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EMLA: An Alternative to Transdermal Lidocaine for the Treatment of Post Herpetic Neuralgia in CRF Patients

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Case Report

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Abstract: The present case report describes use of eutectic mixture of local anaesthetic (EMLA) cream as an effective alternative to lidocaine patches for PHN treatment in patient with concomitant renal failure. In institutional setting, a 50 year old female patient of post herpetic neuralgia in right frontal region with concomitant chronic renal failure was treated by EMLA ointment. The response was evaluated in terms of reduction in scores of Numeric Rating Scale (NRS) up to three months. Patient reported significant pain relief with local application of EMLA after first and second line agents were discontinued on account of chronic renal failure of the patient. Hence, local application of EMLA cream could be a promising alternative for the treatment of neuropathic painful conditions like post herpetic neuralgia in special situations where other agents are contraindicated or not available.
Keywords: Postherpetic neuralgia; chronic renal failure; 5% lidocaine patch; EMLA ointment.

INTRODUCTION

Post herpetic neuralgia (PHN) is a persistent neuropathic pain of more than 3 month duration after healing of the lesions of herpes zoster (HZ) [1]. After a primary chicken pox infection, the Varicella-zoster virus (VZV) establishes latency in sensory ganglia throughout the nervous system [2, 3]. HZ (shingles) is the reactivation and spread of virus from a dorsal root or cranial nerve ganglion to the corresponding dermatome and neural tissue of the same segment [2, 3].

Thoracic dermatomes are the most commonly affected and account for 50% to 70% of all cases; cranial (especially the ophthalmic division of the trigeminal nerve), cervical, and lumbar dermatomes each account for 10% to 20% of cases, and sacral dermatomes are affected in 2- 8% of cases [4].

Early diagnosis and treatment with antiviral agents is believed to shorten the duration and severity of acute HZ and reduce the risk of PHN [5]. Once developed, it is a difficult condition to treat. It is being treated with anticonvulsants, antidepressants, non-steroidal anti-inflammatory drugs, and lidocaine and capsaicin transdermal patches. However availability of these drugs is not uniform across the globe.

The present case report describes use of topical application of EMLA cream as an effective alternative to lidocaine patches for PHN treatment in patient with concomitant renal failure.

CASE REPORT

A female patient aged 50 years presented to the pain clinic with complaints of pain in the right frontal region for past 4 months. Her pain was burning in character and associated with paresthesia and itching. It was episodic in nature, severe in intensity, with a severity of 80/100 as assessed with numeric rating scale, and partially relieved on taking a combination of paracetamol and tramadol. Her Doeuleur Neuropathique en four score (DN4 Score) was 4/10 and Diagnostic and Statistical Manual of Mental (DSM) Disorders four score was 13/27. Four months back patient was diagnosed with herpes zoster characterized by symptoms like fever, multiple lesions and pain in right frontal region. Patient was prescribed tab acyclovir, tab paracetamol and tab amitriptyline. After getting 3 weeks of treatment, all the symptoms subsided except for pain and 3 scar marks in the right frontal region. Patient was a renal transplant recipient and was also taking tab methylprednisolone 7.5 mg OD, tab tacrolimus 0.25 mg BD, tab calcium carbonate 500 mg BD for past 2 years. Along with this she was also taking tab carvedilol 3.125 mg BD and tab amlodipine 5mg OD for hypertension from past 10 years. She was also on insulin therapy for diabetes from last 1 year.

Her physical examination was only remarkable for 3 scar marks in the right frontal region with presence of allodynia in the affected area. Her investigations revealed serum urea 36mg/dl, creatinine 3.69 mg/dl, hemoglobin 9.6 gm%, TLC 8000/mm [3] and fasting blood sugar was 106mg/dl.

Based on the history and physical examination a diagnosis of PHN was established and therapy was started with tab gabapentin 100 mg TDS, tab amitriptyline 10 mg OD. Since acceptable pain relief was not there thus we increased the dose of tab gabapentin to 300 mg TDS. Patient reported 75% pain relief after 1 week of treatment with a reduction in pain (NRS score reduced to 20/100). But she was still having itching in the affected area. Her DSM score reduced to 4/27 and the size of the scars was also reduced. However, we were compelled to stop the above treatment on account of raised serum creatinine levels of 4.4 mg/dl[6].

Subsequently she was advised local application of EMLA cream thrice daily in the affected area followed by an occlusive dressing for one hour, as 5% lidocaine patches are not available at our location. On subsequent visits patient reported complete relief in both itching and pain with the use of EMLA cream. Patient was symptom free up to 3 months in the follow up.

DISCUSSION

Local application of EMLA cream in a patient suffering with PHN (right frontal region) was associated with improvement in her symptoms i.e. itching and pain.

Gabapentin, pregabalin, 8 % capsaicin patch and 5 % lidocaine patch provide an evidence-based approach as first line agents for the treatment of PHN, whereas opioid analgesics, tramadol and TCAs are more typically considered as second-line treatments because they generally require greater caution in the often elderly patient with PHN[7]. Based on the current evidence, we first started the treatment with gabapentin in the standard doses but later stopped it due to raised serum creatinine[6]. Then we thought of using topical agents, but the use of these topical agents is often limited by their non-availability and occurrence of mild to moderate localized skin reactions (erythema, rashes) [7]. This novel use of EMLA cream as an alternative to 5% lidocaine patch was done on account of the difference in mechanism of action and pharmacokinetics between two and non-availability of 5% lidocaine patch in India. To the best of our knowledge, this report is the first in literature using EMLA cream as an alternative treatment to 5% lidocaine patch in a patient of PHN with concomitant renal failure. The eutectic mixture of local anesthetics (EMLA) contains 2.5% lidocaine and 2.5% prilocaine which is being used for short therapeutic procedures [8]. On application of lidocaine patch to the skin, drug pass through epidermis and anesthetizes only superficial nerve endings with no effect on deep tissues. On the other hand, topically applied EMLA penetrates through the epidermis to act on sensory nerve endings (Aδ and C- fibres) in the dermis in order to provide effective anesthesia [8]. EMLA has a high water content (which softens the stratum corneum, making it more permeable) together with high proportion of the lipophilic, un-ionized (basic) form of anesthetic, which makes EMLA membrane permeable [8]. Another advantage of EMLA over conventional topical anesthetics is that, although the final proportion of anesthetic in EMLA cream is only 5%, which reduces the possibility of toxicity, the oil droplets within the emulsion are composed of 80% anesthetic, which provides a highly effective analgesic concentration [8]. As a result of which, EMLA is efficacious as a sole agent without any major adverse effects. Also it is easy to apply and is easily available. In terms of pharmacokinetics, all the amide local anesthetics are metabolized by microsomal enzymes in liver. The principal metabolite of lidocaine is xylidide and in humans 75% of xylidide is excreted in the urine as 4-hydroxy-2, 6-dimethylalanine [9]. The prilocaine metabolite o-toluidine and the hydroxylated metabolites of o-toluidine are excreted mainly in the urine [9]. The metabolites of lignocaine are more metabolically active as compared to metabolites of prilocaine which may accumulate in patients with impaired renal function. On application of 60 g EMLA Cream over 400 cm2 for 3 hours per day, 54 mg out of total 1500 mg lidocaine gets absorbed and peak blood levels of lidocaine are approximately 1/40 the systemic toxic level (0.12 µg/ml). Likewise, the maximum prilocaine level is about 1/70 the toxic level (0.07 µg/ml)[10]. Similarly with application of 3 patches of 5% lidocaine over 420 cm2 area for 11 hrs per day, around 64 ± 32 mg of lidocaine out of total 2100mg lidocaine gets absorbed and peak plasma concentration achieved will be approximately 0.13 ± 0.06 µg/ml, which is higher as compared to that with EMLA [11]. Moreover, EMLA cream contains lignocaine in lower concentration as compared to that in 5% lidocaine patch, thus chances of side effects due to the accumulated metabolites could be less with the use of EMLA cream as compared to lidocaine patch. The observed improvement in the patient's itching and pain following local application of EMLA cream and that too without any local anesthetic related side effect seems promising and needs to be evaluated further

CONCLUSION

In conclusion we suggest that local application of EMLA cream could be a promising alternative to 5% lidocaine patch for the treatment of neuropathic painful conditions in special situations like patients of PHN with concomitant renal failure.

Role of EMLA cream could also be evaluated in conditions of non-availability of 5% lidocaine patch or in situations where first line agents may be contraindicated like pregnancy, lactating mother, patients with suicidal behavior.

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