HTX-011: Another game changer multimodal analgesic or an ephemeral, experimental drug!

To the Editor,

Moderate to severe pain is experienced by the majority of patients postoperatively if multimodal analgesia (MMA) using several analgesics with a different mechanism of action is not used after surgery. Opioid analgesics are quite effective in managing postoperative pain but the issues with rampant perioperative use of opioids are well established. Opioid sparing strategies are extensively used by researchers in an attempt to reduce opioid use and also provide comprehensive, MMA in the perioperative period.[1] Liposomal bupivacaine was developed with the idea of prolonging the duration of action of conventional bupivacaine from 8–10 hrs to 72–96 hrs using nanotechnology.[2] Liposomal bupivacaine, marketed as Exparel (Pacira Pharmaceuticals, Inc., Parsippany, N.J.) comprises of vesicles of bupivacaine loaded in the aqueous chambers using DepoFoam® technology (Pacira Pharmaceuticals Inc, San Diego, CA). The safety of liposomal bupivacaine has been established after reviewing its use in epidurals, abdominal wall blocks, peripheral nerve blocks, and surgical incision sites.[3]

The research continued and later Heron Pharmaceuticals developed HTX-011, which is another member of the armamentarium of MMA. HTX-011 is an extended-release, fixed-ratio product that comprises of bupivacaine as the main drug along low-dose meloxicam to enhance the effectiveness of infiltrated bupivacaine. This combination is integrated into a bioerodible polymer (Biochronomer). When HTX-011 is injected in the surgical site, there is controlled hydrolysis of the polymer as a result of which there is sustained release of both bupivacaine and meloxicam for 3 days.[4] The efficacy of bupivacaine is reduced when the pH is acidic. Inflammation at the surgical site reduces the pH and thus efficacy of infiltrated bupivacaine is affected. Meloxicam owing to its anti-inflammatory effects normalizes the pH (which starts at around 8 hrs after the infiltration) thereby restoring and enhancing the efficacy of infiltrated bupivacaine.[5] The paper by Ottoboni *et al*. described preclinical animal and clinical results (for bunionectomy and herniorrhaphy) about the use of HTX-011 in providing good analgesia when compared to liposomal bupivacaine and placebo.[6] Studies showed that HTX-011 was well tolerated in patients and safety was equivalent to bupivacaine. Other issues of concern like local anesthesia systemic toxicity (LAST) and interference with wound healing was negligible with the use of HTX-011.

There are several ongoing studies that might throw light on safety, efficacy, and opioid-sparing capabilities of HTX-011 when compared to other agents subsequently. Unlike liposomal bupivacaine, which has been used in epidurals and peripheral nerve blocks, the use of HTX-011 will be limited to wound infiltration only due to the presence of meloxicam thus limiting its indications. The cost of the product is currently not known and availability would be another issue with its use. The company has not yet made clear the concentration of bupivacaine/meloxicam and the volume of the drug in a unit of HTX-011. As of now, the United States- Food and Drug Administration (US-FDA) has not approved HTX-011 and is under review.

To conclude, HTX-011 appears as a safe and effective modality in managing postoperative pain. The drawbacks could be limitations in use, i.e., only at the incision site and not in peripheral nerve blocks. The popularity and use will depend on the cost of the product after approval and availability all over.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 20-Mar-2020, **Accepted:** 21-Mar-2020, **Published:** 30-May-2020

References

1. Kumar K, Kirksey MA, Duong S, Wu CL. A review of opioid-sparing modalities in perioperative pain management: Methods to decrease opioid use postoperatively. Anesth Analg 2017;125:1749-60.
2. Chahar P, Cummings KC 3rd. Liposomal bupivacaine: A review of a new bupivacaine formulation. J Pain Res 2012;5:257-64.
3. Vyas KS, Rajendran S, Morrison SD, Shakir A, Mardini S, Lemaine V, *et al*. Systematic review of liposomal bupivacaine (exparel) for postoperative analgesia. Plast Reconstr Surg 2016;138:748e-56e.
4. Balocco AL, Van Zundert PGE, Gan SS, Gan TJ, Hadzic A. Extended release bupivacaine formulations for postoperative analgesia: An update. Curr Opin Anaesthesiol 2018;31:636-42.
5. Kaye AD, Novitch MB, Carlson SF, Fuller MC, White SW, Haroldson AR, *et al*. The role of exparel plus meloxicam for postoperative pain management. Curr Pain Headache Rep 2020;24:6.
6. Ottoboni T, Quart B, Pawasauskas J, Dasta JF, Pollak RA, Viscusi ER. Mechanism of action of HTX-011: A novel, extended-release, dual-acting local anesthetic formulation for postoperative pain Reg Anesth Pain Med 2020;45:117–23.

Access this article online	
Website: www.saudija.org	**Quick Response Code**
DOI: 10.4103/sja.SJA_227_20	

How to cite this article: Nair A, Mantha SS, Suvvari P, Anne P. HTX-011: Another game changer multimodal analgesic or an ephemeral, experimental drug! Saudi J Anaesth 2020;14:419-20.