CLINICAL TOPIC REVIEW

Is cocaine needed in topical anaesthesia?

S Bush

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). This method is painful but does give good anaesthesia. Topical anaesthesia (TA) has been used in the United States for two decades. 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% cocaine although a number of departments use different concentrations of the three drugs.

Application of TAC is less painful than infiltration of lidocaine in wounds of the face and scalp the anaesthetic effectiveness of TAC is equivalent to 1% lignocaine. Some studies have demonstrated equivalence with extremity wounds but other publications report that TAC is inferior to 1% lidocaine in this situation. Wound complication rates are similar for both drugs. Most comparisons with lidocaine have been made only in children but some have included adults.

There are a number of drawbacks associated with the use of TAC. TAC is expensive 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. 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. Cocaine has been detected in the plasma of children treated with TAC. The majority of departments that use TAC avoid its use on mucous membranes but not all.

Reducing the concentration of cocaine in TAC has been proposed to improve its safety profile 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 anaesthesia 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 anaesthesia” 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 compared an agent comprising lignocaine, tetracaine, and vasoconstrictor with either TAC or 1% lidocaine infiltration. In all but one study the agent performed at least as well as the control. Application of the topical agent is less painful than infiltration. Tetralidophen performed less well. Lignocaine with epinephrine works well.

Tetracaine alone is a poor topical agent as it is with adrenaline or 2.5% phenylephrine but with 5% phenylephrine 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 but in one study the results were similar. TAC is superior to prilophen. EMLA cream works better than TAC on extremity wounds in children but is not licensed for use on broken skin in the UK.

Mepivacaine, etidocaine, and bupivacaine 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)

<table>
<thead>
<tr>
<th>Group</th>
<th>Agents Population</th>
<th>Score</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ernst et al⁵⁷</td>
<td>3 ml of TAC v 3 ml of LAT (4% lidocaine, 1/2000 adrenaline, 1% tetracaine) Applied for up to 30 minutes.</td>
<td>Adults. Wound &lt;7 cm on face or scalp.</td>
<td>VAS of suturing by patient + physician.</td>
</tr>
<tr>
<td>Ernst et al⁵⁸</td>
<td>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.</td>
<td>5 years and older. Wound 1.5–10 cm and linear.</td>
<td>VAS of application and suturing by patient + physician.</td>
</tr>
<tr>
<td>Schilling et al⁶⁰</td>
<td>3 ml of TAC v 3 ml of LET (4% lidocaine, 1/1000 epinephrine, 0.5% tetracaine). Applied for 15 minutes.</td>
<td>Children. Wound covered by 2×2 cm gauze on face or scalp.</td>
<td>Adequacy of anaesthesia. Duration of anaesthesia.</td>
</tr>
<tr>
<td>Ernst et al⁶¹</td>
<td>3 ml TAC gel v 3 ml LAT gel (4% lidocaine, 1/2000 adrenaline, 0.5% tetracaine). Applied for up to 30 minutes.</td>
<td>Children 5–17 years. Wound &lt;7 cm on face or scalp.</td>
<td>VAS of suturing by patient or parent and physician.</td>
</tr>
<tr>
<td>Resch et al⁶²</td>
<td>3 ml LET (4% lidocaine, 1/1000 epinephrine, 0.5% tetracaine solution v 3 ml LET gel). Applied for 20 minutes.</td>
<td>Children. Wound covered by 5×5 cm gauze on face or scalp.</td>
<td>Adequacy to needle probe Efficacy of anaesthesia</td>
</tr>
<tr>
<td>Blackburn et al⁶³</td>
<td>10 ml TAC v 10 ml TLE (5% lidocaine, 1/2000 epinephrine). Applied for 20 minutes.</td>
<td>Adults. Wound of face or scalp.</td>
<td>Facial effective scale (9 points)</td>
</tr>
</tbody>
</table>

Adler et al⁶⁴ demonstrated that LET (4% lidocaine, 1/1000 epinephrine, 0.5% tetracaine) worked significantly better than sterile water.

Table 2  Non-cocaine TAC derivatives

<table>
<thead>
<tr>
<th>Group</th>
<th>Agents Population</th>
<th>Score</th>
<th>Results</th>
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<tbody>
<tr>
<td>Schaffer et al⁶⁷</td>
<td>2 ml TAC v 2 ml TA (No cocaine). Applied for 10 minutes.</td>
<td>Children 10 years and younger. Wound above the neck.</td>
<td>Physician effectiveness.</td>
</tr>
<tr>
<td>White et al⁶⁷</td>
<td>5 ml 0.5% tetracaine v 5 ml TAC. Applied for up to 10 minutes.</td>
<td>Over 18 years. Wound &lt;5 cm</td>
<td>VAS of procedure. Not scored if infiltration used.</td>
</tr>
</tbody>
</table>

Bupivacaine 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,⁶⁵ is bupivacaine,⁶ and tetraphen³⁴ 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 VAS or 1% lidocaine infiltration. One paper,⁶⁸ however, was a case series, and another⁶⁹ used sterile water as the control.
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.

We define 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 inclusion and exclusion criteria, blinded randomisation and used as part of a trial. This trial is needed to identify a genuine alternative to lidocaine infiltration 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 3 Other agents

<table>
<thead>
<tr>
<th>Group</th>
<th>Agents</th>
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<th>Score</th>
<th>Results</th>
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<tbody>
<tr>
<td>Smith et al</td>
<td>3 ml tetradilophen (TDP) (1% lidocaine, 2.5% phenylephrine, 1% tetracaine) v 1% lidocaine infiltration. Solution applied for 20 minutes.</td>
<td>Children over 1 year Wound &lt;3 cm on or near mucous membrane. 45 Lido 45 TDP</td>
<td>VAS of procedure by suturer, observer, video observer, parent and patient Likert scale by all except patient</td>
<td>VAS scores of suturers, observers and video observers higher with TDP than lido. Likert scores of suturers, observers, video observers and parents favour lido.</td>
</tr>
<tr>
<td>Wase et al</td>
<td>Up to 5 ml of XAP (1% lidocaine, 1/4000 norepinephrine, 0.5% tetracaine). Applied for up to 20 minutes.</td>
<td>‘Minor lacerations’ 192 XAP. No controls</td>
<td>Infiltration rate</td>
<td>1% required infiltration.</td>
</tr>
<tr>
<td>Zempsky et al</td>
<td>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.</td>
<td>Children 5–18 years. Extremity lacerations &lt;5 cm. 16 TAC 16 EMLA</td>
<td>VAS of procedure by suturer, patient, parent.</td>
<td>55% of TAC wounds required infiltration, 15% of EMLA (p=0.03). No significant difference of VAS scores by any group.</td>
</tr>
<tr>
<td>Smith et al</td>
<td>3 ml prilocain (3.56% prilocain, 1/1000 phenylephrine) v 1% lidocaine infiltration. Solution applied for 20 minutes.</td>
<td>Children over 1 year Wound &lt;3 cm on or near mucous membrane. 20 Lido 20 Prilocain</td>
<td>VAS for suturing by suturer, observer, video observer, patient and parent</td>
<td>VAS scores lower with lidocaine than prilocain 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% lidocaine, 3 prilocain (p=0.60).</td>
</tr>
<tr>
<td>Smith et al</td>
<td>3 ml mepivanor (2% mepivacaine, 1/100000 norepinephrine) v 3 ml TAC v 1% lidocaine infiltration. Solution applied for 20 minutes.</td>
<td>Children 2 years and older. Wound &lt;3 cm on face or scalp. 24 Mepivacain 24 TAC 24 Lido</td>
<td>VAS for suturing by suturer, observer, video observer, patient and parent Likert score for suturing by parent and suturers.</td>
<td>VAS scores lower with lidocaine or TAC than with mepivanor by suturers and observers. No difference with video observer, patient or parent. Likert scores by parents were higher with mepivanor than with lidocaine or TAC (p=0.02).</td>
</tr>
</tbody>
</table>

Likert scale is a 7 point pain 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. 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.

### Table 4: Multiple agents

<table>
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<th>Score</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td>Smith et al</td>
<td>3 ml prilophen (5.36% prilocaine, 1/1000 phenylephrine) v 3 ml bupivacaine (0.67% bupivacaine, 1/1000 phenylephrine) v 3 ml TAC.</td>
<td>Children 1 year and older. Wound &lt;5 cm.</td>
<td>VAS for suturing by suture, observer, parent and patients &gt;5 years.</td>
<td>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 patients.</td>
</tr>
<tr>
<td>Smith et al</td>
<td>3 ml prilophen (5.36% prilocaine, 0.99% phenylephrine) v 3 ml tetralidophen (1% tetracaine, 5% phenylephrine) v 3 ml tetralidophen (1% lidocaine, 2.5% phenylephrine, 1% tetracaine) v 3 ml of TAC.</td>
<td>Children 1 year and older. Wound &lt;5 cm.</td>
<td>VAS for suturing by suture, observer, parent and patients &gt;5 years.</td>
<td>No significant difference in VAS or Likert scores for any group between tetralidophen and TAC. TAC Likert scores lower than prilophen and tetralidophen by suturers. VAS scores with prilophen greater than with TAC by suturers.</td>
</tr>
<tr>
<td>Smith et al</td>
<td>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.</td>
<td>Children 2 years and older. Wound &lt;5 cm.</td>
<td>VAS for suturing by suture, observer and patients &gt;5 years. Likert score for suturing by parent and suture. RICDRS distress behaviour for suturing by suture. Anaesthetic effectiveness by suture.</td>
<td>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 suturer. 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.</td>
</tr>
</tbody>
</table>

RICDRS = restrained infant and child distress rating scale.

## REFERENCES