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CLINICAL PRACTICE

Heated lidocaine/tetracaine patch (Synera™, Rapydan™) compared with lidocaine/prilocaine cream (EMLA®) for topical anaesthesia before vascular access

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Background. We compared the lidocaine/tetracaine patch [Synera™ (USA), Rapydan™ (Europe)], a novel heat-aided patch using a eutectic mixture of lidocaine 70 mg and tetracaine 70 mg, with a eutectic mixture of lidocaine 25 mg ml^{-1} and prilocaine 25 mg ml^{-1} (EMLA® Cream). The agents were administered at different time periods for local topical anaesthesia before a vascular access procedure.

Methods. In this double-blind, paired study, 82 adult volunteers were randomized to receive the lidocaine/tetracaine patch on one anticubital surface and lidocaine/prilocaine cream on the other concurrently for 10, 20, 30, or 60 min before a vascular access procedure. Subjects rated pain intensity using a 100 mm visual analogue scale (VAS). Skin reactions and adverse events were also evaluated.

Results. Median VAS scores were significantly lower for the lidocaine/tetracaine patch than for lidocaine/prilocaine cream in the 10 min (P=0.010), 20 min (P=0.042), and 30 min (P=0.001) application groups. The lidocaine/tetracaine patch was associated with significantly more erythema than lidocaine/prilocaine cream at 20, 30, and 60 min, whereas lidocaine/prilocaine cream produced more blanching than the lidocaine/tetracaine patch at 30 and 60 min. Two subjects reported nausea and faintness associated with the vascular access procedure; one was withdrawn from the study.

Conclusions. The lidocaine/tetracaine patch provided effective anaesthesia with an application time as short as 10 min and was better than lidocaine/prilocaine cream at all application times shorter than 60 min, demonstrating a substantial improvement in time to onset of anaesthesia. The lidocaine/tetracaine patch provided an important alternative to lidocaine/prilocaine cream for topical local anaesthesia.

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Many clinical procedures, including venepuncture, arterial puncture, lumbar puncture, percutaneous venous catheter placement, and dermatological procedures, may be associated with pain or discomfort. Consequently, the procedural pain and associated stress and anxiety involved for some patients represent a significant clinical concern,

†*Declaration of interest*. J.S. has received honoraria for work conducted on behalf of ZARS Pharma. S.M. owns shares of ZARS Pharma. M.A.A is a co-founder of ZARS Pharma, the sponsor of the clinical trial on which this paper is based. He also holds shares in ZARS Pharma and, during the conduct of the study, was an employee of ZARS. His role was to design the trial and act as a medical monitor. J.C.C. is an employee of Endo Pharmaceuticals.

which is often addressed by the use of topical anaesthesia. But, intact skin presents a significant barrier to available topical anaesthetic preparations. This means that many topical anaesthetic preparations must be applied at least 45–60 min before the clinical procedure to achieve the desired level of anaesthesia. In addition, current creams or gel-based preparations may require the use of occlusive dressings, adding to the time required for their application.[1 2] These factors place an additional burden on clinical staff and can lead to delays in administering the planned procedure.

The lidocaine/tetracaine patch (lidocaine 70 mg/tetracaine 70 mg, Synera™, known in Europe as Rapydan™) is a novel drug delivery system designed to warm the skin and enhance the delivery of local anaesthetics through the skin.[3–5] EMLA® Cream, a widely used topical anaesthetic, is a eutectic mixture of lidocaine 25 mg ml^{-1} and prilocaine 25 mg ml^{-1}.[1 6] The objective of this study was to compare the efficacy and tolerability of the lidocaine/tetracaine patch with lidocaine/prilocaine cream when applied within 1 h of conducting vascular access procedures in adult volunteers.

Methods

This randomized, double-blind, paired study compared the effectiveness of the lidocaine/tetracaine patch with that of lidocaine/prilocaine cream when administered for 10, 20, 30, and 60 min periods to provide dermal anaesthesia for vascular access procedures in adult volunteers. The study received approval from the Bro Taf Local Research Ethics Committee, Glamorgan, Wales, UK, and all subjects gave written informed consent before participation.

Eligible subjects were adults 18 yr of age or older of any race and gender who did not meet any of the following exclusion criteria: known allergies or sensitivities to lidocaine, tetracaine, prilocaine, or other local anaesthetic; known sensitivity to any components of the test materials (e.g. sulphites and adhesives); damaged, denuded, or broken skin at the designated patch site; pregnant or breastfeeding; concomitant use of a prescription-strength analgesic within the previous 24 h; or previous use of lidocaine/prilocaine cream.

Subjects received concurrent applications of the lidocaine/tetracaine patch (ZARS Pharma, Salt Lake City, UT, USA) (Fig. 1) and lidocaine/prilocaine cream (AstraZeneca Pharmaceuticals, Macclesfield, UK). The lidocaine/tetracaine patch was activated by removing the patch from its air-tight pouch, peeling the release liner, and applying it to the skin. Lidocaine/prilocaine cream was applied under occlusion, according to the product's instructions for use.[7]

Eligible subjects were randomized into one of the four groups, according to the duration of time the treatment was to be applied: 10, 20, 30, or 60 min. Within each treatment group, subjects received a lidocaine/tetracaine patch on one anticubital surface and lidocaine/prilocaine cream concurrently on the other. Individual treatments were applied to the left or right arms according to a random scheme, by a study nurse who took no part in the study evaluations. Lidocaine/prilocaine cream was applied using an oval plastic template similar in size to the lidocaine/tetracaine patch so that the investigator could not determine treatment allocation. The study nurse then removed the study treatments before treatment evaluations. Immediately after removal of the treatments, the investigator, who remained blinded to the study drug applied to each arm, evaluated the treatment sites for skin reactions. After skin evaluation, the investigator performed a venepuncture of each right and left anticubital vein using a standard 18 gauge angiocatheter. In all cases, the procedure was performed on the right arm first. The investigator obtained a flash of blood to confirm that venous access was achieved. Once the flash was obtained, the angiocatheter was removed and the blood was discarded. After each procedure, the subject and investigator completed study evaluations. Before leaving the study site, subjects were asked to call the study site if a skin reaction developed.

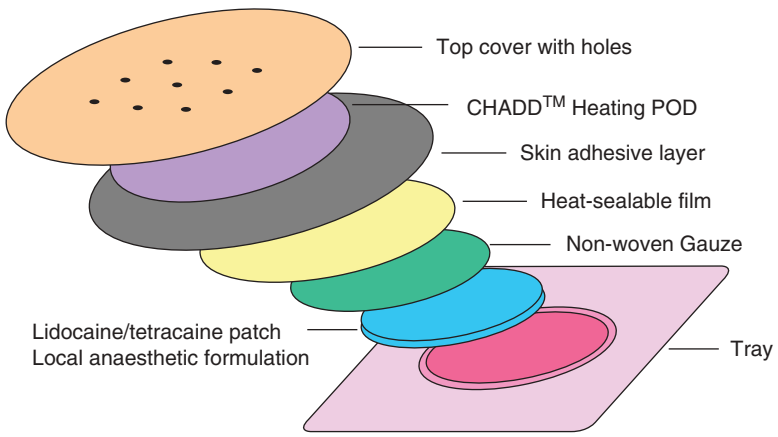

Fig 1 Diagram of the heated lidocaine/tetracaine patch.