

**1. The formula analyzed in this study is unique, but the Amethocaine is far better than EMLA for pain control in an experimental model in rats.**

Anesth Analg. 2004 May;98(5):1407-12

**Rapid skin anesthesia using a new topical amethocaine formulation: a preclinical study.**

**Arevalo MI, Escribano E, Calpena A, Domenech J, Queralt J.**

Departament de Fisiologia-Divisio IV, Universitat de Barcelona, Spain.

We developed a fast-acting topical amethocaine emulsion and tested its analgesic activity against heat or mechanically induced pain in a rat paw model. The first experiment was performed in rats made hyperalgesic or allodynic after carrageenan-induced inflammation. Rats were distributed in five subgroups, each receiving topically one of the following: amethocaine microemulsion, amethocaine gel (Ametopgel), EMLA (Eutectic Mixture of Local Anesthetics) cream, amethocaine infiltration, or nothing (controls). The second experiment was conducted on healthy, selected heat- or touch-hypersensitive rats, which were distributed as in the first experiment. Paw withdrawal time from a heat and a mechanical stimulus was used as a pain index. In the first experiment, antihyperalgesic activity appeared at 4.2, 13.8, and 14 min after amethocaine microemulsion, gel, or EMLA cream, respectively. Amethocaine microemulsion was the only topical formulation with an antiallodynic effects, although less than with amethocaine infiltration. In healthy rats (second experiment), all topical formulations produced similar analgesic effects in heat-induced pain of the ipsilateral paw. Activity in the contralateral paw appeared earlier with amethocaine microemulsion, which was also the only one that increased touch-induced withdrawal time in the ipsi- and contralateral paws. Therefore, the microemulsion could be valuable for improving amethocaine skin penetration and thus bringing rapid pain relief. **IMPLICATIONS: Topical anesthetics are used in several painful clinical procedures, but they tend to have a slow onset time. A new amethocaine microemulsion with a faster onset of analgesia than commercial formulations was developed and its activity tested in pain states induced by heat or mechanical stimulus in inflamed and healthy rat paws.**

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## **2. Association study of lidocaine 7% and amethocaine 7% vs placebo. Useful to show that high associations have been used without problems.**

Dermatol Surg. 2003 Oct;29(10):1012-8.

**Two randomized, double-blind, placebo-controlled studies evaluating the S-Caine Peel for induction of local anesthesia before long-pulsed Nd:YAG laser therapy for leg veins.**

**Chen JZ, Alexiades-Armenakas MR, Bernstein LJ, Jacobson LG, Friedman PM, Geronemus RG.**

Laser and Skin Surgery Center of New York, New York 10016, USA.

**BACKGROUND:** Topical anesthetics are valuable tools for many dermatologic procedures. **OBJECTIVE:** To evaluate the efficacy and safety of S-Caine Peel composed of 1:1 (wt:wt) **mixture of 7% lidocaine and 7% tetracaine** in the induction of local anesthesia before long-pulsed Nd:YAG laser therapy for leg veins. **METHODS:** Two randomized, double-blinded, placebo-controlled trials were performed. In study 1, 60 adults received S-Caine Peel and placebo cream for 30 or 60 minutes. Efficacy was evaluated by a patient visual analog scale and impression. The pain scale and impression were evaluated by the investigator and an independent observer. In study 2, 40 adults received 60- and 90-minute applications. **RESULTS:** In study 1, the 30- and 60-minute application times were grouped: Patients had adequate pain relief in 48% of S-Caine sites versus 23% of placebo sites ( $P < 0.001$ ). Investigators reported none-to-mild pain in 50% of active sites versus 33% of placebo sites ( $P = 0.007$ ), with adequate anesthesia in 65% of active sites versus 43% of placebo sites ( $P = 0.002$ ). The independent witness assessed none-to-mild pain in 52% of active sites versus 37% of placebo sites ( $P = 0.067$ ). In study 2, investigators rated none-to-mild pain in 75% of 60-minute and 85% of 90-minute S-Caine sites versus 30% and 50% of placebo sites ( $P = 0.012$  and  $P = 0.002$ , respectively), with adequate anesthesia in 70% and 85% of 60- and 90-minute of active sites versus 25% and 20% of placebo sites ( $P = 0.029$  and  $P = 0.001$ , respectively). The independent witness rated none to mild pain in 80% and 85% of 60 and 90 minute of S-Caine sites versus 35% and 50% of placebo sites ( $P = 0.008$  and  $P = 0.004$ ). **CONCLUSION:** The S-Caine Peel provides safe and highly effective local anesthesia when applied for at least 60 minutes for laser therapy of leg veins. Facile removal of the peel provides a unique advantage and ease in administration.

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### **3. Potential benefits of Amethocaine.**

Drug Dev Ind Pharm. 2003 May;29(5):505-12.

#### **Formulation and efficacy studies of new topical anesthetic creams.**

**Kang L, Jun HW.**

Department of Pharmaceutical and Biomedical Sciences, The University of Georgia College of Pharmacy, Athens, Georgia 30602, USA.

Local anesthetics (lidocaine or tetracaine) spontaneously melted at 25 degrees C when mixed with thymol and aqueous isopropyl alcohol solution (IPA) at proper ratios and formed novel two-phase melt systems (TMS). The TMS consisted of a homogeneous oil phase containing primarily a local anesthetic agent (lidocaine or tetracaine) and thymol, and a homogeneous aqueous phase containing primarily IPA and pH 9.2 buffer. The relationship between melting of the solid components and system composition was determined from the phase diagram obtained by a titration method. A select TMS of a local anesthetic agent (lidocaine or tetracaine) was directly emulsified to prepare an O/W cream and tested for the anesthetic efficacy on intact human skin. While both lidocaine (6%) and tetracaine (4%) creams were highly effective for dermal anesthesia with a similar onset time, **the tetracaine cream exhibited a significantly longer duration of action than the lidocaine cream**. An accelerated stability study indicated that lidocaine was significantly more stable than tetracaine in the creams.

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## **4. Radial artery cannulation: topical amethocaine gel versus lidocaine infiltration.**

Br J Anaesth. 2002 Apr;88(4):580-2.

### **Radial artery cannulation: topical amethocaine gel versus lidocaine infiltration.**

**Olday SJ, Walpole R, Wang JY.**

Department of Anaesthesia, Royal Infirmary of Edinburgh, UK.

**BACKGROUND:** In a prospective randomized study, we compared topical 4% amethocaine gel (Ametop) with 2% lidocaine infiltration for analgesia for radial artery cannulation. A previous study had shown topical analgesia with EMLA cream reduced pain, shortened cannulation time, and improved success rates when compared with lidocaine infiltration. **METHODS:** One hundred adult patients undergoing elective cardiac surgery were randomized. Cannulation times and success rates were compared between the two groups. The quality of analgesia was assessed using a visual analogue scale (VAS) and four-point verbal pain scoring system. **RESULTS:** Ninety-nine sets of data were analysed using Mann-Whitney U and chi-squared tests. Mean time to cannulation was 56 s in the amethocaine group (interquartile range (IQR) 41-142) and 59 s in the lidocaine group (IQR 40-105). The median pain score on the VAS was 2 in both groups (IQR 1-3.5 for amethocaine and 0-4 for lidocaine). **CONCLUSIONS:** There was no significant difference between these two methods of analgesia for any measured variable.

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**5. VERY IMPORTANT. Systematic review shows that the superposition of lidocaine-prilocaine and amethocaine for analgesic effect. The tetracaine is more effective when applied for the same period of lidocaine-prilocaine.**

**Lidocaine-prilocaine cream versus tetracaine gel for procedural pain in children.**

**Taddio A, Gurguis MG, Koren G.**

Department of Pharmacy, The Hospital for Sick Children, Toronto, Ontario, Canada.

OBJECTIVE: To determine the relative efficacy of lidocaine-prilocaine and tetracaine for procedural pain in children. METHODS: **Systematic review** was performed (MEDLINE1990-June 2001) of all studies comparing the efficacy of these 2 modalities of pain relief in children undergoing painful cutaneous procedures. Search terms included lidocaine, prilocaine, tetracaine, and anesthesia. RESULTS: Eight studies compared lidocaine-prilocaine with tetracaine in children for 4 different procedures: intravenous cannulation, venipuncture, Port-a-Cath puncture, and laser therapy. When used as labeled (60 min for lidocaine-prilocaine, 30 min for tetracaine), the 2 modalities provided similar analgesic efficacy. When both anesthetics were applied for a similar duration of time (40 min, 60 min, 2 h), tetracaine provided superior anesthesia. Tetracaine was commonly associated with erythema, and lidocaine-prilocaine was associated with blanching of the skin. CONCLUSIONS: **Lidocaine-prilocaine and tetracaine appear to be comparable for procedural pain relief when used as recommended. Tetracaine is more efficacious than lidocaine-prilocaine when both anesthetics are applied for the same amount of time.**

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## **6. Rarity of adverse effects from amethocaine**

Anaesth Intensive Care. 1998 Jun;26(3):312-4.

### **Adverse local reactions to amethocaine cream--audit and case reports.**

**Wongprasartsuk P, Main BJ.**

Department of Anaesthesia, Royal Children's Hospital, Melbourne, Victoria.

Amethocaine has recently been introduced as a topical local anaesthetic preparation. Following sporadic reports of severe local adverse effects, we conducted an audit of 372 children attending our hospital for day surgery. We conclude that 4% amethocaine cream is a safe and effective topical anaesthetic and that the incidence of severe local adverse reactions is rare. We also report two of these local reactions, one involving occupational exposure.

Publication Types:

- Case Reports

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## 7. VERY IMPORTANT. Study of systemic absorption of amethocaine

Br J Anaesth. 1991 Oct;67(4):432-6.

**Preliminary study to assay plasma amethocaine concentrations after topical application of a new local anaesthetic cream containing amethocaine.**

**Mazumdar B, Tomlinson AA, Faulder GC.**

Department of Anaesthetics, City General Hospital, Stoke-on-Trent.

Plasma concentrations of amethocaine were measured after topical application of amethocaine cream 2 g (5% w/w) to the dorsum of the right hand of 10 adult volunteers. The cream was applied for 240 min and plasma was assayed for amethocaine and its metabolite p-n-butylaminobenzoic acid at 0, 30, 60, 90, 120 and 240 min in all 10 volunteers, and at 360 min in seven volunteers, by high pressure liquid chromatography. No amethocaine was detected in the plasma of seven volunteers. Plasma concentrations of amethocaine up to 0.20 mg litre<sup>-1</sup> were observed in three volunteers. No significant side effects were seen and pain scores on insertion of a 16-gauge cannula were 0 in all subjects. We conclude that the absence of clinical toxicity in the 10 healthy volunteers was a reflection of slow absorption and tissue hydrolysis of amethocaine after topical dermal application.

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