Comparison of amethocaine gel versus 1% lidocaine infiltration on wound healing. A pilot study in animals

Rodrick K Lim[1], Bertha Garcia[2], Michael J Rieder[1,3,4], Priya Iyer[3], Jamie A Seabrook[1]

[1] *Department of Paediatrics, Children's Health Research Institute, Children's Hospital of Western Ontario, University of Western Ontario, London, Canada*

[2] *Department of Pathology, University of Western Ontario, London, Canada*

[3] *Department of Medicine, University of Western Ontario, London, Canada*

[4] *Department of Physiology and Pharmacology, Children's Health Research Institute, Children's Hospital of Western Ontario, University of Western Ontario, London, Canada*

Corresponding author

Dr Michael Rieder, Children's Hospital of Western Ontario, 800 Commissioners Road East, London, Ontario, N6H 5B8, Canada. Email: mrieder@uwo.ca

***Aim*: The purpose of this pilot study was to determine whether subcutaneous lidocaine and topical amethocaine were similar in their effects on wound healing.**

***Methods*: Ten rats were used in this study with incisions made to right and left shoulder and right and left flank. The incisions were randomly assigned to either topical amethocaine gel for a period of 30 minutes or subcutaneous lidocaine injected 5 minutes prior to suturing. The wounds were assessed on days 1, 2, 4, 7, 10 and 14 for evidence of dehiscence, infection defined as purulent discharge, erythema, induration, necrosis or ulceration, and widened scar formation. On day 14 the rats were euthanised and biopsies of the wounds were taken. The biopsies were examined histologically for degree of inflammation and cellular infiltrates.**

***Results*: The results demonstrate that there was no significant difference in wound healing with the use of topical amethocaine when compared to subcutaneous lidocaine both macroscopically and histologically.**

***Conclusions:* Topical amethocaine gel is an effective alternative to subcutaneous lidocaine in laceration repairs as demonstrated in this small animal study. Thus it has the potential to be an alternative form of anaesthetic in Paediatric Emergency Departments for laceration repair.**

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Introduction

Children presenting with lacerations comprise a significant proportion of all visits to the Paediatric Emergency Department (ED), with an estimated annual rate of 50 to 60 per 1000 children in the United States[1]. Lacerations account for 30–40% of all injuries for which care is sought in a paediatric ED[2]. Currently, the most widely used local anaesthetic in laceration repair remains lidocaine which is infiltrated into the wound edges. This is despite the development, in the past 20 years of numerous topical anaesthetics, as well as tissue adhesives. The infiltration of any local anaesthetic is a painful procedure, producing anxiety in children[3], and which can distort the edges of the wound to be repaired. Buffering the anaesthetic with bicarbonate and warming the solution to be infiltrated can lower the pain associated with the technique[4,5].

Tetracaine, adrenaline, cocaine (TAC) and lidocaine, epinephrine, tetracaine (LET) solutions are the two main topical anaesthetic compounds that have been used in wound repair. LET solution has virtually replaced TAC in most centres because of cheaper cost and diminished risk of toxicity from the cocaine component[6]. Amethocaine is a compound consisting of 4% tetracaine hydrochloride in a lecithin gel, which has been developed to reduce the pain associated with venous cannulation[7]. Its short application time and long duration of anaesthesia[8] make it interesting in laceration repair. However, the effects of amethocaine on wound healing have not been firmly established. One of the product's properties, local vasodilatation, could theoretically be detrimental to adequate healing when used as a topical anaesthetic for wound repair.

The objective of this pilot study was to compare the effects of amethocaine gel on wound healing to 1% lidocaine infiltration. It was hypothesised that the use of amethocaine gel for laceration repair does not adversely affect wound healing when compared to the use of 1% lidocaine local infiltration.

Methods

This was a prospective, single-blind, animal study conducted using our previously described protocol[9]. Ten healthy adult Wistar rats (Harland–Sprague–Dawley, Indianapolis, IN) were subjected to general anaesthesia using intramuscular ketamine (7.5 mg/100 g) and xylozine (1.5 mg/100 g). Dorsal hair was clipped from the animal, and under sterile conditions 3 cm longitudinal full thickness incisions were made on the right and left shoulders and right and left flanks. The wounds were then randomly allocated to the lidocaine group (1% lidocaine infiltration with a 25-gauge needle) or the amethocaine gel group (1.5g of topical amethocaine applied directly into the wound and covered by an occlusive sterile dressing). The lidocaine treated wounds were sutured five minutes after lidocaine infiltration while the amethocaine gel was left in the wound for 30 minutes and gently wiped away with sterile gauze prior to suturing. This period of exposure was chosen, as we estimate this to be the time required to achieve anaesthesia in the clinical setting.

All wounds were closed with 4-0 monofilament prolene, using simple interrupted sutures. Following closure, the animals were cared for in the usual manner in the medical vivarium. All sutures were removed on the seventh day under methoxyflurane inhalation anaesthesia.

The wounds were assessed clinically on days 1, 2, 4, 7, 10 and 14 by a single observer who was blinded to the local anaesthetic used. Wound healing was measured both on gross pathology and with microscopic investigation of inflammatory infiltrates. The following macroscopic pathological observations were noted: evidence of dehiscence, infection defined as purulent discharge, erythema, induration, necrosis, or ulceration, and widened scar formation. Widened scar formation was defined as a scar measuring greater than 2 mm wide. Swabs were obtained from wounds showing clinical evidence of infection and sent for bacterial culture.

On day 14, the animals were euthanised using inhaled carbon dioxide and biopsies of all wounds were obtained. These biopsies were fixed in formalin, mounted in wax, sectioned and stained with Haematoxaline-Eosin. The histological sections were then reviewed by a senior pathologist (BG) who was blinded to the anaesthetic agent used.

Inflammation

The densities of inflammation of epidermis, papillary dermis, reticular dermis, and subcutaneous fat were measured in millimetres. In the statistical analysis the degree of inflammation present was classified as negative (<1 mm), mild (1–3 mm), moderate (3.1–6 mm), or severe (>6.1 mm). The Pearson Chi-square test was used to determine whether there was any statistical difference in the gross pathology, particularly the density of inflammation in those wounds treated with injectable lidocaine versus topical amethocaine. The statistical analysis was done by a faculty member statistician (JS).

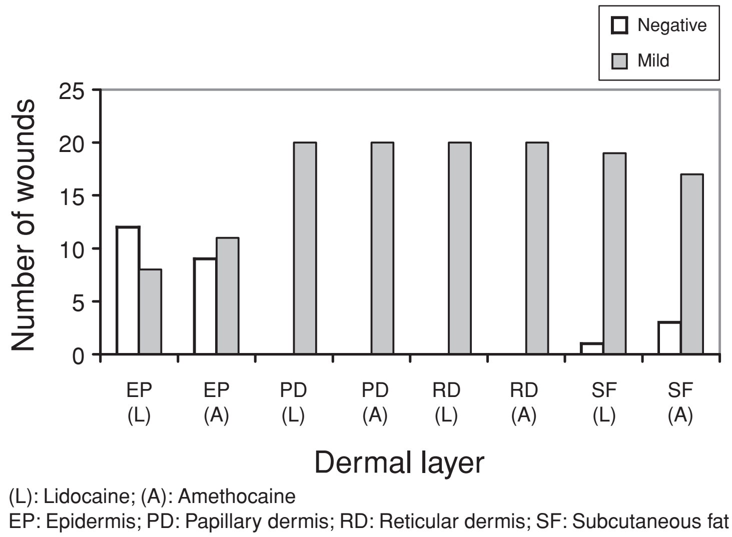

Figure 1 Degree of inflammation in the dermis layer as observed by gross pathology

Cellular infiltration

The histological samples were reviewed for evidence of cellular infiltrates in both the lidocaine and amethocaine groups. The number of cells per field of view was recorded. In the statistical analysis, the degree of cellular infiltrates was classified as negative (<1 cell), mild (1–3 cells), moderate (4–6 cells), and severe (>6 cells). Polymorphic neutrophils, monocucleated lymphocytes/macrophages, eosinophils, and giant cells were identified on microscopic analysis as evidence of inflammation. The differences in inflammatory infiltrates were compared using the Pearson Chi-square test or Fisher's exact test when necessary. A P value ≤ 0.05 was considered statistically significant.

Approval for this study was obtained from the University of Western Ontario Council on Animal Care in accordance with the Canadian Council on Animal Care guidelines.

Results

The epidermis showed no significant difference in wound healing between the lidocaine and amethocaine group (P=0.34). The papillary dermis and reticular dermis had identical values for inflammatory density, with all incisions demonstrating mild inflammation, in both the lidocaine and amethocaine group. The subcutaneous fat showed no significant difference in wound healing between the two anaesthetics (P=0.53, Figure 1).

Each wound sample was recorded as negative, mild, moderate, or severe for cellular infiltrates as identified in the field of vision. There were no neutrophils in all the incisions in both the

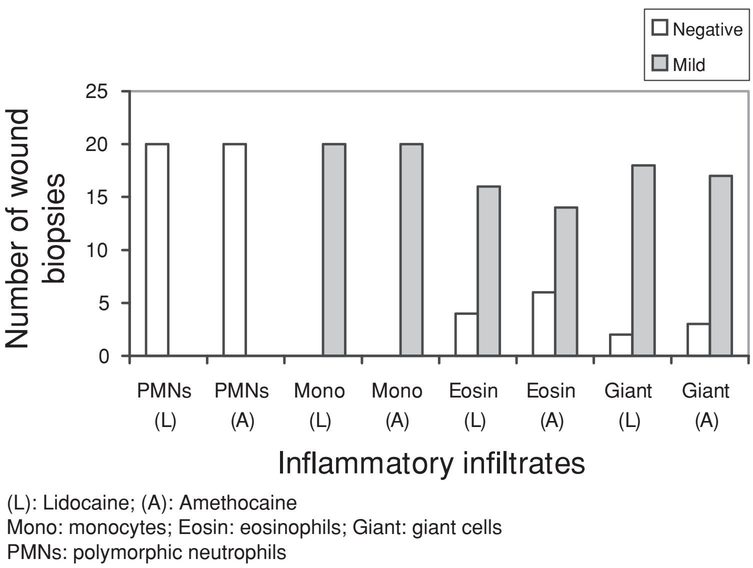

Figure 2 Degree of inflammation as assessed by histology

injectable lidocaine and topical amethocaine treated wounds. Mononucleated lymphocytes were identical in the recorded values, with all incisions classified as mild in both groups. Eosinophils were classified as both mild and negative, and no statistically significant difference was found between groups (P=0.72, Figure 2).

Discussion

This pilot study was designed to compare wound healing with topical amethocaine with the clinical gold standard of injectable lidocaine. The results of this study agree with the initial hypothesis and show no significant differences in wound healing between these two forms of local anaesthetic. Gross pathology and histological analysis demonstrated similarity in inflammation between wounds treated with lidocaine and amethocaine. As such, this animal model implies a potential use for topical amethocaine in paediatric laceration repairs. However, given that only 10 rats were observed, these negative findings should be taken with caution given that it was a pilot study.

Pain management in paediatrics has made great bounds in the last 25 years[10]. Lacerations are a common presentation to the paediatric ED. In the paediatric population, the anxiety associated with suturing wounds can have adverse effects on subsequent encounters with medical care[11]. The effects of painful medical encounters include psychological effects such as adverse pain behaviours during immunisation[11].

Paediatric laceration repairs are most commonly done with the aid of injectable lidocaine. This does provide anaesthesia, but unfortunately distorts wound edges and results in patient anxiety and pain. Needle insertion is the most frightening experience amongst hospitalised children[12]. An effective, fast-acting, topical anaesthetic may be of value in minimising the pain and anxiety associated with a laceration repair. LET is the most commonly used topical anaesthetic used for laceration repair. EMLA has also been suggested for use in laceration closure[13]. However, the greater lipophilicity of amethocaine renders its time to action shorter and its duration of action longer than lidocaine/prilocaine based EMLA[14]. Amethocaine has a relatively fast onset of action of 20–30 minutes in comparison with a 60–90 minute onset of action of EMLA[13,14]. Amethocaine is used for intact skin in many paediatric EDs, but its potential role in lacerations is unclear.

Amethocaine is indicated for a number of procedures requiring topical anaesthesia, including ophthalmological procedures, as well as skin and mucous membrane procedures; furthermore, it is also indicated for spinal anaesthesia[15]. Lacerations are not discussed as a specific indication for amethocaine, notably as the adverse effects of amethocaine typically relate to amount of systemic absorption[15]. Adverse reactions are often hypersensitivity reactions or anaphylaxis. Other possible adverse effects include depression of the central nervous system or excitation[15]. These reactions are unusual even when used on mucous membranes, which have the potential for systemic absorption. Ideally, a comparison between amethocaine alone and LET would permit evaluation of amethocaine against the most commonly used topical anaesthetic in paediatric ED laceration repairs. This study has not yet been performed to our knowledge.

This animal model demonstrates the similarity in inflammation between wounds treated with amethocaine versus the gold standard injectable lidocaine. Future research needs to include studies in patients to determine the effectiveness of this approach in reducing pain compared with existing topical anaesthetics used in laceration repair.

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