

EFFICACY OF 5% LIDOCAINE MEDICATED PLASTER IN LOCALIZED PERIPHERAL NEUROPATHIC PAIN IN ADULTS

Ciaramitaro P., *Stella M., *Risso D., *Germano P., °Faccani G., °Cocito D.

Clinical Neurophysiology, °Neurosurgery Div., CTO, Neuroscience Department, AOU Città della Salute e della Scienza di Torino

*Department of Plastic Surgery, Burn Center, CTO, AOU Città della Salute e della Scienza di Torino

°°Clinical Neurophysiology, Neuroscience Department, AOU Città della Salute e della Scienza di Torino

Background

Localized peripheral neuropathic pain (NP) may be defined as “a type of neuropathic pain characterized by consistent and circumscribed area(s) of maximum pain”. 5% Lidocaine medicated plaster (LMP) is a topical peripheral noninvasive analgesic approved (FDA) as the first line of medication for treating allodynia generated by post-herpetic neuralgia; LMP has recommended as the first line of treatment for localized peripheral NP in USA, Europe, and Latin America. According to recent reports, LMP is an effective, safe and comfortable therapeutic option in patients with localized peripheral NP secondary to traumatic neuropathies.

Objectives: 1) to evaluate the efficacy of LMP in localized peripheral NP secondary to post-burn plastic surgery; 2) to confirm safety, tolerability and absence of side effects in a short term treatment in adults.

Material and Methods

In a prospective study we enrolled consecutive patients with painful post-burn scars and localized NP treated with 5% Lidocaine medicated plaster-Versatis®.

Demographic variables, the size of painful area and pain intensity (VAS) were recorded. The possible neuropathic origin of this pain was defined on the basis of a DN4 questionnaire score ≥ 4 . Inclusion criteria: age 18-75 years; DN4 ≥ 4 ; VAS ≥ 4 ; localized peripheral pain (painful area $< 70 \text{ cm}^2$). Exclusion Criteria: polyneuropathy, major depressive disorders, treatment with other analgesic drugs. The mean duration of pain before starting treatment with LMP was calculated. NRS was measured before starting treatment (T0), after 1 (T1) and 3 (T2) months. VAS at T0 and T2, PGIC and functional recovery at T2 were performed to evaluate the efficacy of the treatment. Pain reduction $\geq 50\%$, percentage of functional recovery and of PGIC ≤ 2 was calculated at T2 to evaluate the efficacy.

Results

Twenty patients were included (8 males, 12 females; age 32-65, mean $52.4 \pm 9.6 \text{ SD}$). Localized neuropathic pain affected upper (15 patients) and lower (5 patients) limbs. The mean duration of pain before starting treatment with LMP was 3.6-15.0 months; DN4 score was 6.8 ± 1.2 . 13/20 (65%) patients used LMP as monotherapy. Functional recovery after treatment was observed in 14/20 (70%) patients; pain and painful area reduction respectively in 75% (15/20) and in 90% (18/20). None of the patients reported adverse local or systemic reactions to the use of LMP.

Conclusions

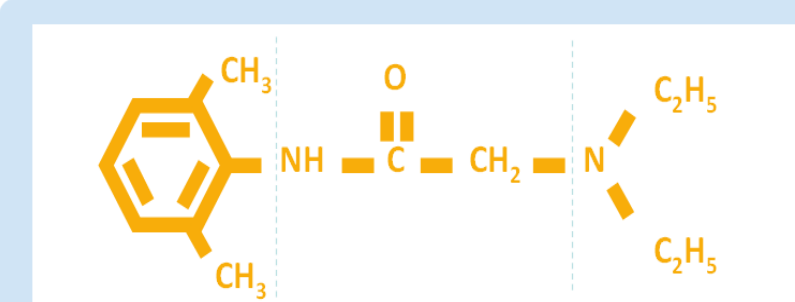
This study suggests LMP-Versatis® efficacy in short term treatment of localized peripheral NP secondary to post-burn plastic surgery, reducing both pain intensity and size of the painful area; moreover, our results would confirm safety, tolerability and absence of side effects.

Bibliography

- [1] Mao J and Chen LL. Pain. 2000;87:7-17.
- [2] Dougherty PM et al. Brain Res.1992;570:109-15.
- [3] Chaplan SR et al. Anesthesiology. 1995;83:775-85
- [4] Versatis® (Lidocaina cerotto 5%) RCP.
- [5] Grünenthal. Data on file.
- [6] Comer AM and Lamb HM. Drugs 2000; 59 (2):245-249
- [7] Attal N et al. Eur J Neurol 2010.
- [8] Dworkin RH et al. Pain 2007; 132:237-251.
- [9] Dworkin RH et al. Mayo Clin Proc.2010;Mar;85(3 Suppl):S3-14. Review
- [10] Rowbotham, MC, Davies, PS, Verkempinck, C et al (1999). Lidocaine patch: double-blind controlled study of a new treatment method for Post-herpetic neuralgia. Pain 1996; 65; 39-44 (MSK)
- [11] Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, Cunin G, Fermanian J, Ginies P, Grun-Overdyking A, Jafari-Schlupep H, Lanteri-Minet M, Laurent B, Mick G, Serrie A, Valade D, Vicaut E. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain. 2005;114(1-2):29-36.

LIDOCAINA

- L'efficacia della lidocaina nella nevralgia è documentata da diversi studi in vivo [1,2,3]
- La lidocaina:
 - sopprime gli impulsi ectopici dopo un danno nervoso periferico
 - riduce le modifiche comportamentali nel dolore neuropatico sperimentale
 - riduce l'iperalgesia e l'allodinia

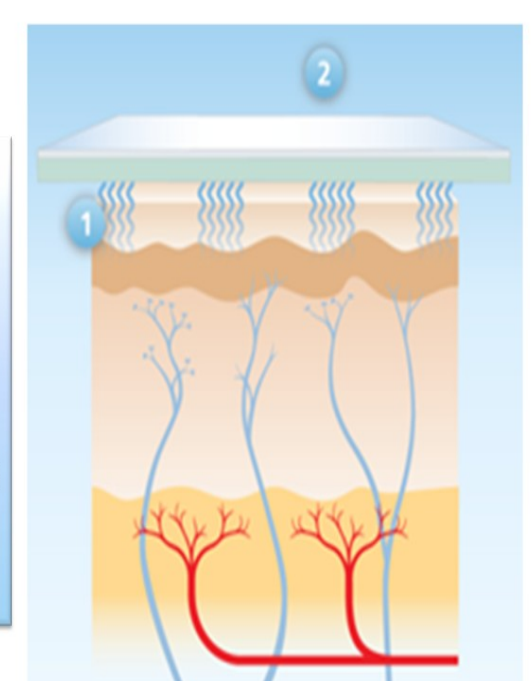


Lidocaina cerotto 5% Meccanismo d'azione [10]

- 1 Componente farmacologica
- 2 Componente meccanica

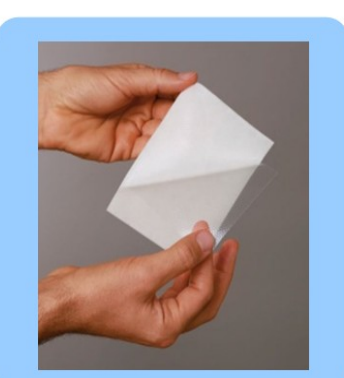
*Azione specifica sulle fibre sensitive danneggiate, con stabilizzazione del potenziale di membrana neurale

*Specificità d'azione: effetto analgesico senza effetto anestetico locale



Lidocaina cerotto 5% Tecnologia

- Formulazione galenica: Cerotto idrogel, autoadesivo
- Principio attivo: Lidocaina
- Dimensioni: 10 cm x 14 cm
- Dosaggio per cerotto: 5% (50 mg/grammo di base adesiva)
- Dose di carico totale: 700 mg a cerotto



- Schema di applicazione: 12 ore on/off con un sollievo dal dolore per 24 ore
- Da uno ad un massimo di tre cerotti applicati contemporaneamente

Lidocaina cerotto 5% Proprietà farmacocinetiche

Parametro	Valore	Unità
Assorbimento	3 ± 2%	%
C _{max} (3 cerotti per 12 ore/giorno)	85 ± 36 ng/ml (volontari sani) 52 ± 31 ng/ml (pazienti con PHN)	ng/ml
AUC (3 cerotti per 12 ore/giorno)	1259 ± 487 ore ng/ml (giorno 5)	ore ng/ml
T _{max} (3 cerotti per 12 ore/giorno)	11 ore	ore
Steady State	Entro 4 giorni	giorni
Legame alle proteine plasmatiche	70% (soprattutto alla albumina)	%
Metabolismo (epatico)	Deacilazione (CYP1A2, CYP3A4) e idrolisi	%
Eliminazione	Eliminazione renale; >85% escreto come metaboliti	%
Emivita di eliminazione (t _{1/2})	7,6 ore	ore

Lidocaina cerotto 5% Tollerabilità

Modalità d'azione topica

Assorbimento sistemico della lidocaina molto basso

- L'insorgenza di reazioni avverse sistemiche è improbabile
- Circa il 16% dei pazienti sperimenta reazioni avverse localizzate
- Queste reazioni sono in genere reversibili e di intensità da lieve a moderata
- Meno del 5% di queste porta alla sospensione del trattamento

DN4 Questionnaire [11]

Please complete this questionnaire by ticking one answer for each item in the 4 questions below:

INTERVIEW OF THE PATIENT

Question 1: Does the pain have one or more of the following characteristics?

1 - Burning	yes	no
2 - Painful cold		
3 - Electric Shocks		

Question 2: Is the pain associated with one or more of the following symptoms in the same area?

4 - Tingling	yes	no
5 - Pins and Needles		
6 - Numbness		
7 - Itching		

EXAMINATION OF THE PATIENT

Question 3: Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?

8 - Hypoesthesia to touch	yes	no
9 - Hypoesthesia to prick		

Question 4: In the painful area, can the pain be caused or increased by:

10 - Brushing	yes	no
---------------	-----	----

Attal et al. 2010 [7] Linee guida EFNS

Raccomandazioni per il trattamento farmacologico di prima, seconda e terza linea nella PHN

Raccomandazioni per la prima linea	Raccomandazioni per la seconda o terza linea	Livello A per efficacia	Livello B per efficacia	Livello A/B per inefficacia o risultati discordanti
Gabapentin Pregabalin TCA Cerotto con lidocaina	Capsaicina Oppioidi	Cerotti con capsaicina 8%*** Gabapentin Gabapentin RP** Cerotto con lidocaina Oppioidi [†] Pregabalin TCA [‡]	Capsaicina in crema Valproato*	Benzidamide topico Destrometorfano Flufenazina Memantina Lorazepam Mexiletina Inibitori della COX-2** Tramadol

*** Sono stati riportati solo i farmaci a dosaggi ripetuti in eccezione dei trattamenti con effetti prolungati come i cerotti con capsaicina.
† Lidocaina raccomandata specificamente in pazienti anziani.
‡ Morfina, ossicodone, metadone.
* Amitriptilina, nortriptilina, desipramina, imipramina.
** Non ancora disponibile per l'uso. PHN = Nevralgia post-erpetica; TCA = Antidepressivi triciclici; RP = rilascio prolungato

Dworkin et al. 2007/2010 [8-9] Linee guida NeuPSIG

Trattamenti di prima linea per il dolore neuropatico

- Antidepressivi
 - Antidepressivi triciclici, in particolare nortriptilina e desipramina
 - Duloxetina e venlafaxina
- Ligandi $\alpha 2-\delta$ dei canali del calcio
 - Gabapentin e pregabalin
- Lidocaina per uso topico
 - Per pazienti con dolore neuropatico periferico localizzato: lidocaina topica utilizzata da sola o in combinazione con una delle altre terapie di prima linea

0-10 NUMERICAL RATING SCALE

0 No pain 1 2 3 4 5 6 7 8 9 10 the worst pain imaginable