

Is cocaine needed in topical anaesthesia?

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Are non-cocaine containing topical anaesthetics as effective as cocaine containing topical anaesthetics in the management of lacerations? This review examines the current medical literature for effective agents that do not contain cocaine.

"Pain hurts".

The standard local anaesthesia technique used in UK practice before suturing is infiltration with 1% plain lignocaine (lidocaine).¹ This method is painful but does give good anaesthesia.²⁻⁴

Topical anaesthesia (TA) has been used in the United States for two decades.⁵ The rationale behind its use was to avoid the needle prick and pain of infiltration while producing effective anaesthesia. There is also no tissue distortion with topical anaesthesia unlike subcutaneous infiltration.

The original mixture used for topical anaesthesia was TAC—0.5% tetracaine, 0.05% adrenaline (epinephrine), and 11.8% cocaine⁷ although a number of departments use different concentrations of the three drugs.⁶⁻⁹

Application of TAC is less painful than infiltration of lidocaine.^{5 9-11} In wounds of the face and scalp the anaesthetic effectiveness of TAC is equivalent to 1% lignocaine.^{5 12-15} Some studies have demonstrated equivalence with extremity wounds^{5 7 10} but other publications report that TAC is inferior to 1% lidocaine in this situation.^{13 14} Wound complication rates are similar for both drugs.^{6 7-11 15 16} Most comparisons with lidocaine have been made only in children but some have included adults.⁵

There are a number of drawbacks associated with the use of TAC. TAC is expensive^{6 9 15 16} and as a controlled drug, it is inconvenient to store and use. The most significant problems with TAC, however, are the rare but catastrophic complications of its use. There are several reports of seizures associated with its use in children.¹⁷⁻²⁰ There is also a case report of the death of a child that has been attributed to the rapid absorption of cocaine via mucous membranes.²¹ Cocaine has been detected in the plasma of children treated with TAC.²² The majority of departments that use TAC avoid its use on mucous membranes but not all.¹⁹

Reducing the concentration of cocaine in TAC has been proposed to improve its safety profile⁶⁻⁹ but the safety issues remain, as do the cost and inconvenience factors. It is logical, therefore, to seek an agent that does not contain cocaine but is as effective in topical anaesthesia as TAC. The purpose of this review is to examine the literature for evidence of such an agent.

METHODS

The Medline database (1966–2000) was searched using the Ovid search engine. MeSH headings of "Anesthesia, local", "Anesthetics, local" and "Administration, topical" were used. Searches were also made using "topical anesthesia" and "topical anaesthesia" as keywords. The results generated were combined with those from the MeSH headings "Wounds, nonpenetrating" and "Wounds, penetrating" and the keywords "laceration" and "incision". The combined articles were limited to "English language" and "randomised controlled trial".

Another electronic search was made of Medline using the Internet Grateful Med search engine. The query terms were "topical anesthesia or topical anaesthesia" with limitation to "Human" and "Randomised Controlled Trial". The databases EMBASE, COCHRANE LIBRARY and BEST EVIDENCE CD were also searched in a similar manner. The internet was searched for "topical anesthesia" and "topical anaesthesia" using the Dogpile site.

All of the references of the chosen papers were examined to identify other relevant papers. The journals *Annals of Emergency Medicine* and *Journal of Accident and Emergency Medicine* were hand searched from 1994–2000.

RESULTS

Tables 1, 2, 3, and 4 show the results of the literature search.

Sixteen relevant papers have been identified by the search strategy. Five studies^{2 16 23 24 29} compared an agent comprising lignocaine, tetracaine, and vasoconstrictor with either TAC or 1% lidocaine infiltration. In all but one study²⁹ the agent performed at least as well as the control. Application of the topical agent is less painful than infiltration.² Tetralidophen^{29 34} performed less well. Lignocaine with epinephrine works well.¹⁵

Tetracaine alone is a poor topical agent²⁸ as it is with adrenaline²⁷ or 2.5% phenylephrine^{29 34} but with 5% phenylephrine³⁴ it is similar to TAC.

Prilophen has been used in three studies by the same investigators. In two studies, it was less effective than lidocaine infiltration and TAC^{32 34} but in one study the results were similar.³³ TAC is superior to prilonor.⁷ EMLA cream works better than TAC on extremity wounds in children³¹ but is not licensed for use on broken skin in the UK.

Mepivonor,^{7 8} etidonor,⁷ and bupivaphen³³ alleviate less pain than TAC or lidocaine infiltration.

Abbreviations: TA, topical anaesthesia; TAC, tetracaine, adrenaline, cocaine

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Table 1 Agents using strong lignocaine (lidocaine)

Group	Agents	Population	Score	Results
Ernst <i>et al</i> ³	3 ml of TAC v 3 ml of LAT (4% lidocaine, 1/2000 adrenaline, 1% tetracaine) Applied for up to 30 minutes.	Adults. Wound <7 cm on face or scalp. 47 TAC 48 LAT	VAS of suturing by patient + physician. Number of painful sutures by physician.	LAT caused fewer painful sutures $p=0.036$ Median VAS for TAC + LAT by both groups = 0
Ernst <i>et al</i> ²	1% buffered lidocaine with epinephrine v 3 ml LAT gel (4% lidocaine, 1/2000 adrenaline, 0.5% tetracaine). Gel applied for up to 20 minutes.	5 years and older. Wound 1.5–10 cm and linear. 33 Lido 33 LAT gel	VAS of application and suturing by patient + physician Number of painful sutures by physician.	VAS for application strongly favours LAT $p=0.001$ 13% sutures caused pain with LAT, 6% with lidocaine $P=0.28$ No difference in VAS for suturing
Schilling <i>et al</i> ⁶	3 ml of TAC v 3 ml of LET (4% lidocaine, 1/1000 epinephrine, 0.5% tetracaine). Applied for 15 minutes.	Children. Wound covered by 2x2 cm gauze on face or scalp. 73 TAC 78 LET	Adequacy of anaesthesia. Duration of anaesthesia.	Equivalent adequacy of anaesthesia (TAC 79.5%, LET 74.4% $p=0.45$). Equivalent numbers with complete duration of anaesthesia (TAC 75.9%, LET 82.4% $p=0.18$).
Ernst <i>et al</i> ⁴	3 ml TAC gel v 3 ml LAT gel - (4% lidocaine, 1/2000 adrenaline, 0.5% tetracaine). Applied for up to 30 minutes	Children 5–17 years Wound <7 cm on face or scalp. 47 TAC 48 LAT	VAS of suturing by patient or parent and physician. Number of painful sutures by parents or patients.	No difference in number of painful sutures (TAC 13%, LAT 18% $p=0.51$). No difference between LAT and TAC ranked sum ratings for physicians ($p=0.80$) or patients ($p=0.71$).
Resch <i>et al</i> ²⁵	3 ml LET (4% lidocaine, 1/1000 epinephrine, 0.5% tetracaine) solution v 3 ml LET gel. Applied for 20 minutes.	Children. Wound covered by 5x5 cm gauze on face or scalp. 91 Gel 103 Solution	Adequacy to needle probe Efficacy of anaesthesia	No difference in adequacy between solution and gel (95% CI –8% to 13%) Similar numbers with complete effectiveness (95% CI –3% to 22%)
Blackburn <i>et al</i> ¹⁵	10 ml TAC v 10 ml TLE (5% lidocaine, 1/2000 epinephrine) Applied for 20 minutes.	2 years and older. Wound of face or scalp. 18 TAC 17 TLE	Facial effective scale (9 points) by physician or older child.	Similar results TAC mean score 2.66, TLE 3.29 ($p=0.33$). Both scores within "complete anaesthesia" range

Adler *et al*⁶ demonstrated that LET (4% lidocaine, 1/1000 epinephrine, 0.5% tetracaine) worked significantly better than sterile water.

Table 2 Non-cocaine TAC derivatives

Group	Agents	Population	Score	Results
Schaffer <i>et al</i> ²⁷	2 ml TAC v 2 ml TA (No cocaine). Applied for 10 minutes	Children 10 years and younger. Wound above the neck. 56 TAC 51 TA	Physician effectiveness.	More in the TA group required extra infiltration 27.5% TA v 8.9% of TAC ($p=0.01$). 82% TAC had completely effective anaesthesia, 65% TA ($p=0.13$)
White <i>et al</i> ²⁸	5 ml 0.5% tetracaine v 5 ml TAC Applied for up to 10 minutes.	Over 18 years Wound <5 cm 36 TAC 32 Tetracaine	VAS of procedure. Not scored if infiltration used.	36% TAC required extra infiltration, 59% tetracaine. TAC group had less pain, Mean VAS TAC 1, tetracaine 3.7, ($p<0.05$).

Bupivacort⁷ is as effective as TAC and lidocaine infiltration. The wound infection rate was low in all studies.

DISCUSSION

Principal results

Fourteen different non-cocaine containing topical anaesthetics have been studied. Of these, agents with 4% or 5% lidocaine,^{2 15 16} bupivacort,⁷ and tetracaine³⁴ have similar effectiveness to TAC or 1% lidocaine infiltration.

There have been no significant complications reported in any study.

Strengths and weaknesses of the search

The question chosen was one that was clinically relevant to A&E practice in the UK and should allow a number of papers to be identified.

Multiple electronic databases were used using a variety of search engines. Keywords were used in addition to MeSH

headings in an attempt to improve sensitivity. Alternative spellings of certain keywords further increase the sensitivity. By using the references of the articles chosen to generate further papers and hand searching the two journals thought most likely to be relevant, more articles were found.

Despite this strategy, it is unlikely that all the relevant papers will have been chosen. There may be other journals that may produce a relevant article but that may be unavailable for hand searching. It is impracticable to attempt to hand search every title that possibly has a useful paper and electronic searches, though extremely useful, do not identify every paper.

Strengths and weaknesses of the papers

The studies were all prospective in design and almost all used a "gold standard" control of either TAC or 1% lidocaine infiltration. One paper,³⁰ however, was a case series, and another²⁶ used sterile water as the control.

Table 3 Other agents

Group	Agents	Population	Score	Results
Smith <i>et al</i> ⁹	3 ml tetrilodophen (TLP) (1% lidocaine, 2.5% phenylephrine, 1% tetracaine) v 1% lidocaine infiltration. Solution applied for 20 minutes.	Children over 1 year Wound <5 cm on or near mucous membrane. 45 Lido 45 TLP	VAS of procedure by suturer, observer, video observer, patient and parent. Likert scale by all except patient	VAS scores of suturers, observers and video observers higher with TLP than lido. Trend favouring lido from scores by patient and parent. Likert scores of suturers, observers, video observers and parents favour lido. 16% required infiltration.
Wase <i>et al</i> ⁰	Up to 5 ml of XAP (1% lidocaine, 1/4000 norepinephrine, 0.5% tetracaine). Applied for up to 20 minutes.	'Minor lacerations' 192 XAP. No controls	Infiltration rate	
Zempsy <i>et al</i> ¹	3 ml TAC v 5 g EMLA cream (2.5% lidocaine, 2.5% prilocaine). TAC applied for up to 30 minutes, EMLA for up to 60 minutes.	Children 5–18 years. Extremity lacerations <5 cm. 16 TAC 16 EMLA	VAS of procedure by suturer, patient, parent.	55% of TAC wounds required infiltration, 15% of EMLA (p=0.03) No significant difference of VAS scores by any group.
Smith <i>et al</i> ²	3 ml prilophen (3.56% prilocaine, 1/1000 phenylephrine) v 1% lidocaine infiltration. Solution applied for 20 minutes.	Children over 1 year. Wound <5 cm on or near mucous membrane. 20 Lido 20 Prilophen	VAS for suturing by suturer, observer, video observer, parent and patients >5 years.	VAS scores lower with lidocaine than prilophen by suturers (p=0.003) and video observer (p=0.02). No difference with observer, patient or parent. No significant difference in the additional infiltration rate, 1 lido, 3 prilophen (p=0.60).
Smith <i>et al</i> ⁸	3 ml mepivonor (2% mepivacaine, 1/100000 norepinephrine) v 3 ml TAC v 1% lidocaine infiltration. Solution applied for 20 minutes.	Children 2 years and older. Wound <5 cm on face or scalp. 23 Lido 24 TAC 24 Mepivonor	VAS for suturing by suturer, observer, video observer, parent and patient. Likert score for suturing by parent and suturers.	VAS scores lower with lidocaine or TAC than with mepivonor by suturers and observers No difference with video observer, patient or parent. Likert scores by parents were higher with mepivonor than with lidocaine or TAC (p=0.02)

Likert scale is a 7 point pain scale.

All papers had clearly defined inclusion and exclusion criteria but many recruited convenience samples, which could introduce selection bias. Random number generators were generally used but some papers may have suffered bias because of the "arbitrarily assigned vials" and the use of the patient's unit number for randomisation. A number of papers introduced blocking to maintain similar numbers in each group as the trial progressed. Bias could have resulted if the number of patients in each block was known. The randomisation process resulted in similar groups in the vast majority of papers.

Double blinding was the rule in those studies whose design allowed it. In those that compared infiltration with topical anaesthesia, a blinded video observer was used. Well defined outcome measures were used to assess the results of the papers. Not all papers used previously validated scales however. Several papers excluded patients after randomisation without further analysis.

Topical anaesthesia was introduced in an attempt to avoid the pain associated with lidocaine infiltration. It is surprising, therefore, that of the five studies comparing topical agents with infiltration^{2, 7, 8, 29, 32} only one compares the pain of application separately from the pain of suturing.²

The serious complications with the use of TAC have been associated with its use on mucous membranes. Only two studies^{29, 32} allowed wounds on or near mucous membranes to be included. As a result of this (understandable) caution, there are a paucity of data relating to the safety of managing wounds in these areas where TAC is contraindicated.

Implication for practice in the UK

Few A&E departments in the UK use topical anaesthesia before wound suture.¹ The reasons given include "topical anaesthesia ineffective" and "no experience". There is little evidence in the literature for the first conclusion.

Almost all the trials included here have been performed in the United States and the unfamiliarity with topical anaesthesia in the UK may both contribute to and result from this. The reasons given, together with the case reports of serious harm with the use of TAC and the inconvenience of its use, have resulted in the almost universal use of lidocaine infiltration in the UK. It is unlikely that further USA based trials of topical anaesthesia will affect the management of patients in the UK as 20 years of USA research have had little effect on UK practice.

Topical anaesthesia should be used in the UK for the suturing of lacerations in children. The reluctance to use this technique in the UK may be to some extent reduced by the use of non-cocaine containing agents. The most effective agents available are ones that contain strong lidocaine^{2, 15, 16, 23, 24–26} and it is one these that should be introduced into UK practice. There has been recent correspondence in this journal of the use of such an agent in a UK A&E department.³⁵ Other promising agents include bupivonor⁷ or tetrphen.³⁴ All of these agents are not commercially available but may be manufactured and used as part of a trial. This trial is needed to identify that a genuine alternative to lidocaine infiltration exists and demonstrate its suitability in UK A&E practice.

FUTURE RESEARCH

Two areas have been identified. Firstly, as mentioned above, a UK based trial of a non-cocaine containing agent compared with infiltration. This should be a prospective randomised controlled trial of one of the above mentioned agents compared with 1% lidocaine. The study should have well defined inclusion and exclusion criteria, blinded randomisation, a clear treatment policy, and blinded outcome variables. If the agent is shown to have similar anaesthetic properties to 1% lidocaine infiltration and is less painful on

Table 4 Multiple agents

Group	Agents	Population	Score	Results
Smith <i>et al</i> ³	3 ml prilophen (3.56% prilocaine, 1/1000 phenylephrine) v 3 ml bupivaphen (0.67% bupivacaine, 1/1000 phenylephrine) v 3 ml TAC. Solution applied for 20 minutes.	Children 1 year and older. Wound <5 cm. 60 TAC 60 Prilophen 60 Bupivaphen	VAS for suturing by suturer, observer, parent and patients >5 years.	No significant difference in VAS scores between TAC and prilophen by any group. Bupivaphen VAS scores higher than TAC and prilophen by suturers, observers and parents.
Smith <i>et al</i> ⁴	3 ml of prilophen (3.56% prilocaine, 0.99% phenylephrine) v 3 ml of tetraphen (1% tetracaine, 5% phenylephrine) v 3 ml of tetralidophen (1% lidocaine, 2.5% phenylephrine, 1% tetracaine) v 3 ml of TAC. Solution applied for 20 minutes.	Children 1 year and older. Wound <5 cm. 60 TAC 60 Prilophen 60 Tetraphen 60 Tetralidophen	VAS for suturing by suturer, observer, parent and patients >5 years. Likert score for suturing by parent, observers and suturers. Anaesthetic effectiveness by suturers.	No significant difference in VAS or Likert scores for any group between tetraphen and TAC. TAC Likert scores lower than prilophen and tetralidophen by suturers. VAS scores with prilophen greater than with TAC by suturers. No difference in anaesthetic effectiveness between anaesthetics. No significant differences between anaesthetics when wounds of the face and scalp analysed separately.
Smith <i>et al</i> ⁵	3 ml Bupivanor (0.48% bupivacaine, 1/26000 norepinephrine) v 3 ml etidonor (0.95% etidocaine, 1/26000 norepinephrine) v 3 ml mepivanor (1.9% mepivacaine, 1/26000 norepinephrine) v 3 ml prilonor (3.81% prilocaine, 1/26000 norepinephrine) v 3 ml TAC v 1% lidocaine infiltration. Solution applied for 20 minutes.	Children 2 years and older. Wound <5 cm. 60 Lido 60 TAC 30 Bupivanor 30 Etidonor 30 Mepivanor 30 Prilonor	VAS for suturing by suturer, observer and patients >5 years. Likert score for suturing by parent and suturers. RICDRS distress behaviour for suturing by suturers. Anaesthetic effectiveness by suturers.	No difference with any scale by any group between TAC and lidocaine. No difference with any scale by any group between bupivanor and TAC or lidocaine except anaesthetic effectiveness by suturers. Complex matrix of comparisons between agents using the 4 scores by the 4 groups. All other agents had some statistically significant poorer results than TAC or lidocaine.

RICDRS = restrained infant and child distress rating scale.

application, there would be a compelling reason for its use in routine UK practice. If this does occur, surveillance of safety is essential as even with TAC use, complications are rare and are unlikely to be identified in a single trial.

Secondly, wounds near mucous membranes may need suture. The concern with absorption of anaesthetic is attributable to the nature of the tissue, not the wound. Topical anaesthesia is routinely and safely used on intact mucous membranes in ophthalmology, urology, and dentistry.³⁶ It is logical to suspect that agents that have similar efficacies to TAC and do not contain cocaine would be safe and effective when used on mucous membrane wounds and therefore may be studied in larger trials.

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