Sublingual Buprenorphine: A Feasible Alternative for Treating Breakthrough Chronic Pain

Sir,

Chronic cancer pain manifests in two forms. The first is background pain which is the pain experienced by the patient throughout the day. The second is breakthrough pain (BTP) which is acute exacerbation of the pain.[1] BTP is defined as a transient exacerbation of the pain that occurs either spontaneously (incidental) or in relation to a specific predictable or unpredictable trigger, despite relatively stable and adequately controlled background pain.[2] BTP is severe, unbearable most of the times and is a reason for depression and anxiety among all patients as it affects the quality of life. Almost 65% of cancer patients suffer from BTP. A prescription for BTP is essential for all pain clinic patients who have chronic cancer or noncancer pain. The medication needs to be rapid in onset and has minimal first-pass metabolism.

BTP is usually managed with sublingual (SL)/buccal tablets or films, lozenges, SL spray, and intranasal delivery of medication. Fentanyl and buprenorphine are the drugs available in such preparations. In resource-limited areas, BTP is managed with intravenous or subcutaneous opioids.[3] This is usually not very practical, especially for a patient who is an outpatient.

Buprenorphine hydrochloride is a partial μ-receptor agonist, an oxidized low-density lipoprotein receptor-1 agonist, and a delta and kappa receptor antagonist. It is classified as a Schedule III controlled substance. It is used for managing acute surgical pain and cancer and non-cancer pain.[4] It has a unique distinction of being having the US-FDA approval for three unrelated indications: opioid detoxification, opioid maintenance, and pain management. Buprenorphine is available for intravenous use, as a per rectal suppository, as a transdermal patch, and as an SL preparation (tablet and film). Due to its extensive first-pass metabolism enzyme CYP3A4 in the gastrointestinal tract when taken orally, it is not effective by this route. When used SL, there is 30%–60% of bioavailability as hepatic first-pass metabolism is avoided. This property makes SL buprenorphine an effective drug for treating BTP.

SL buprenorphine is available as a 200 μg/tablet. The tablet usually takes 10 min to dissolve and around 60–90 min to achieve maximum plasma concentration. A single dose offers pain relief for up to 6 h after SL administration. Other issues with commonly used opioids such as addiction, abuse, and tolerance are less with buprenorphine as it is not a pure agonist but is a partial agonist. Buprenorphine is also used in combination with naloxone for reducing opioid dependence and for opioid substitution therapy.[5] The dose used for opioid dependence is different. It is started as 2 mg SL tablet and gradually increased as tolerated up to 24 mg/day along with naloxone. Such high dose is not indicated in opioid-naïve patients and is reserved for treating opioid dependence. At present, there is no clarity regarding equianalgesic dose of buprenorphine and other opioids. In the systematic review published by Cote and Montgomery, they felt that although SL buprenorphine has all properties of being a useful analgesic in treating chronic pain conditions, the current evidence is insufficient.[6] Being a partial agonist and also actions at several receptors, regular dose of naloxone does not reverse its clinical effects.

To conclude, SL buprenorphine is another alternative for treating BTP as it gets absorbed fast, has a rapid onset of action, and has a better adverse effect profile compared to other opioids.

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Conflicts of interest

There are no conflicts of interest.

Abhijit S Nair, Srinivasa Shyam Prasad Mantha, Kodisharapu Praveen Kumar, Basanth Kumar Rayani

Department of Anaesthesiology, Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad, Telangana, India

Address for correspondence: Dr. Abhijit S Nair, Department of Anaesthesiology, Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad - 500 034, Telangana, India.
E-mail: abhijitnair95@gmail.com

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