions for severe chronic daily headache. *Medical Journal of Australia* 2000;**172**:157-9.

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Taal 1997

Taal LA, Faber AW. Burn injuries, pain and distress: exploring the role of stress symptomatology. *Burns* 1997;**23**:288-90.

Ulmer 1998

Ulmer JF. Burn Pain management: a guideline based approach. *Journal of Burn Care and Rehabilitation* 1998;**19**:151-9.

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Cassuto 2003	Case report
Holthsuen 2000	Did not report on relevant primary outcome measures
Jönsson 1991	Case series
Koppert 2004	Did not report on relevant primary outcome measures
Mattsson 2000	Did not report on relevant primary outcome measures

APPENDICES

Appendix 1. MEDLINE search strategy

via Ovid

1. exp BURNS/
2. (burn or burns or burned).mp
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4. burn.ti. or burn.ab. or burns.ti. or burns.ab. or burned.ti. or burned.ab.) and (burn$ or burns$ or burned$).au
5. 2 not 3
6. 4 or 5
7. burn.ti. or burn.ab. or burns.ti. or burns.ab. or burned.ti. or burned.ab.
8. 2 not (1 or 3 or 7)
9. 6 or 8
10. 1 or 9
11. thermal injur$.mp
12. 10 or 11
13. Lidocaine/
14. (lidocaine or lignocaine).mp
15. 13 or 14
16. 12 and 15

In addition we checked the reference lists of the relevant trials and reviews. We did not contact current researchers in the field for unpublished data and ongoing trials.

WHAT'S NEW

Date	Event	Description
24 September 2010	Amended	Contact details updated.

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HISTORY

Protocol first published: Issue 1, 2006
Review first published: Issue 3, 2007

Date	Event	Description
30 October 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

JW: principal author, conception, guarantor of the review, Cochrane methodology expert.
HC: co-author, burn surgeon, content expert.

DECLARATIONS OF INTEREST

None known

INDEX TERMS

Medical Subject Headings (MeSH)

Analgesia [methods]; Anesthetics, Intravenous [*administration & dosage]; Anesthetics, Local [*administration & dosage]; Burns [*complications] [therapy]; Lidocaine [*administration & dosage]; Pain [*drug therapy] [etiology]; Pain Management [methods]; Randomized Controlled Trials as Topic

MeSH check words

Humans

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