

Month/Year of Review: March 2013

PDL Classes: Topical Analgesics/Anesthetics

Date of Last Review: April 2010

Source Document: Provider Synergies

Current Status of PDL Class:

- Preferred Agents: CAPSAICIN CREAM
- Non Preferred Agents: CAPSAICIN PATCH, DICLOFENAC GEL AND SOLUTION, DICLOFENAC TRANSDERMAL PATCH (FLECTOR) LIDOCAINE CREAM, LIDOCAINE TRANSDERMAL PATCH (LIDODERM),

Previous Recommendations:

- Evidence does not support a difference in efficacy/effectiveness
- Evidence does not support a difference in harm/adverse events
- Efficacy and safety not established in patients under 18
- Consider including capsaicin and lidocaine by PA criteria.

Methods:

A Medline OVID search was conducted with the following search terms: capsaicin, benzocaine, tetracaine, lidocaine, prilocaine, ketorolac, diclofenac, methyl salicylate, menthol, amlexanox, dibucaine, bromfenac, nepafenac, trolamine, aphthous mouth ulcer, acute pain, actinic keratosis, myalgia, osteoarthritis, eye pain, rheumatoid arthritis, corneal abrasion, extraction of cataract eye pain, burn, diabetic neuropathy, local anesthetic, topical analgesic, otitis, skin irritation, stomatitis, toothache, ulcer, dental prosthesis pain, arthritis, musculoskeletal pain, neuropathic pain, postherpetic neuralgia, neuropathy, psoriasis. The search was limited to English language articles of controlled trials conducted on humans published from 2010 to January week 2 2013.

The Cochrane Collection, Dynamed and Medline OVID were searched for high quality systematic reviews. The FDA website was searched for new drugs, indications, and safety alerts. Finally, a search for new or updated guidelines was conducted at the AHRQ National Guideline Clearinghouse (NGC).

New Trials:

A total of 157 citations resulted from the initial MEDLINE search. Articles were excluded due to the wrong study design (observational), comparator (placebo), or outcome (non-clinical). After a review of titles and abstracts for inclusion, four relevant head-to-head clinical trials were identified and are discussed below. Please see Appendix 1 for the full abstracts.

Ravishankar¹ et al conducted a small (n=100), fair quality study which compared 4% tetracaine gel with tetracaine-lidocaine (both 7% strength) patches for topical anesthesia prior to venous cannulation. Patients were randomized to receive either the gel or the patch prior to needle insertion. Pain after insertion was measured by a visual analogue scale of 0 (no pain) to 100 (the worst pain imaginable). No significant difference in pain response was found between the median group score for the gel versus the patch (11 versus 10; p = 0.63).

Another comparison of topical anesthetics in venous cannulation by Poonai² et al also measured the efficacy of lidocaine versus tetracaine for pain reduction. This small (n=60), fair quality trial randomized children aged 5 to 12 years old to either 4% liposomal lidocaine cream or 4% tetracaine gel prior to IV insertion. Pain was measured on an analogue scale; in this study children picked a face from the Revised Faces Pain Scale that best demonstrated their pain level. The faces corresponded to a numerical value between 0 (no pain) and 10 (very bad pain). Again no difference was found in pain response between the two treatments: mean score for the lidocaine group 3.4, for the tetracaine group 4.3 (p=0.28).

Bourolias³ et al compared 10% lidocaine spray with 2% tetracaine solution for preventing pain and discomfort during transnasal fiber optic laryngoscopy. Forty-eight patients were randomized prior to the procedure to receive nasal sponges soaked either in lidocaine or tetracaine as an anesthetic. Pain was measured on a visual analogue scale of 0 (no pain) to 10 (intolerable pain). The tetracaine solution group had a lower mean pain score than the lidocaine group (2.29 versus 3.04; $p < 0.001$). This was a low quality study with poorly defined methodology; blinding, randomization and allocation concealment were not described.

Lastly, a postoperative pain relief trial by Hardy⁴ et al compared 2% viscous lidocaine solution with rectal diclofenac suppositories. This small ($n=130$) study recruited children 5 to 12 years old and measured pain relief after tonsillectomy through a visual analogue scale designed for children (similar to the one described in the Poonai study). No statistical difference in pain scores was seen between the two treatments ($p=0.474$). This was a low quality trial: blinding, randomization and concealment were not discussed, and results were published without treatment differences.

New drugs:

None

New Formulations/Indications:

None

New FDA safety alerts:

In September 2012⁷, the FDA released a safety communication for OTC menthol, methyl salicylate, and capsaicin use. After several instances of serious burns were reported, the FDA advised consumers to stop using all OTC topical muscle and joint pain-relievers and seek medical attention if they experience signs of skin injury where the product was applied, such as pain, swelling, or blistering of the skin.

Also in 2012, a safety communication regarding the use of oral benzocaine was released. In April⁸ the FDA issued a warning of rare cases of methemoglobinemia reported with benzocaine use. The majority of cases occurred in children under the age of two; because of this, the FDA recommended not using benzocaine in children under two years old.

New Systematic Reviews:

No new or updated, relevant, head-to-head systematic reviews were identified. A protocol⁹ from the Cochrane Collaborative was published in 2010. The authors proposed to conduct a systematic review to measure any difference between topical analgesics to treat acute and chronic pain in adults. No estimated date of completion is listed.

Guidelines:

The 2012 updated guideline for osteoarthritis¹⁰ treatment from the American College of Rheumatology was reviewed. The 2010 guidance¹¹ on neuropathic pain treatment from the UK's National Institute for Clinical Excellence was also reviewed; as was the 2011 guideline¹² published by the American Academy of Neurology, the American Association of Neuromuscular Medicine and the American Academy of Physical Medicine and Rehabilitation. In 2010, the American Society of Anesthesiologists updated guidelines on chronic pain¹³; they published new guidelines for acute pain¹⁴ in the perioperative setting in 2012. No changes regarding the use of analgesics or anesthetics were found.

Recommendations:

- No further research or review needed at this time.
- Evaluate comparative costs in executive session.

References:

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3. Bourolias C, Gkotsis A, Kontaxakis A, Tsoukarelis P. Lidocaine spray vs tetracaine solution for transnasal fiber-optic laryngoscopy. *Am J Otolaryngol*. 2010;31(2):114–116.
4. Rhendra Hardy MZ, Zayuah MS, Baharudin A, et al. The effects of topical viscous lignocaine 2% versus per-rectal diclofenac in early post-tonsillectomy pain in children. *Int. J. Pediatr. Otorhinolaryngol*. 2010;74(4):374–377.
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13. Practice guidelines for chronic pain management: an updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. *Anesthesiology*. 2010;112(4):810–833.
14. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology*. 2012;116(2):248–273.

Appendix 1

Randomized Control Trials

Ravishankar N, Elliot SC, Beardow Z, Mallick A. A comparison of Rapydan® patch and Ametop® gel for venous cannulation. *Anaesthesia*. 2012; 67(4):367–370.

Ametop(®) gel (4% tetracaine) is used to provide topical anaesthesia for venous cannulation. Rapydan(®) patch (7% lidocaine and 7% tetracaine) has been developed to provide topical anaesthesia by a different mechanism, that of heat assisted delivery. We compared the topical anaesthetic effect of these agents for venous cannulation. One hundred healthy adults undergoing day-case surgery were randomly assigned to receive either Rapydan (n = 50) or Ametop (n = 50) before venous cannulation. Pain on insertion was scored on a visual analogue scale between 0 and 100 (where 100 = unbearable pain). Median(IQR[range]) pain scores were not different between groups with 11 (5-20 [0-72]) for Rapydan and 10 (5-24 [0-95]) for Ametop (p = 0.63). Adequate topical anaesthesia was achieved in over 90% of patients in both groups. Rapydan produces topical anaesthesia comparable with Ametop for venous cannulation.

Poonai N, Alawi K, Rieder M, Lynch T, Lim R. A comparison of amethocaine and liposomal lidocaine cream as a pain reliever before venipuncture in children: a randomized control trial. *Pediatr Emerg Care*. 2012;28(2):104–108.

OBJECTIVE: Although the use of anesthetic creams before intravenous (IV) insertion has been shown to be both safe and effective in decreasing pain during IV cannulation, the use of any single agent based on efficacy is not yet considered the standard of care in children. We sought to compare a commonly used preparation, 4% liposomal lidocaine (Maxilene), with 4% amethocaine (Ametop), a newer agent with reportedly good efficacy and an intrinsic vasodilatory effect. **METHODS:** A total of 60 children aged 5 to 12 years were randomized to receive topically either 4% amethocaine or 4% liposomal lidocaine before IV cannulation. The primary outcome variable was the child's rating of pain using the Faces Pain Scale - Revised. Secondary outcomes included success rate on first IV cannulation attempt, cannulation difficulty ratings by the nurses, and adverse skin reactions. **RESULTS:** We found no statistically significant differences in self-reported scores in the Faces Pain Scale-Revised with the use of 4% amethocaine versus 4% lidocaine before IV cannulation. There was a trend toward fewer IV cannulation attempts in the 4% amethocaine group. Adverse skin reactions were uncommon, and there were no statistically significant differences between groups. **DISCUSSION:** This study demonstrates that there is no difference between 4% amethocaine and 4% liposomal lidocaine in reducing pain associated with IV cannulation in children. Amethocaine confers no advantage in improving IV cannulation success rate over lidocaine. Both agents are associated with few local adverse skin reactions.

Bourolias C, Gkotsis A, Kontaxakis A, Tsoukarelis P. Lidocaine spray vs tetracaine solution for transnasal fiber-optic laryngoscopy. *Am J Otolaryngol*. 2010;31(2):114–116.

STATEMENT OF PROBLEM: The aim of this study was to evaluate the efficacy of lidocaine spray 10%, compared with tetracaine 2% solution, as a local anesthetic for patients undergoing transnasal fiber-optic laryngoscopy. **METHOD OF STUDY:** A prospective study was conducted on patients undergoing transnasal fiber-optic laryngoscopy. Microsurgical sponges were applied in each side of the nose for 10 minutes before laryngoscopy. Patients were randomly classified into group A and group B, in which tetracaine 2% solution and lidocaine spray 10% were used, respectively. Patients were asked to evaluate the severity of pain during the procedure by a visual analog scale. Patients data, pain score, and potential complications were placed in a database and statistically assessed. **MAIN RESULTS:** Our series consisted of 48 patients. Statistical analysis showed significant lower mean nasal discomfort score in favor of the tetracaine group (2.29 vs 3.04 [P < .001]). No tetracaine complications or side effects occurred. **PRINCIPAL CONCLUSION:** Neurosurgical sponge application of tetracaine 2% solution is an easy, safe, inexpensive, and effective analgesia for transnasal fiber-optic laryngoscopy.

Rhendra Hardy MZ, Zayuah MS, Baharudin A, et al. The effects of topical viscous lignocaine 2% versus per-rectal diclofenac in early post-tonsillectomy pain in children. *Int. J. Pediatr. Otorhinolaryngol*. 2010;74(4):374–377.

INTRODUCTION: Tonsillectomy is frequently associated with postoperative pain of considerable duration, which is usually accompanied by the substantial consumption of both opioid and non-opioid analgesic such as NSAIDs and local anaesthetics. **OBJECTIVE:** The aim of this study was to evaluate the efficacy between 2% viscous lignocaine and sodium diclofenac based upon the visual analogue scores (VASs), consumption of pethidine 0.5mgkg(-1) as the rescue drug postoperatively and time taken to resume feeding. **METHODS:** 130 patients aged between 5 and 12 years old were randomly allocated into 2 groups to be given either 2% viscous lignocaine 4mgkg(-1) body weight topically post-tonsillectomy or sodium diclofenac 1mgkg(-1) per-rectal post-induction of anaesthesia. Postoperatively visual analogues score was done for 24h, the amount of pethidine given and time when the patient start taking oral feeding of clear fluid, soft diet and normal diet were documented. **RESULTS:** There was no significant difference in the visual analogue scores in both groups, however the requirement of pethidine as the rescue drug postoperatively was significant 2h post-tonsillectomy (p=0.023) in viscous lignocaine group compared to sodium diclofenac. The time taken to resume oral feeding and soft diet was also significant in viscous lignocaine group (p=0.016 and p=0.007) whereas there was no significant in taking normal diet. **CONCLUSION:** We concluded that 2% viscous lignocaine applied topically post-tonsillectomy is comparable to sodium diclofenac per-rectal in providing analgesia and faster oral feeding.