

# Piroxicam gel, compared to EMLA cream is associated with less pain after venous cannulation in volunteers

*[Un gel de piroxicam, comparé à une crème EMLA, est associé à moins de douleur après une canulation veineuse chez des volontaires]*

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**Purpose:** To evaluate and compare the analgesic efficacy and anti-inflammatory effects of topical piroxicam gel vs eutectic mixture of local anesthetic (EMLA) cream applied to the peripheral venous cannulation site in adult volunteers.

**Methods:** Piroxicam gel and EMLA cream were randomly applied on the dorsum of the right and left hand of ten volunteers who acted as their own control. A venous cannula was inserted (no iv infusion) and removed after one hour. Pain scores and signs of inflammation were noted at the cannulation site up to 48 hr.

**Results:** Pain scores with piroxicam gel were higher on cannulation and on advancement of the cannula ( $P < 0.05$ ). Thereafter, pain scores were significantly higher with EMLA ( $P < 0.05$ ). Blanching was present at all the peripheral venous sites treated with EMLA cream. Signs of inflammation (erythema, edema) were not more frequent with EMLA than with piroxicam ( $P > 0.05$ ). Induration was more frequent with EMLA at six hours.

**Conclusion:** In volunteers EMLA cream is associated with less pain on cannulation and cannula advancement compared to piroxicam gel. Topical application of piroxicam gel before peripheral venous cannulation alleviates pain and, possibly, inflammation in the period subsequent to cannulation itself.

**Objectif :** Évaluer et comparer l'efficacité analgésique et les effets anti-inflammatoires d'un gel de piroxicam topique et d'une crème d'un mélange eutectique d'anesthésique local (EMLA) appliqués autour du site d'une canulation veineuse chez des adultes volontaires.

**Méthode :** Le gel de piroxicam ou la crème EMLA ont été appliqués, aléatoirement, au dos des mains droite et gauche de dix volontaires qui étaient leur propre témoin. Une canule veineuse a été insérée

(sans perfusion iv) et enlevée une heure plus tard. Les scores de douleur et les signes d'inflammation ont été notés au site de canulation pendant une période allant jusqu'à 48 h.

**Résultats :** Les scores de douleur ont été plus élevés avec le gel de piroxicam pendant la canulation et la poussée de la canule ( $P < 0,05$ ). Par la suite, les scores de douleur ont été significativement plus élevés avec le EMLA ( $P < 0,05$ ). La blancheur était présente à tous les sites veineux périphériques traités avec la crème EMLA. Les signes d'inflammation (érythème, œdème) étaient comparables avec les deux médicaments ( $P > 0,05$ ). L'induration a été plus fréquente avec le EMLA à six heures.

**Conclusion :** Chez des volontaires, la crème EMLA est associée à moins de douleur, que le gel de piroxicam, au site de canulation et pendant la poussée de la canule. L'application topique de gel de piroxicam avant la canulation veineuse atténue la douleur et, possiblement, l'inflammation après la canulation elle-même.

**P**AIN upon venous cannulation continues to be a shortcoming with respect to the smooth initiation of anesthesia. In addition, patients may continue to have pain and discomfort at the cannulation site even after removal of the cannula. It is one of the common problems at the end of the day in surgical inpatients and constitutes an important complaint in outpatients after discharge, adding to morbidity. Local inflammation at the cannulation site is one of the mechanisms of pain. The incidence of peripheral venous thrombophlebitis

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(PVT) is 10–57% in patients with peripheral *iv* lines.<sup>1</sup> Payne-James *et al.* described that topical non-steroidal anti-inflammatory drugs (NSAIDs) prevent PVT, but they did not study pain scores specifically.<sup>2</sup>

Local anesthetics in one form or the other are commonly employed to overcome pain on cannulation.<sup>3</sup> Apart from the benefit of rapidity of onset and effective pain relief, the use of local anesthetic agents is associated with a number of disadvantages, such as pin-prick pain on lidocaine *sc* infiltration<sup>4</sup> and blanching of the skin and vasoconstriction following the topical application of eutectic mixture of local anesthetic (EMLA) cream.<sup>5</sup> These agents do not seem to have any effect on subsequent inflammation. Topical NSAIDs, by virtue of their capacity to inhibit prostaglandin synthesis are expected to provide analgesia and decrease the inflammatory response to cannulation. Smith *et al.* found that topical ibuprofen did not alleviate pain secondary to venous cannulation, but they did not study its effect on inflammation.<sup>4</sup> Topical piroxicam, a long-acting NSAID<sup>6</sup> has been used as an adjuvant for postoperative analgesia in patients undergoing inguinal hernia repair.<sup>7</sup>

We evaluated the efficacy of topical piroxicam to prevent pain during and after venous cannulation and subsequent inflammation in adult volunteers.

## Methods

After Ethics Committee approval and written informed consent from the subjects, a prospective and randomized study was conducted in ten healthy volunteers who acted as their own control. Volunteers belonged to either sex, were 20–60 yr of age and American Society of Anesthesiologists physical status I or II. Subjects with asthma, NSAID allergy, chronic NSAID intake, any psychiatric disease, alcohol or drug dependence and with any local skin condition were excluded from the study.

A vein was marked on the dorsum of both hands. Piroxicam gel (Cipla, Ahmedabad, India) was applied on one hand and EMLA cream on the other hand (Astra Pharmaceuticals, NSW, Australia) of each subject based upon a computer generated random number. It was then covered with an occlusive dressing (Tegaderm, 3M Health Care, St. Paul, MN, USA) and a gauze bandage. The area of skin covered with gel (3.8 cm × 1.9 cm) and the amount of topical drug preparation (2 g) were standardized. Volunteers were blinded to the gel applied. The gel was wiped off with an alcohol swab before cannulating the vein. Only successful cannulations at the first attempt with a 20-G venous cannula (Venflon, Ohmeda, BOC Ohmeda, AB, Sweden) entered the study. A single and dedicated observer unaware of the gel applied recorded the

TABLE I Visual analogue scale scores [median (range)] on cannulation and up to 48 hr

Time	Eutectic mixture of local anesthetic	Piroxicam
On cannulation	2.0 (1–5)	4.5 (3–8)**
Cannula advancement	2.0 (1–3)	3.5 (1–7)*
1 hr	2.5 (1–4)	2.5 (1–4)
6 hr	3.5 (1–5)**	1.5 (1–3)
12 hr	4.0 (1–5)**	1.5 (1–3)
24 hr	4.0 (1–7)**	1.0 (1–2)
48 hr	3.0 (1–6)*	1.0 (1–2)

\* $P < 0.05$ ; \*\* $P < 0.01$ ; Wilcoxon sum rank test.

pain scores as marked by subjects on a visual analogue scale (VAS) 1–10 cm (1 = no pain, 10 = worst possible pain). In addition, the observer rated local skin condition (blanching, erythema, induration, edema) at predetermined intervals. Cannulation was attempted one hour following application of the gel. The cannula was removed after one hour and local compression with pressure gauze lasted for 30 min.

VAS scores on cannulation, during cannula advancement and at regular intervals over the next 48 hr were compared using Wilcoxon rank sum test with continuity correction. Skin condition between the two drugs was compared using Pearson's Chi squared test with Yates' continuity correction. A  $P < 0.05$  was considered significant. A difference of 2 cm on the VAS to assess pain was considered significant. To detect this difference with a statistical power of 80% or more we calculated that we would need ten subjects.

## Results

VAS scores for pain on venous cannulation, during cannula advancement and at regular intervals over the subsequent 48 hr are summarized in Table I. Pain scores were significantly higher with piroxicam on cannulation ( $P < 0.01$ ) and with cannula advancement ( $P < 0.05$ ). Conversely, the scores were significantly higher with EMLA at six, 12, 24 and 48 hr intervals ( $P < 0.01$ ).

Skin condition *i.e.*, blanching, erythema, induration and edema, and their overall frequency at various intervals are presented in Table II. All subjects exhibited blanching with EMLA at the time of cannulation as compared to none in the piroxicam group. Blanching was still present in 50% of the volunteers at six hours.

Occurrence of erythema and edema with EMLA or with piroxicam was not different. Induration was more frequent with EMLA at six-hour interval.

TABLE II Skin condition up to 48 hr

<i>Skin condition</i>	<i>Time interval of local anesthetic</i>	<i>Eutectic mixture</i>	<i>Piroxicam</i>
Blanching	OC	10*	0
	1 hr	10*	0
	6 hr	5*	0
	12 hr	1	0
	24 hr	0	0
	48 hr	0	0
Erythema	OC	0	0
	1 hr	3	2
	6 hr	6	2
	12 hr	7	2
	24 hr	6	1
	48 hr	4	0
Edema	OC	0	0
	1 hr	4	2
	6 hr	6	4
	12 hr	6	3
	24 hr	3	2
	48 hr	1	1
Induration	OC	0	0
	1 hr	5	1
	6 hr	5*	0
	12 hr	3	2
	24 hr	1	2
	48 hr	0	1

OC = on cannulation. \* $P < 0.05$ ; Pearson's Chi squared test.

## Discussion

The emergence of outpatient surgery has underlined the importance of complications like pain, postoperative nausea and vomiting, shivering, myalgia and their contribution towards overall patient morbidity.<sup>8</sup> Pain upon venous cannulation has been the focus of few studies.<sup>4</sup> Pain and/or discomfort at the cannulation site is one of the common complaints following surgery in inpatients. For outpatients undergoing minor surgical procedures, protracted pain at the cannulation site may be important. NSAIDs act as analgesic and anti-inflammatory agents and their utility in providing analgesia and prevention of thrombophlebitis has been reported earlier.<sup>2,4</sup> We chose topical piroxicam, a long-acting NSAID<sup>9</sup> to alleviate pain on cannulation and inflammation after venous cannulation.

Piroxicam gel was less effective in preventing pain on cannulation and on advancement of the venous cannula but was associated with a lesser incidence of skin induration and subsequent pain compared to EMLA. The vasoconstrictive effect of EMLA at the time of cannulation might be responsible for blanching,<sup>9,10</sup>

Blanching was present in all patients at the time of venous cannulation. Extravasation of blood in the surrounding tissue following decannulation may also contribute to inflammation. When the vasoconstrictive effects of EMLA wear off, there is a generalized local vasodilation, which may lead to erythema and swelling. In our study, EMLA treated hands were more painful over the 48 hr following venous cannulation.

Our study shows the advantageous analgesic effects of topical piroxicam in the period subsequent to the cannulation whereas the reduction of incidence of inflammatory skin signs was inconclusive. This warrants a larger study sample to substantiate clinical significance. Though inclusion of a placebo control would have better highlighted the analgesic efficacy of local piroxicam gel at the cannulation site, we felt it was not justified in volunteers. Although piroxicam did not fare well as compared to EMLA cream in decreasing pain during cannulation and cannula advancement, the advantageous analgesia profile of topically applied piroxicam in the period following cannulation may prove beneficial in adult outpatients as well as inpatients.

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