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BURN

ANALGESIA FOR DRESSING CHANGES IN BURNS: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Intense and prolonged pain often caused by burn injuries. The greatest pain is mostly experienced during dressing changes to maintain healing and banish the infection. This review is conducted to assess the effectiveness and safety of different analgesia agents or methods for dressing changes in burn patients.

Method: Searches of studies conducted from 4 electronic databases, using keywords "Analgesia", "Dressing", "Bandages", "Changes" and "Burns". We included randomized and quasi-randomized trials assessing and comparing the effects of different analgesia agents, analgesia methods for dressing changes in burns patients. We excluded trials reporting only pharmacokinetic and physiological outcomes, comparing drug dosages, with exception for those using different drugs in the same class.

Result: Multiple databases search retrieved 144 studies. 17 trials are eligible involving 700 patients. Analgesia using pharmacological agents in 7 trials; 5 trials elaborating primary treatments and 2 trials as the adjunct treatment complementing the major analgesia. Two primary analgesia treatments were studying the role of patient-controlled analgesia (PCA), while 3 trials using caregiver delivered. Ten trials were observing the role of non-pharmacological analgesia.

Conclusion: There was inadequate evidence from comparisons tested in randomized trials to confirm the dependent effectiveness of various techniques of analgesia, individual methods, or to assess the administration of different drug adjuncts for providing analgesia during dressing changes. Given the unresolved questions about the management of these conditions, we suggest that preference should be focused on the large scale, optionally, multi-center randomized observations of the primary methods.

Keywords: *Burn Injury, Dressing Changes, Analgesia*

Latar Belakang: Nyeri hebat dan berkepanjangan sering disebabkan karena luka bakar, Rasa nyeri terhebat seringkali dialami selama pergantian perban yang dilakukan untuk untuk menjaga proses penyembuhan dan mencegah infeksi. Studi ini dilakukan untuk menilai efektivitas dan keamanan dari agen analgesik yang berbeda atau metode pergantian perban pada pasien luka bakar.

Metodologi: Pencarian dilakukan dari 4 *database* elektronik, menggunakan kata kunci *"Analgesia", "Dressing", "Bandages", "Changes"* dan *"Burns"*. Kami menyertakan uji coba acak dan kuasi acak yang menilai dan membandingkan efek dari agen analgesia yang berbeda, metode analgesia untuk pergantian perban pasien luka bakar. Kami mengekslusi penelitian yang melaporkan hanya hasil farmakokinetik dan fisiologis, membedakan dosis obat, dengan pengecualian yang menggunakan obat berbeda di kelas yang sama.

Hasil: Ditemukan 144 studi dari hasil pencarian. Terdapat 17 uji coba yang memenuhi syarat dan melibatkan 700 pasien. Analgesia dipertimbangkan sebagai agen farmakologis dalam 7 uji coba; 5 uji coba menjelaskan analgesia sebagai terapi primer dan 2 uji coba sebagai terapi tambahan untuk analgesia utama. Dua terapi analgesia primer mempelajari peran analgesia yang dikontrol pasien, sementara tiga uji coba diberikan oleh tenaga kesehatan. Sepuluh uji coba mengamati peran analgesia non-farmakologis.

Kesimpulan: Terdapat bukti yang tidak cukup dari perbandingan uji coba acak untuk mengkonfirmasi efektivitas yang bergantung dari teknik analgesia, metode individual, atau untuk menilai pemberian obat tambahan analgesia selama pergantian perban. Mengingat banyak pertanyaan yang belum terjawab mengenai kondisi ini, kami menyarankan preferensi harus difokuskan pada skala besar, secara opsional, pengamatan acak *multicenter* dari metode primer.

***Keywords**: Burn Injury, Dressing Changes, Analgesia*

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BACKGROUND

Great and extended pain often caused by burn injuries; the pain is exaggerated by the need to remove dressings often to maintain healing and banish the infection. There are some modern techniques such as skin replacement therapy and early excision that already decreased the amount of dressing changes in a burn injury.[1]

Choiniere et al, investigated the characteristics of pain suffered by burn patients and studied that the time of greatest pain is mostly experienced during procedural dressing changes.[2] The big goal to achieve of zero pain in procedural burn management is an achievable and entirely realistic goal. However, pain arisen by procedural dressing changes is difficult to assess and manage[3], and there is best treatment available that is agreed among burn specialists on how best to determine or control this pain. Most procedural pain is widely undertreated; even in sophisticated burn centers settings[4,5]. In addition, pain management, even though, is necessary, often constrained and forgotten by lack of caregiver training, time and monitoring skill. Unmanaged pain in burn patients could lead to non-compliance with hospital regiment, disorganized care[6] and increased post-traumatic stress disorders occurrence.[7]

Following acute phase of a burn injury, an intense inflammatory response and the release of chemical mediators will elicit the active nociceptors at the site of harm. The wound will become sensitive to mechanical stimuli such rubbing and debridement, also chemical stimuli such as antiseptics cleaning or other topical agents.[9]

If nociceptive afferent fibers is continuously stimulated it will induces a significant increase in dorsal horn excitability via N-methyl-D-aspartate (NMDA) receptors[10], which will cause increased sensitivity to unburned areas of skin. The phenomenon is called 'wind-up' pain, as investigated in a study by Pedersen and Kehlet those comprises the post-burn hyperalgesia, and frequent dressing change and its mechanical stimulation will exacerbate this condition.[11] This 'wind-up' mechanism is the explanation of patient's increased sensitivity during the course of burn management and somehow the main reason for greater opioid requirement for dressing changes over time[2].

Atchison et al, studied pain at different stages of the dressing procedure in burn and investigated that worst pain come when the innermost layer of gauze is removed, which usually adheres partly to the wound bed. This removal frequently followed by another debridement and topical agents applications.[12]

Often dressing changes are performed in an operating theater. However, considering the cross-infection risk, dressings changes are carried mostly out in the patient ward. Speaking of the ideal criteria for optimal analgesia for burn dressing changes we have to ensure that there are adequately staffed and safe environment in which to care for sedated patients. The control for severe acute pain due to nociception (inflammatory response) while painful dressing change is applied (i.e. dressing removal, wound cleansing) should be alleviated by titrating analgesics agents to individual requirements. One must avoid over sedation during and following the dressing change, but always ensure enough post-procedural analgesia by considerable amount of pain assessment and monitoring of vital signs. The ideal analgesia method also needs to reduce prolonged fasting as little as possible while adequate nutrition and hydration are essential to the healing process.

Among those criteria mentioned above, there're many medications well suited to fulfill the requirements such as general anesthesia, the intravenous medications (IV opioids), Oral medications for mild pain (morphine), inhaled medication (nitrous oxide/Entonox), and non-pharmacological therapies such as distraction therapies.

Sufficient analgesia should aid to assure that the patient remains as comfortable as possible throughout the dressing change procedure and subsequently, which should also help the burn team complete the method safely. While the plan of analgesia is to give adequate coverage with the least amount of pain and less adverse effects, various analgesic agents and methods will vary in their capability to balance anesthetic coverage, pain support and the avoidance of disadvantageous effects.

Disclosure: *The authors have no financial interest to disclose.*

It is important to assess the effects of different types/methods of analgesia for burn dressing change in order to inform patients and caregiver of the most efficient and safe methods, associated with fewest adverse consequences for patients.

METHOD

We included any randomized controlled trials and quasi-randomized trials (use of a system of designating participants to a therapy that is not rigidly random such as DOB, medical record numbers) evaluating and analyzing the effects of different analgesics or methods or techniques for providing analgesia, for dressing changes in burns patients. We intended to involve studies given as abstracts. Types of participants are burns patients, male or female, in any age group, who undergoes procedural burns wound dressing changes for any indication for burns treatment.

All trials assessing and comparing different methods of analgesia, any method or mixture of analgesics associated with placebo or no treatment or matched with an alternative method or pharmacological agent. Also involved are trials investigating the use of drug adjuncts/supplements. We excluded cluster-randomized trials and trials reporting only pharmacokinetic and physiological outcomes, also trials comparing drug dosages, with one exception for those using different medications in the same class.

Types of outcome measures are effect of Intervention (pain relief as measured by the author of the trials) and adverse effects directly attributed to anaesthetic drugs and techniques; complications were resulting directly from the administration of anesthesia (including cardiac and respiratory arrest).

Online searches of multiple databases from Ovid MEDLINE(R), EMBASE Classic+EMBASE, CINAHL, and COCHRANE LIBRARY conducted on 12th January 2015, at 20:00 pm. Searches from Ovid MEDLINE(R) database at http://ovidsp.ovid.com (1946 until presents), from EMBASE Classic+EMBASE database at http://ovidsp.ovid.com (1947 to 9th of January 2015), from CINAHL database at https://web-b-ebscohost-com (all year), and last from COCHRANE LIBRARY at http://onlinelibrary.wiley.com (all year). No language restrictions were applied. Online search ends on Tuesday, 12th January 2015 at 21:25 pm. The search strategies used are utilizing search terms and keywords such as "Analgesia", "Dressing", "Bandages", "Changes" and "Burns". Boolean operator were incorporated into search terms to distinguish more particular studies, in general, using following strategy: (("Dressing" OR "Bandages") AND "Changes" AND "Analgesia" AND "Burns"). Searches were performed on all fields, and no search limitation was applied initially.

Data collection and analysis

All studies retrieved from 4 databases were exported to Endnote X7 for Mac, duplicate studies are identified and excluded. One authors assessed for inclusion all the potential and the methodological quality of the studies independently. Full texts were searched, and we also planned to include studies presented as abstract. Titles of journals, names of authors or supporting institutions were not masked at any stage. We contacted the trialist of the studies for additional details of key items of trial methodology or data.

A modification of the Cochrane Bone, Joint, and Muscle Trauma Group quality assessment tool was employed in the evaluation of the added studies. The scoring plot for 12 aspects of trial validity, plus brief notes of coding guidelines for some items, is shown in **Table 1.** Despite the numbers of the particular items were summed, this was to gain an overall impression rather than for quantitative purposes.

Data analysis

of equivalent groups of trials were merged utilizing the fixed effects model, and 95 per cent confidence limits. Heterogeneity among comparable trials was examined using a regular chi-squared test and judged to be statistically significant at $p < 0.1$. Where there was significant heterogeneity in the outcomes of individual trials. We viewed the results of the random effects model and presented these, when considered appropriate, instead of those from the fixed effects model.

No subgroup analyzes were initiated; if they had happened, every test of interaction measured to define if the outcomes for subgroups are significantly different. Those were based on Peto odds ratio results. Sensitivity analyzes testing various aspects of trial and review methodology, involving the effects of missing data and study quality were also estimated but rarely possible

T**able 1.** Methodological quality assessment scheme

Code	Items	Scores	Notes
Q1	1. Was the assigned treatment adequately concealed prior to allocation?	3 = method did not allow disclosure of assignment. 1 = small but possible chance of disclosure of assisgnment or unclear. 0 = quasi-randomised or open list/ table	Cochrane code (see Handbook) Clearly Yes = A; Not Sure = B; Clearly No = C
Q2	2. Were the outcomes of patients who withdrew described and included in the analysis (intention to treat)?	3 = withdrawals well described and ac-counted for in analysis. 1 = withdrawals described and analysis not possible, or probably no withdrawals. 0 = no mention, inadequate mention, or obvious differences and no adjusment	
Q3	3. Were the outcome assessors blinded to treatment status	3 = effective action taken to blind assessors. 1 = small or moderate chance of unblinding of assessors, or some blinding of outcomes attempted. 0 = not mentioned or not possible	
Q4	4. Were important baseline characteristics reported and compared	3 = good comparability of groups, or con-founding adjusted for in analysis. 1 = confounding small, mentioned but not adjusted for, or comparability reported in text without confirmatory data. 0 = large potential for confounding, or not discussed.	the principal confounders considered were gender, age, type of burns, type of treatment, existing co-morbidities (cardiac disease, inhalation trauma, prior functional and mental status, and existing complications).
Q5	5. Were the patients blind to assignment status after allocation?	3 = effective action taken to blind patients. 1 = small or moderate chance of unblinding of patients. 0 = not possible, or not mentioned (unless double-blind), or possible but not done.	
Q6	6. Were the treatment providers blind to assignment status?	3 = effective action taken to blind treatment providers. 1 = small or moderate chance of unblinding of treatment providers. 0 = not possible, or not mentioned (unless double-blind), or possible but not done	
Q7	7. Were care programers other than the trial options, identical?	3 = care programmes clearly identical 1 = clear but trivial differences, or some evidence of comparability. 0 = not mentioned or clear and important differences in care programmes.	Example of clinical important differences in other interventions were: differences in anesthesia method, subsequent treatment (pharmacological and non-pharmacological),clinician experience and specialty
Q8	8. Were the inclusion and exclusion criteria for entry clearly defined	3 = clearly defined (including type of treatment). 1 = inadequately defined. 0 = not defined.	

Q9	9. Were the interventions clearly defined (including who provided the care)?	3 = clearly defined interventions are applied with a standardised protocol and care providers identified. 1 = clearly defined interventions are applied but the application protocol is not standardised or care providers identified. 0 = intervention and/or application protocol are poorly or not defined.
Q10	10. Were the outcome measure used clearly defined?	3 = clearly defined. 1 = inadequately defined 0 = not defined
Q11	11. Were the accuracy and precision, with consideration of observer variation, of the outcome measure adequate (and were these clinically useful?) - including active follow-up	3 = optimal 1 = adequate 0 = not defined, not adequate.
Q12	12. Was the timing (e.g. duration of surveil-lance) clinically appropriate?	3 = optimal. (> 1 year) 1 = adequate. (3 months - 1 year) 0 = not defined, not adequate. (< 3 months)

Data analysis

Results of equivalent groups of trials were merged utilizing the fixed effects model, and 95 per cent confidence limits. Heterogeneity among comparable trials was examined using a regular chi-squared test and judged to be statistically significant at $p < 0.1$. Where there was significant heterogeneity in the outcomes of individual trials. We viewed the results of the random effects model and presented these, when considered appropriate, instead of those from the fixed effects model.

No subgroup analyzes were initiated; if they had happened, every test of interaction measured to define if the outcomes for subgroups are significantly different. Those were based on Peto odds ratio results. Sensitivity analyzes testing various aspects of trial and review methodology, involving the effects of missing data and study quality were also estimated but rarely possible.

RESULT

Description of studies

Searches from Ovid MEDLINE(R) database started from year 1946 until presents revealed 39 studies, from EMBASE Classic+EMBASE database started from year 1947 to 9th of January 2015 resulted 56 studies, from CINAHL database with all year spans search retrieved 20 studies, and last from COCHRANE LIBRARY also all year span search found 29 studies. Online search ends on Tuesday, 12th January 2015 at 21:25 pm. Total of 144 studies retrieved from 4 databases were exported to Endnote X7 for Mac, duplicate studies are identified and excluded, thus yield remaining 74 studies. Hand searches to studies derived from search strategy are performed using inclusion criteria above; full texts were searched, and we also include studies presented as abstract. Finally after exclusion of 54 studies, the remaining 17 studies are selected and accounted for the final analysis.

METHOD

We included any randomized controlled trials and quasi-randomized trials (use of a system of designating participants to a therapy that is not rigidly random such as DOB, medical record numbers) evaluating and analyzing the effects of different analgesics or methods or techniques for providing analgesia, for dressing changes in burns patients. We intended to involve studies given as abstracts. Types of participants are burns patients, male or female, in any age group, who undergoes procedural burns wound dressing changes for any indication for burns treatment.

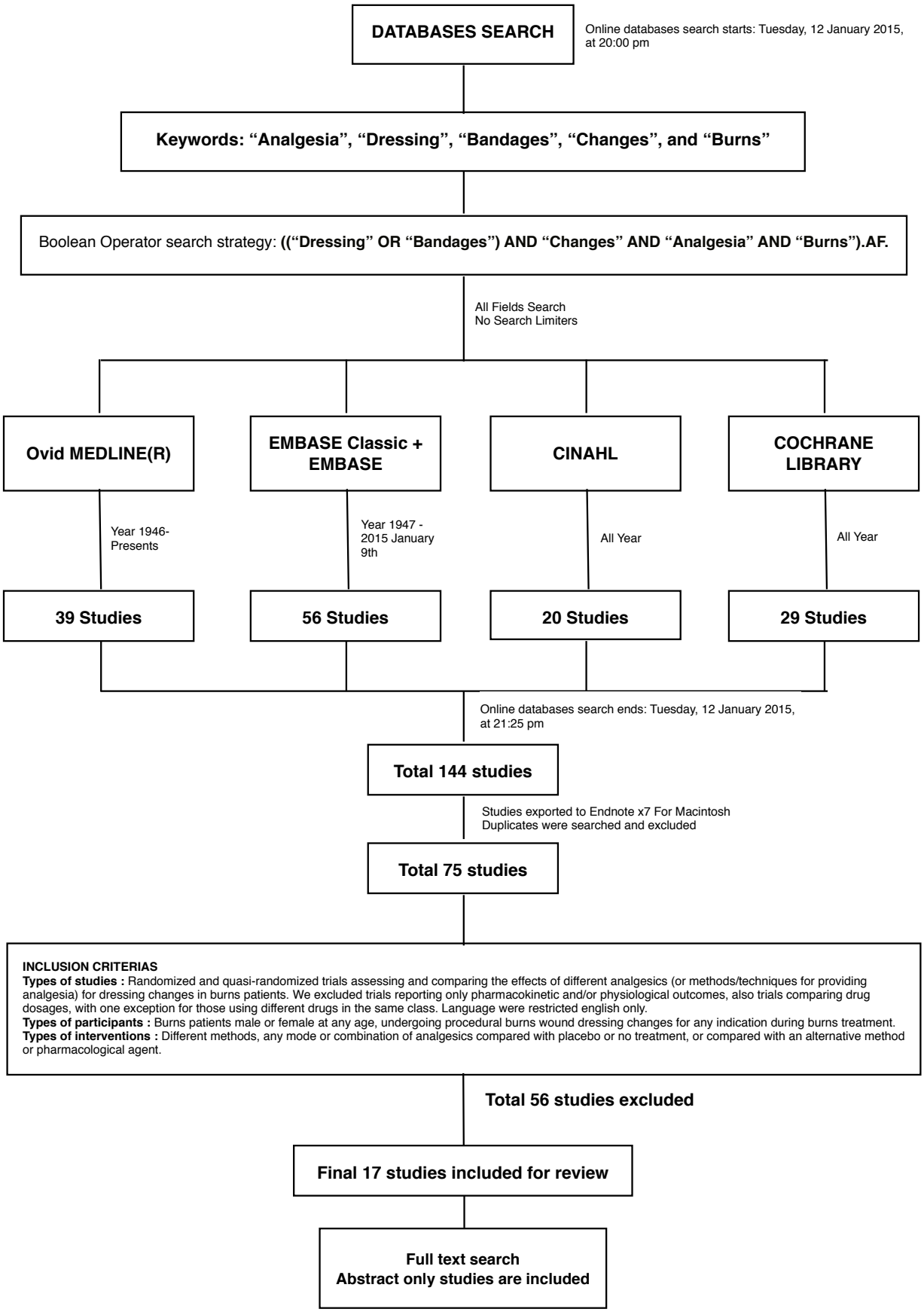

Figure 1. Detailed search history diagrams

T**able 2.** Studies retrieved from the search

1.	Prakash (2004)	"Patient-controlled analgesia with fentanyl for burn dressing changes. "Anesthesia and analgesia**99**, 552-555, table of contents DOI: 10.1213/01.ANE.00001251 10.56886.90.	Included
2.	Das (2005)	"The efficacy of playing a virtual reality game in modulating pain for children with acute burn injuries: a randomised controlled trial [ISRCTN87413556]. "BMC paediatric**5**, 1 DOI: 10.1186/1471-2431-5-1.	Included
3.	Frenay (2001)	"Psychological approaches during dressing changes of burned patients: a prospective randomised study comparing hypnosis against stress reducing strategy." Burns**27**, 793-799.	Included
4.	Konstantatos (2009)	"Predicting the effectiveness of virtual reality relaxation on pain and anxiety when added to PCA morphine in patients having burns dressing changes." Burns**35**, 491-499 DOI: 10.1016/j.burns.2008.08.017.	Included
5.	Miller (2010)	"Multi-modal distraction. Using technology to combat pain in young children with burn injuries. "Burns**36**, 647-658 DOI: 10.1016/j.burns.2009.06.199.	Included
6.	Mohammadi (2013)	"The effect of jaw relaxation on pain anxiety during burn dressing: Randomised clinical trial. "Burns**39** 61-67 DOI: 10.1016/j.burns.2012.03.005.	Included
7.	Mott (2008)	"The efficacy of an augmented virtual reality system to alleviate pain in children undergoing burns dressing changes: a randomised controlled trial. "Burns**34**, 803-808 DOI: 10.1016/j.burns.2007.10.010.	Included
8.	Nilsson (2008)	"Patient controlled sedation using a standard protocol for dressing changes in burns: patients' preference, procedural details and a preliminary safety evaluation." Burns**34**(7):929-934.	Included
9.	Wasiak (2011)	"Adjuvant use of intravenous lidocaine for procedural burn pain relief: a randomised double-blind, placebo-controlled, cross-over trial." Burns**37** (6): 951-957.	Included
10.	Wright (2000)	"Rapid induction analgesia for the alleviation of procedural pain during burn care." Burns**26**, 275-282.	Included
11.	Zhang (2013)	"Effects of puerarin on the inflammatory role of burn-related procedural pain mediated by P2X7 receptors." Burns**39** (4): 610-618.	Included
12.	Zor (2010)	"Pain relief during dressing changes of major adult burns: Ideal analgesic combination with ketamine," Burns**36** (4): 501-505.	Included
13.	Borland (2005)	"Intranasal fentanyl is an equivalent analgesic to oral morphine in paediatric burns patients for dressing changes: a randomised double blind crossover study." Burns (03054179)**31**(7): 831-837	Included
14.	Lewis (1990)	"Effects of auricular acupuncture-like transcutaneous electric nerve stimulation on pain levels following wound care in patients with burns: A pilot study." Journal of Burn Care and Rehabilitation**11**(4): 322-329.	Included
15.	Miller (1992)	"A distraction technique for control of burn pain." Journal of Burn Care and Rehabilitation**13**(5): 576-580.	Included
16.	VerLee (2012)	"The utility of virtual reality in minimizing procedural distress with pediatric burn patients. "Journal of Burn Care and Research**1**): S178.	Included

17.	Tosun (2008)	"Propofol-ketamine vs propofol-fentanyl combinations for deep sedation and analgesia in pediatric patients undergoing burn dressing changes." Paediacticanaesthesia**18**, 43-47 DOI: 10.1111/ j.1460-9592.2007.02380.x.	Included
18.	Sheridan (1994)	"Midazolam infusion in pediatric patients with burns who are undergoing mechanical ventilation." Journal of Burn Care and Rehabilitation**15**(6): 515-518.	Included

The periods over which individual tests were conducted spanned over twenty-five years, from the early 1990s by Lewis et al. 1990 (21) on- wards. All trials took place at single centres in eight countries (Australia (7 trial); USA (3); Belgium (1); India (1); Turkey (1); Sweden (1); Iran (1); China (11)). All trials using non-English language were excluded.

The 17 included studies involved at least 700, mainly male and distributed on all ages, participants who received burns wound care that requiring dressing changes. There was a minimum of 716 randomized patients with these injuries. The number of randomised patients in Lewis et al 1990 (21) and Nillson et al 2008(22)was not explicitly stated but was probably the same as deduced from a table in the article.

With the exception of two trials Wright 2000 (23) and Zhang 2013 (24)most trials presenting data on patient gender recruited more male than female patients; the proportion ranged from 50 percent from Frenay et al 2001 (25)to 83.3 percent in studies by Zor et al 2010 (26). Where provided, median or mean ages of trial populations ranged between 6.2 years from Miller et al 2010 (27)and 57.5 years Nillson et al 2008 (22). The youngest patient (3.5 years) appeared in Mott et al 2008 (28). Lower age limits were set by seven trials (Das 2005: 5 years; Miller 2010: 3 years; Verlee 2012: 7 years, Tosun2008 ; 5 months) (27, 29-31). While six trials (Das 2005, Miller 2010, Mott 2008, Borland 2005, Verlee 2012, Tosun 2008)(28-30, 32-34)actually includes children only for their subject. However, it was clear that the majority of patients were from adult age group. An upper limit of 80 years was applied in Konstantos2009 (35).

Injury classification was broadly defined as burns caused by any agents that require dressing changes. A burns injury classification scheme that based on TBSA (Total Burn Surface Area) was specified in nine trials: The lowest cut-off points for TBSA was defined in Miller 2010 (36)for burns involving more than 1% of TBSA, and the highest cut-off points was applied in Wright 2000 (23)for more burns than 45% TBSA. Eight trials from Verlee 2012, Tosun 2008, Konstantos 2009, Mohammadi 2013, Wasiak 2011, Miller 1992, Lewis 1990, Zor2000 (21, 26, 30, 33-35, 37, 38)did not specified the TBSA criteria for trial inclusion. Two trials from Zhang 2013 and Nilsson 2008(22, 24)actually specified the burn categories to first, second and third degree classification, showing more detailed classification of burn injuries. Analgesia was for considered using pharmacological agents in 7 trials; which further comprises 5 trials elaborating primary treatments and 2 trials as the adjunct treatment complementing the major analgesia. Two primary analgesia treatments by Nilsson 2008 and Prakash 2004 (22, 39)were studying the role of patient-controlled analgesia (PCA), while 3 trials using caregiver delivered analgesia (Borland 2005, Tosun 2008, Wright 2000) (23, 32, 34). Ten trials were observing the role of non-pharmacological analgesia, in which seems like to be the new study trends in this population nowadays. The role of non-pharmacological analgesia for burn dressing changes were evidently adjunctive as described in 6 trials (Das 2005, Frenay 2001, Konstantatos 2009, Miller 1992, Mohammadi 2013, Mott 2008) (25, 28, 29, 33, 35, 37), while four trials (Lewis 1990, Miller 2010, Verlee 2012, Zhang 2013) deliberately using non-pharmacological trials as the primary treatment for analgesia in burns dressing changes.

These are short description of the interventions compared in the 17 trials.

1. Main types of analgesia:

a. PUE versus normal saline

One comparison for analgesia given by Zhang (2013) studies the role PUE for reducing pain in dressing changes (24).PUE-treated burn patients were applied with 100 ml puerarin glucose injection (Yangtze River Pharmaceutical Group, SFDA License No. H20020450, including puerarin 200 mg). The NS-treated burn patients were administered with 100 ml 0.9% sodium chloride injection

b. Intranasal fentanyl versus placebo

Study by Borland (2005) (32)compares Oral Morphine and intranasal placebo on first day continued by oral placebo (40) also INF on second for treatment group and INF and OP on first day followed by INP and OM on day 2 for control group.

c. Acupuncture versus placebo

Lewis (1990)(21)patient who received one experimental treatment consisting of bilateral acupuncture-like transcutaneous electrical nerve stimulation to six ear points, while control treatment consisting of a placebo pill.

d. Propofol-ketamine versus propofol-fentanyl

Tosun (2008) (31) examines combination of propofol-ketamine compared to propofol fentanyl for effective sedation during dressing changespediatric burn patients.

2. Techniques of analgesia

a. PCA (Patients Controlled Analgesia)

Two studies by Prakash (2004) and Nillson (2008) compare the uses of PCA (Patients Controlled Analgesia). One trial by Prakash2004 (39)compares doses of PCA-Fentanyl for analgesia during dressing changes. Every participant administered by an initial loading dose of IV fentanyl 1 microg/kg 10 min before the procedure. The patients were allocated to receive on-demand analgesia with one of the four PCA-fentanyl demand doses—10, 20, 30, and 40 microg. The demand treatment was given IV at a steady rate by a PerfusorFm PCA pump (Braun) with a 5-min lockout interval. The participants were ordered to press the PCA hand control device during the dressing procedure whenever their pain intensity VAS score was >2. Nilsson (2008) (22)comparison started with dressing changes under sedation by an anesthetist using routine sedating techniques. The second dressing change was done using PCS as described below. At the third dressing change, the patients were asked to choose one of the two techniques.

b. Attention Distraction Techniques

There were five studies from Das (2005), Konstantatos(32), Miller (2010), Mott (2008), Miller (1992) and Verlee (2012) that explore the roles of attention distraction techniques to combat pain in dressing changes. Studies by Das 2005(41) and Konstantatos (2009) (35)compares routine pharmacological analgesia coupled with virtual reality versus routine pharmacological analgesia coupled with virtual reality versus routine pharmacological analgesia only. However, Das (2005) uses children as their subjects, and Konstantatatos (2009) uses adults as their subjects. Virtual reality relaxation plus intravenous morphine patient-controlled analgesia (PCA) infusion were the protocol used to treatment arms in Konstantatos (2009) studies.

Various multi-modal distraction techniques are used such as Standard (SD), off the shelf handheld video game (VG), MMD procedural preparation (MMD-PP), and MMD Distraction (MMD-D) by Miller[27] in their studies. Children entered the treatment room individually and were set up with the distraction as per outlined by their group. The nursing staff completed standard burn dressing removal procedures. All children were treated with Acticoat, a silver-based dressing that was changed every three days.

Mott (2008)[37] examines the comparison of Augmented Reality versus multidimensional cognitive techniques. The AR group used the handheld system both before and during the dressing change. The control group employed primary multi-dimensional cognitive techniques, such as attention– distraction, positive reinforcement, relaxation and an age appropriate video program. Analgesic medications were administered prior to randomization and all children received standard drug dosages, calculated on a dose per weight basis.

The experimental arm watched video programs that were comprised of scenic beauty accompanied by music, and the other group received standard care in a study by Miller (1992)[33]. In study by Verlee (2012)[30] patients were randomly assigned to VR or standard care. Children in the VR group used a headset containing the VR program during initial dressing change. The usual care group received traditional forms of distraction (ex: TV, talking).

c. Psychotheraphy

Two studies uses psychotherapy techniques in the form of hypnosis to alleviate pain associated with dressing changes. Frenay et al[25] compares hypnosis versus stress reducing strategies, along with usual standardized premedication that was injected intramuscularly 20 minutes before dressing change (analgesic drug, piritramide 20 mg, anxiolytic drug, midazolam 5 mg without weight adjustment). RIA (Rapid Induction Analgesia) patients and standard care were compared to Standard care only in studies by Wright (2000).[23]

3. Treatment adjuncts or supplements

a. Lidocaine

The treatment arm from Wasiak (2011)[38] were given an initial bolus doses of lidocaine of 1.5 mg/kg accompanied by two boluses of 0.5 mg/kg at 5-min intervals and an infusion run at 2 mg/min throughout the duration of the dressing, these were compared to In the alternative treatment arm, 0.9% sodium chloride (normal saline) was given at an similar volume, dose and rate to that of lidocaine All subjects received patient-controlled analgesia (PCA) according to pain service protocol.

b. Tramadol, dexmedetomidine, and midazolam

Zor (2010)[26] examines three groups in his comparison Group I: 2 mg/kg intramuscular (IM) ketamine was administered. Group II: 1 mg/kg IM tramadol was administered. After 30 min, 1 mg/kg IM dexmedetomidineHCl and 2 mg/kg im ketamine was administered. Group III: 1 mg/kg IM tramadol was administered. After 30 min, 0.05 mg/kg IM midazolam HCl and 2 mg/kg IM ketamine was administered.

c. Jaw relaxation techniques

Mohammadi (2013) studies one particular method: jaw relaxation compared to standard care. Patients in the experimental group practiced jaw relaxation technique for 20 min. Fifteen to twenty minutes after the dressing change, when patients were resting comfortably in their bed, they were asked to rate their pain anxiety during the dressing change.

Risk of bias among studies included

The methodological quality scores based on included studies were considered vary. Lack of recognition of the concealment of allocation and insufficiencies in the estimation of the outcome, including only short-term follow-up, were typical causes for lower quality scores. A summary of the individual aspects of trial quality follows the table of the scores for individual tests presented in **Table 5.** Information unique to the first three items of the quality score is given in the methods section of the

Characteristics of Included Studies.

Effect of intervention

The summary for intervention, comparator and available outcomes among trials are presented at **Table 4.**

T**able 3.** Summary of methodological quality assessment

Study ID	Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Total (Max 36)
1	Prakash (2004)	3	1	1	3	3	3	3	1	1	3	1	0	23
2	Das (2005)	1	1	3	1	1	0	0	1	1	3	0	0	12
3	Frenay (2001)	1	1	0	1	1	1	1	3	1	1	0	0	11
4	Konstantatos (2009)	1	1	0	3	0	0	1	3	3	3	1	0	16
5	Miller (2010)	1	3	1	3	0	0	1	3	1	3	1	0	17
6	Mohammadi (2013)	1	3	0	3	0	0	1	3	3	3	1	0	18
7	Mott (2008)	1	1	0	1	0	0	1	1	3	3	1	0	12
8	Nilsson (2008).	0	1	0	1	0	0	1	1	3	3	1	0	11
9	Wasiak (2011).	3	1	3	3	3	3	1	3	3	3	1	0	27
10	Wright (2000)	1	1	0	3	0	0	1	1	1	1	0	0	9
11	Zhang (2013).	3	1	1	3	1	1	1	3	1	3	1	0	19
12	Zor (2010).	1	0	0	1	0	0	0	1	1	3	1	0	8
13	Borland (2005).	1	1	1	3	0	1	1	1	3	3	1	0	16
14	Lewis (1990).	0	1	0	1	0	0	1	1	1	1	0	0	6
15	Miller (1992).	1	1	0	1	0	0	1	1	1	1	0	0	7
16	VerLee (2012).	1	1	0	1	0	0	1	3	1	1	0	0	9

Table 4. Summary of intervention, comparator and outcomes available

Study	Participants Assessed	Intervention	Comparator	Primary Outcomes	Secondary Outcomes	Comments
Prakash (2004)	60/60, 15 for each froup of PCA-fentanyl demand doses—10, 20, 30, and 40 micrograms	On-demand analgesia with one of the four PCA-fentanyl demand doses—10, 20, 30, and 40 microg.	On-demand analgesia with one of the four PCA-fentanyl demand doses—10, 20, 30, and 40 microg	Available	Available	Mean VAS scores in the 10 and 20 microg groups (7.73 +- 1.33 and 7.20 +- 1.21, respectively) were significantly higher than those in the 30 and 40 microg groups (4.47 +- 0.83 and 3.90 +- 0.63, respectively) (all P= 0.000). Demand/delivery ratios were significantly larger in the 10 and 20 microg groups (3.03 1.06 and 2.54 +- 0.49, respectively) than those in the 30 and 40 microg groups (1.36 +- 0.34 and 1.37 +- 0.36, respectively) (all P = 0.000). VAS scores and demand/delivery ratios were comparable in the 30 and 40 microg groups (P=0.260 and P= 0.977, respectively), which suggests comparable analgesic efficacy.
Das (2005)	7/9, 3 trials were undertaken from 9 children, 1 subject participating in 3 trials, 2 subjects in 2 trials, and the remainder in 1 trial each	Routine pharmacological analgesia coupled with virtual reality	Routine pharmacological analgesia	Available	Available	With pharmacological analgesia only, the mean pain score (using the Faces Scale), over all included trials was 4.1 (SD 2.9), whilst for VR coupled with pharmacological analgesia, the average pain score was 1.3 (SD 1.8). Over all included trials, the mean pain score difference between administrations was 3.2 (SD 2.1), which was significant using paired t-tests ($p < 0.01$). This indicated the importance of the effect of using VR (coupled with analgesia) in reducing pain experiences during burns dressing changes
Frenay (2001)	26/30, 15 patients in the hypnosis group and 15 in the SRS group.	Hypnosis adjunctively to routine intramuscular pre-dressing change analgesia and anxiolytic drugs	Stress reducing strategies (SRS) adjunctively to routine intramuscular pre-dressing change analgesia and anxiolytic drugs	Available	None	Although the VAS scores after wound care did not differ significantly in the two groups, they were still higher in the SRS group. Likewise, pain VAS scores before, during and after wound care in the hypnosis group were consistently lower than in the SRS group, however, the differences did not reach statistical significance. To test for an overall effect of psychological interventions, hypnosis and SRS patients were combined and VAS scores recorded were compared by Student's paired t-test, psychological support did significantly decrease pain and increase patient satisfaction.

Konstantatos (2009)	86/88 44 allocated to VRR plus PCA, 45 allocated to PCA Alone	Virtual reality relaxation plus intravenous morphine patient controlled analgesia (PCA) infusion	Intravenous morphine patient controlled analgesia infusion alone	Available	None	The group receiving virtual reality relaxation plus morphine PCA infusion reported significantly higher pain intensities during the dressing change (mean = 7.3) compared with patients receiving morphine PCA alone (mean = 5.3) (p = 0.003) (95% CI 0.6–2.8). The addition of virtual reality guided relaxation to morphine PCA infusion in burns patients resulted in a significant increase in pain experienced during awake dressings changes
Miller (2010)	70/80, SD group 20, PS group 20, MMD procedural preparation group 20, MMD distraction group 20	(1) Standard (SD), (2) off the shelf hand held video game (VG), (3) MMD procedural preparation (MMD-PP), and (4) MMD Distraction (MMD-D)	(1) Standard (SD), (2) off the shelf hand held video game (VG), (3) MMD procedural preparation (MMD-PP), and (4) MMD Distraction (MMD-D)	Available	None	MMD-D and MMD-PP were both shown to significantly relieve reported pain (p = 0.05) and reduce the time taken for dressings (p=0.05) compared to SD and VG. The positive effects of both MMD-D and MMD-PP were sustained with subsequent dressing changes.
Mohammadi (2013)	100/107, 55 allocated to experimental group, 52 allocated to control group	Patients in the experimental group then practiced jaw relaxation technique for 20 min.	Standard usual care	Available	None	An independent t-test showed no significant difference between mean pain anxiety scores in the experimental and control group before intervention (p = 0.787). A dependent t-test showed significantly less pain anxiety after intervention (before dressing) in the experimental group (p<0.05). However, the dependent t-test showed no significant difference between before and after dressing pain anxiety (after intervention) in the experimental group (p = 0.303).
Mott (2008)	42/42 Treatment (AR) group (n = 20 with a total of 24 dressing changes) and a control group (n = 22 with 32 dressing changes)	The AR group used the hand held system both before and during the dressing change.	The control group employed basic multi-dimensional cognitive techniques, such as attention–distraction, positive reinforcement, relaxation and an age appropriate video program.	Available	None	The pain in the altered reality treatment was significantly less severe (2.81 +- 0.89) than the pain felt by the control group (5.38 +- 0.58). A Repeated Measures of Analysis test showed that pain significantly increased over time (p<0.0006 for medium dressing times, p < 0.0001 for long dressing times) as the dressing progressed. There was a significant decrease in pain over time in the altered reality treatment group (p = 0.0060), compared to control for the long dressing time group (>30 min duration).

Nilsson (2008).	11/11 Patients were their own control group	PCS (Patients Controlled Sedation)	Routine sedating techniques.	Available	None	The highest mean (S.D.) pain ratings recorded, during wound treatment were greater for PCS (4.9 (2.4)) than for ACS (1.5 (1,0)). Immediately and 10 min after dressing changes there were no differences. Procedural pain was higher during PCS but lower after the procedure.
Wasiak (2011).	45/45, active treatment n=22, placebo=23	treatment arm were given an initial bolus does of lidocaine of 1.5 mg/kg/ body weight followed by two boluses of 0.5 mg/kg at 5-min intervals and an infusion run at 2 mg/ min throughout the duration of the dressing. All subjects received patient controlled analgesia (PCA) according to pain service protocol.	In the alternative treatment arm, 0.9% sodium chloride (normal saline) was administered at an equivalent volume, dose and rate to that of lidocaine. All subjects received patient controlled analgesia (PCA) according to pain service protocol.	Available	Available	The increase in VRS score was significantly lower for lidocaine [difference (95% CI) = 0.36 (0.17 +- 0.55), $p < 0.001$] as compared to placebo. No significant clinical or statistical differences regarding the effects of lidocaine and placebo on opioid requests and consumption, anxiety or level of satisfaction during the first and second dressing procedures
Wright (2000)	30/30, 15 in treatment and 15 in control group	RIA (Rapid Induction Analgesia) patients and standard care.	Standard care only	Available	None	Self-reported pain intensity and distress during burn care decreased during RIA in treated subjects. The condition x sessions interaction was significant both for sensory and affective ratings ($F(2,27)=12.02$ and 19.08 respectively, $p < 0.001$). I
Zhang (2013).	42/42 NS treated burn patients, n = 15) and puerarin-treated group (PUE treated burn patients, n = 17	The PUE-treated burn patients were applied with 100 ml puerarin glucose injection (Yangtze River Pharmaceuti cal Group, SFDA Licence No. H20020450, including puerarin 200 mg).	The NS-treated burn patients were applied with 100 ml 0.9% sodium chloride injection	Available	None	There was no statistical significance between NS-treated burn patients and PUE-treated burn patients at 10 min pre-dressing on days 1–3 ($P > 0.05$). The mean VAS of 10 min mid- and post-dressing in NS-treated burn patients was significantly increased in comparison with that at 10 min pre-dressing from the first day to the third day ($P < 0.05$). The values in NS-treated burn patients were higher than those in PUE-treated burn patients at 10 min mid- and post-dressing on days 1–3 ($P < 0.05$).

Zor (2010).	24/24 Separated to 3 groups each group of 8	Group II: 1 mg/kg IM tramadol was administered. After 30 min, 1 mg/kg IM dexmedetomidineHCl and 2 mg/kg im ketamine was administered. Group III: 1 mg/kg IM tramadol was administered. After 30 min, 0.05 mg/kg IM midazolam HCl and 2 mg/kg IM ketamine was administered	Group I: 2 mg/kg intramuscular (IM) ketamine was administered.	Available	None	VAS scores obtained following the dressing change showed that group II and group III have statistically lower VAS scores (p< 0.05) than group I. When VAS scores recorded at 2 h following the procedure were evaluated, group II was found to have lower VAS scores than the other groups, and the difference was statistically significant(p< 0.05).
Borland (2005).	24/24 OM and intranasal placebo (INP) on day 1 followed by oral placebo (OP) and INF on day 2 (n =14) or INF and OP on day 1 followed by INP and OM on day 2 (n=10)	INF and OP on day 1 followed by INP and OM on day 2 (n=10)	OM and intranasal placebo (INP) on day 1 followed by oral placebo (OP) and INF on day 2 (n =14) or	Available	Available	Mean pain difference scores (OM-INF) ranged from -0.500 (95% CI = -1.653 to 0.653) at baseline to -0.625 (05% CI = -1.863 to 0.613) for a retrospective rating of worst pain experienced during the dressing procedure.
Lewis (1990).	11/11 Experimental and Control Group (Not Stated)	patient received one experimental treatment consisting of bilateral acupuncture-like transcutaneous electrical nerve stimulation to six ear points	Control treatment consisting of a placebo pill	Available	None	A two-factor repeated measures ANOVA indicated significant effects of measurement time ($p < 0.001$) and treatment by time ($p = 0.002$). Post hoc analysis revealed significant differences ($p < 0.05$) between experimental and control conditions at all times after treatment but not at pretreatment baseline.
Miller (1992).	17/17 Treatment and control group not stated	The treatment group viewed video programs that were composed of scenic beauty accompanied by music.	Standard group	Available	None	A nested general linear model using the 'F' test in multiple regression analysis was adjusted for age, percent partial-thickness burn, and choice of topical agent demonstrated that the use of videos during the dressing changes significantly reduced pain and anxiety: present pain intensity ($F = 8.69$; $p = 0.01$), pain rating index ($F = 5.57$; $p = 0.03$), anxiety ($F = 9.10$; $p = 0.01$).

VerLee (2012).	40/40 23 children at VR group, 17 children at standard care group	Children in the VR group used a headset containing the VR program during initial dressing change.	The standard care group received traditional forms of distraction (ex: TV, talking)	Available	None	Results suggest participants in the control group reported higher post-procedure pain ratings compared to the VR group, although this was not significant (t = 1.17, p = .25). Age of participant was correlated with pain ratings (r = .36, p <.05).
Tosun (2008)	32 Group PK n=17, group=15	Group PK (n = 17) received 1 mgÆkg)1 ketamine (1 mlÆ10 kg)1) and 1.2 mgÆkg)1 propofol	Group PF (n = 15) received 1 lgÆkg)1 fentanyl (1 mlÆ10 kg)1) and 1.2 mgÆkg)1 propofol for induction	None	Available	No primary outcomes stated in the abstract. However, both propofol-ketamine and propofol-fentanyl combinations provided effective sedation and analgesia during dressing changes in pediatric burn patients

DISCUSSION

Most of the comparisons addressed by the 17 included trials are relevant to current practice, at least in some parts of the world. Small test quantities of 50 or less patients in any intervention group, insufficient methodology and lacks in the evaluation of outcome impede the capacity of individual tests to address their own questions, let alone the purposes of this review. Trial methodology was incompletely described in most trials. However, the trialists need to be communicated and involved. Even though, the probability of systematic bias appearing in flawed evidence cannot be commanded out. The notable is the failure to assure or validate the concealment of allocation in every but three trials. Different issue is that of confounding, where factors other than the interventions under examination impact the test results.

Samples of confounders are disproportions in baseline characteristics, such as TBSA category of participants, and variations in care programmes including kind of standard analgesia given, their doses, how they are delivered, by the health professionals. The methodological quality plot used in our study did not score the comprehensiveness of outcome assessment in single trials; rather we looked at the likely for ascertainment bias due to the quality of measurement of the actual outcomes recorded and shortage of blinding of outcome assessor. However, the included trials did not provide a full, or sufficient, 'picture' of the relative effects of the interventions under investigation. This insufficiency was typically correlated with a short length of follow-up. While it is intriguing to concentrate on short-term outcomes, such as pain relievers throughout dressing changes, for assessing analgesic interventions, it is necessary to assemble long-term outcomes given that poor analgesia could have long-term outcomes.

Our principal focus is on examining clinical outcomes. However, information on resource use and costs that would enable a cost-effectiveness analysis is also beneficial, and especially useful when there is no clear evidence for significant differences in the effectiveness of interventions.

Finally, the analysis and administration of trial findings is restricted where, as is often the case with the trials involved in this report, there are short details of the proposed and actual test population and interventions.

Overall completeness and applicability of evidence

There is a significant lack of randomized trials in this area, especially evaluating the methods and agents regularly adopted in current clinical practice for the provision of pain relief throughout dressing change in burns patient.

This review is limited to the inclusion of only 17 small trials. The variety of analgesic agents/ methods used in the 17 included trials suggested that no single data could be joined in the meta-analysis, this the main reason the interpretation was hard. The different methods of measuring pain relief and the safety of interventions also made comparisons between trials difficult. In addition, diverse in age group were determined to be the most burdening factor in combining meta-analysis for this review.

Potential biases in the review process

The evidence for this report is derived from trials identified through a detailed search process. It is possible (but unlikely) those additional trials assessing analgesia for dressing change in burn patients have been issued but not identified. It is also probable that different studies have been conducted but not published. Should such studies

Agreements and conflicts with other studies or reviews

This report authenticates that there is currently inadequate evidence to recommend a specific analgesic agent or method as utmost efficient and safe for affording pain relief throughout dressing changes in burn patients. There have not been another systematic reviews on the use of analgesia for this implication.

CONCLUSIONS

There was inadequate quality evidence from comparisons tested in randomised trials to confirm the dependent effectiveness of various techniques of analgesia or of various techniques of individual methods, or to assess the administration of different drug adjuncts for providing analgesia during dressing changes in burn patients.

Implications for practice

While this review suggests possible benefits of attention-distraction techniques for an analgesia method, the superiority of each method is still uncertain. Given that there are too many mode of analgesia used within studies and the two sub-age group presented in this report also makes it harder to conclude which better analgesia method for better age group. It is essential to remark that the conclusions are based on 17 small, low-quality randomised trials.

Until further evidence from extensive, well-designed randomised trials becomes accessible, prevailing evidence from this review is insufficient to make comprehensive suggestions, or to choose which is the best option in the management for burns patients undergoing dressing changes in regards to the most efficient and safe analgesic agent/method to use.

Implications for research

In the light of the limited current evidence, further randomised controlled trials are required to determine the most efficient and safe agent and method for providing analgesia during dressing change in burns. Such studies must be adequately powered, and well designed to allow principal differences to be detected.

Future research should consider relevant safety outcomes, and should in particular focus on the agents and methods that are regularly used in current clinical practice. In addition to judging effectiveness and safety, such trials may address specific concerns including timing and dosage.

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