ESSAY

Capsaicin topical patches:

Capsaicin [6-nonenamide, N-[(4-hydroxy-3-methoxyphenyl) methyl]-8-methyl-, (6E)] is a mordacious ingredient in hot chili peppers. It is categorized under counterirritant class of drugs[1.] Capsaicin topical patches are the preparations which are used as an analgesic for various neuropathological conditions. It acts as a selective agonist for a ligand gated, non selective cation channel, that is transient receptor potential vanilloid 1 receptor (TRPV1). This receptor mainly expressed on nociceptive nerve fibers of the skin[2, 3.] Initial applications of capsaicin cause painful sensations. However, repeated applications results in temporary diminution of distal epidermal nerve fibers[4], which finally results in pain relief. Relief from pain occurs due to reduced expression of TRPV1 receptors on small diameter sensory axon fibers.

Indications:

- Capsaicin topical patches have FDA approved indication for post herpetic neuralgia management. Neuropathic pain associated with this condition can be successfully treated by capsaicin topical patches.[2]
- HIV associated distal polyneuropathy (DSP) can be managed with the help of capsaicin topical patches.[5,6]
- Several researches indicate the efficacy of capsaicin patches in the treatment of diabetic and other peripheral neuropathies.[7]
- Topical capsaicin is considered as the mainstay treatment regimen for postmastectomy pain syndrome.[7]
- 0.075% concentration topical capsaicin patches demonstrate significant improvement in stabbing pain and other overall painful conditions.[7]

Role in the treatment of neuropathic pain:

Capsaicin topical patches are FDA approved interventions for the management of neuropathic pains associated with post herpetic neuralgia. 8% topical patches are considered the most prophylactic and efficacious regimen for the management of Phase II and III post herpetic

neuralgia[5]. Upon application of patches, capsaicin absorbed fugaciously in the systemic system and its highest plasma level reach up to 4.6 ng/mL, after removal of topically applied patches. But this concentration was no longer detectable in plasma after 3 – 6 hours of patch removal.[2]

To assess the effects of capsaicin in phase III neuralgic conditions, numeric pain rating scale (NPRS) is used. This is an 11 point scale and its rating ranges from 0 to 10. Here, 0 refers to the no pain condition where 10 indicate the worst possible pain. In post herpetic phase III conditions, pain levels of past 24 hr used as a reference[8].

Patient global impression of change (PGIC) was the other parameter used to assess the efficacy of capsaicin topical patches. This scale ranges from +3 (worse pain) to -3 (improved condition). Here 0 refers to no pain. In this, patients were compared before and after the treatment, and PGIC was evaluated at weeks 8 and 12 [8].

Capsaicin 8% patches substantially reduce the NPRS and PGIC scores at 8 and 12 weeks after patch application, when compared to controls. More than 40% patients reported with 30% reduction in NPRS scores, compared to 30% patients with 20% reduction with the control group[8] (NNT=10, 95%CI not calculable).

Capsaicin topical patches (NGX-4010) are also useful in providing analgesia in severe chronic pain from HIV – DSP (Distal sensory polyneuropathy). High concentration dermal patches are designed to deliver high doses of capsaicin in a single short application period. Trials for this study included patients between 18 – 75 years of age. Predominantly male patients (9 male, 3 female) were involved in the study. Average age of patients was 44 years. Six patients (50%) were Caucasian, and six (50%) were African American and all patients presented with symptoms of painful distal polyneuropathy due to HIV. Mean duration of HIV associated polyneuropathy was 3.6 years (range0.5-10.1 years), and mean (SD) pain intensity rate was 5.6 - 1.4 (range, 3.6-8.2) at the time of screening[9].

NPRS scores were used to evaluate the efficacy of capsaicin. Average pain scores required to be 3 – 9 according to this study [10.] Results conclude 40% reduction in pain, when compared to pain rating at the time of screening. These results based upon the pain scoring for past 24 hours. Mean change in NPRS scores from 2 to 12 weeks was - 2.4 (95% CI: -3.9, -0.9; P = 0.006). Pain

reduction after capsaicin patches application, starts from the very first week and persist throughout the 12 weeks period. Mean reduction in pain from the time of screening, at week 12 (n = 9) was - 41% (95% CI: 18%, 65%) [9].

Advantages:

Following are the advantages related to the capsaicin topical patches[9].

- Capsaicin is useful drug regimen for the treatment of neuropathic and non neuropathic pain.
- It shows additive effects when used with other agents.
- There is no particular site as far as capsaicin application is concerned. Multiple sites can be used for its application.
- Capsaicin is particularly efficacious in the treatment of neuropathological conditions in relieving pain, as described above.
- This drug is relatively safer with lack of toxic effects, compare to other available regimens for the treatment of neurogenic pain. Apart from the transient local pain and erythema , capsaicin is a well tolerated drug and no safety issues hamper its use.

Disadvantages:

Capsaicin is an efficacious and safer drug, still some adverse effects argues about its persistence as a future drug regimen. These effects mainly include erythema, pain, papules and pruritis at the site of application[2]. It may also cause hypertension, which is due to treatment related pain. Cardiovascular problems and hypertension cases should be treated with caution[2]. Aerosolization of capsaicin can also occur, if patch does not remove properly[2]. Some other side effects are - bacterial pneumonia, car accident, drug abuse relapse, increased back pain, intermittent increased perspiration, low back pain, lung congestion, vaginal yeast infection, vivid dreams, and weight loss[2].

LIDOCAINE TOPICAL PATCHES:

Lidocaine is categorized under local anesthetic medications[11]. .025 - .075% concentration of topical patches of lidocaine are used to relieve pain in neuropathologic conditions like, shingles

(Herpes zoster infection) [12]. It also helps in reducing sharp, aching pain in overly sensitive skin areas. Topical patches act by transient reduction of sensations at the site of application.

Indications:

- Topical lignocaine patches are mainly used to treat post herpetic neuralgia pain (shingles) in some patients. But this is not considered as a first line therapy[13.]
- Tinnitus can be treated in some cases with topical patches. Complete cure is not reported, but it reduces the illness approx. by two thirds[14].
- Knee osteoarthritis[15] (OA) and chronic low back pain[16] can be managed by topical patches of lignocaine.
- Lidocaine topical is also used to reduce discomfort caused by skin irritations such as sunburn, insect bites, poison ivy, poison oak, poison sumac, and minor cuts, scratches, hemorrhoids, and burns[10].

Role in the treatment of neuropathic pain:

Lidocaine is an aminoethylamide local anesthetic[17]. It acts by blocking voltage gated sodium channels and thus reduces the frequency of ectopic discharges[18]. In this way, it decreases pain sensation. To manage pain associated with PHN, lidocaine 5% medicated plaster is an optimum regimen. It consists of 5% lidocaine (w/w) in aqueous adhesive on a soft hydro gel dressing[19]. It acts in a dual manner to treat PHN pain. Initially topical application reduces pain within an hour of application and also maintains low plasma lidocaine concentration[20] to reduce chances of adverse effects and secondly, plaster helps in reduction of allodynia and brushing[21].

Lidocaine acts on sensitized, hyperactive cutaneous nociceptors. Capsaicin and sun burn models[22, 23] used to investigate the efficacy of topical lignocaine. 32 volunteers were included in this randomized double blinded placebo controlled study. Results indicate marked reduction of hyperalgesia with lignocaine compared to placebo (capsaicin: more than 50% reduction, sunburn: reduction of 73%) [23].

Advantages:

Lignocaine topical plasters have long term tolerability, because it is not associated with any pharmacokinetic interactions. Lignocaine plasters are used mainly for the treatment of focal neuropathic pain syndromes with localized symptoms as single therapy or in combination with

other treatments[24, 25, 26.] Plasters also have practical significance; they are easy to apply and easy to cut. They protect the skin from any kind of mechanical stimulations, which is important in allodynia cases.

Lignocaine is helpful in reduction of refractory polyneuropathy pain. A study of 20 patients, reported that pain relief from the lidocaine plaster was 3.8 on a scale ranging from-5 (extremely dissatisfied) to +5 (extremely satisfied) [27].

To assess the efficacy of lidocaine in pain relief, several studies have been conducted. The first RCT concludes that lidocaine patches significantly improve pain compared with placebo (improvement: 29/32 [91%] with lidocaine *v* 13/32 [40%] with placebo; RR 2.23, 95% CI 1.45 to 3.44; NNT 2, 95% CI 1 to 3)[26].

Disadvantages:

These are application site related reactions, papules (4-28%) and local erythema (14- 15%) [28]. There are no systemic adverse effects associated with lidocaine plasters.

Conclusion:

Neuropathic pain is difficult to manage and many patients have pain that is refractory to existing treatment regimens. On the basis of several studies and researches it has been concluded that lidocaine and capsician both are useful to treat Neuropathological pain. But due to less safety margin and adverse effects associated with the capsaicin it is not considered as a first line drug therapy for this condition. Topical lidocaine (5%w/w) has shown efficacy in NP and recommended as first line of drug for its management. Lidocaine is particularly useful in patients with peripheral NP and allodynia[29.] Another study also favors the use of lidocaine patches over capsaicin for PHN and allodynia and in patients who have allodynia due to different types of peripheral NP[30.]. Thus over all evidences indicate the foremost importance of lidocaine. But capsaicin does not stand as a therapeutic regimen for polyneuropathic pain management.

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