Original Article

Contribution of a Heating Element to Topical Anesthesia Patch Efficacy Prior to Vascular Access: Results From Two Randomized, Double-Blind Studies

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Abstract

Context. Pain associated with superficial procedures, including intravenous (IV) access procedures, should be prevented when possible, especially in children.

Objectives. To evaluate a topical local anesthetic patch containing lidocaine 70 mg/tetracaine 70 mg with a heating element designed to warm the skin and facilitate rapid delivery of local anesthetics into the skin. The pilot study was designed to provide data to inform the design of the definitive study to evaluate the impact of controlled heat on the efficacy of the lidocaine/tetracaine patch (patch) when applied before IV cannulation.

Methods. Subjects in the pilot study were randomized to eight groups that varied by heated vs. unheated patch, 20 vs. 30 minute application, and 16 vs. 18 G catheter. Subjects in the definitive study were randomized in a double-blind manner to receive either the heated or unheated patch, 20 minutes before vascular access, using a 16 G catheter in the antecubital space of the arm. In both studies, the primary efficacy measure was subject-reported pain intensity using a visual analog scale.

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Results. Pilot study: Subjects who received the heated patch ($n = 43$) vs. the unheated patch ($n = 37$) had lower mean pain intensity scores (14.7 vs. 23.5 mm, $P = 0.04$). Pain intensity scores did not differ significantly by application time, but the difference between the 16 and 18 G catheter groups approached statistical significance (22.8 vs. 14.9 mm, $P = 0.05$). Definitive study: Mean pain intensity scores for the heated patch group ($n = 124$) vs. the unheated patch group ($n = 126$) were 14.2 and 20.5 mm, respectively ($P = 0.006$).

Conclusion. Heated patches provided significantly better pain relief compared with unheated patches. All the subjects tolerated the patches well, with few adverse effects. J Pain Symptom Manage 2010;40:510–519.

Key Words

Anesthetics local, tetracaine; anesthetics local, lidocaine; drug delivery, temperature, pain, cannulation

Introduction

There is an increasing awareness that the pain associated with superficial procedures, including intravenous (IV) access procedures, should be prevented when possible, especially in children. In addition, more patients who are undergoing superficial dermatologic procedures could benefit from rapid, effective pain prevention prior to the procedure. Providing a good clinical outcome in an efficient and practical manner requires a topical anesthetic agent to be effective, quick in onset, and without systemic side effects.[1,2]

New anesthetic technologies have emerged that improve drug delivery through the skin. These include a eutectic mixture of local anesthetics, iontophoresis of lidocaine, liposomal agents, and controlled heat.[3–6] The topical local anesthetic patch (approved as Synera® in the U.S. [ZARS Pharma, Inc., Salt Lake City, UT, USA] and as Rapydan™ in the E.U. [Eurocept International B.V., Ankeveen, The Netherlands]) investigated in these trials consists of a patch with a eutectic mixture of lidocaine 70 mg and tetracaine 70 mg (Fig. 1).[7,8] This patch has an integrated heating element intended to enhance the flux of the tetracaine and lidocaine. The patch begins heating once it is removed from the pouch and exposed to atmospheric oxygen and may increase skin temperature by up to approximately 5°C. The maximum skin temperature is expected not to exceed 40°C.[8]

Controlled heat is used in this patch to increase the flux of tetracaine and lidocaine, thus leading to more rapid and effective delivery of the local anesthetics to the target area. Although previous studies have shown the efficacy of this patch when compared with placebo, different local anesthetic formulations, or variable application times, no previous study has demonstrated the contribution of heat to the clinical performance of this patch. Therefore, a pilot study was conducted to preliminarily assess the effect of heat and establish an appropriate application time and stimulus. Based on the results of the pilot study, a definitive study was subsequently conducted to fully characterize the impact of controlled heat on the efficacy of the patch to provide local dermal analgesia prior to vascular access and to add rigor to the results of the pilot study.

Methods

Both studies were multicenter studies that enrolled healthy adult volunteers of any race or sex at four study sites in the United States. Institutional Review Board approval was obtained before the studies were conducted, and written informed consent was obtained from each subject before enrollment. In both studies, subjects were excluded from enrollment if they had a known sensitivity to lidocaine or tetracaine or to any components of the test materials (i.e., sulfites, adhesives), a history of multiple allergies that could indicate hypersensitive skin or a history of contact dermatitis. Subjects also were excluded if they had damaged or denuded skin at the designated skin site, a history of