Calcitonin as an alternative in pain management- present status

To the Editor,

Calcitonin (CT) is a 32-amino acid polypeptide released from the parafollicular C cells of the mammalian thyroid gland [Figure 1]. CT regulates calcium homeostasis in the body, especially during phases like growth, pregnancy, lactation, and menopause, where calcium is of utmost importance. Exogenous CT supplementation is indicated under certain conditions like osteoporotic fractures, pathological fractures, and Paget's disease. This was hypothesized due to an increase in bone mass with its use. US-FDA has approved the use of CT in hypercalcemia of malignancy, Paget's disease, and prevention of acute bone loss in immobilized patients.[1]

CT supplementation is useful under several other conditions like lumbar spinal canal stenosis, diabetic neuropathy, phantom limb pain, trigeminal neuralgia, acute postoperative pain, reflex sympathetic dystrophy, migraine, metastatic pain, post-herpetic neuralgia, and complex regional pain syndrome after stroke all of which are off-label uses. This beneficial effect is not due to its effect on calcium homeostasis. Studies have shown that calcitonin could inhibit the signals associated with melastatin-8 and ankyrin-1 receptor, which possibly contributes to analgesia conferred by calcitonin in peripheral neuropathy.[2]

In a study where salmon CT nasal spray was used successfully in patients suffering from migraine, the authors hypothesized that the pain relief conferred could be due to an increase in the amount of endorphin, adrenocorticotropic hormone, and corticosteroid hormones after CT administration.[3]

The other plausible yet unproven mechanisms of action of CT in analgesia are thromboxane and prostaglandin inhibition, dural mast cell stabilization, inhibition of c-fos expression and thus suppression of the activation of the trigeminovascular system, decreased transcription of the sodium channel in dorsal root ganglion neurons mediated by CT-dependent signal activated by nerve injuries, and to decrease serotonin transporters and increase the expression of the serotonin receptors of the thalamus. Most of the research papers are based on animal studies.[4,5]

Gabopoulou *et al*.[6] investigated the efficacy of 100 IU epidural CT and compared it with local anesthetics and fentanyl epidurally. In this small sample size study, the authors concluded that epidural CT when combined with local anesthetic provided good quality analgesia, stable hemodynamics, with controlled blood sugars intraoperatively without an increase in intraoperative cortisol.

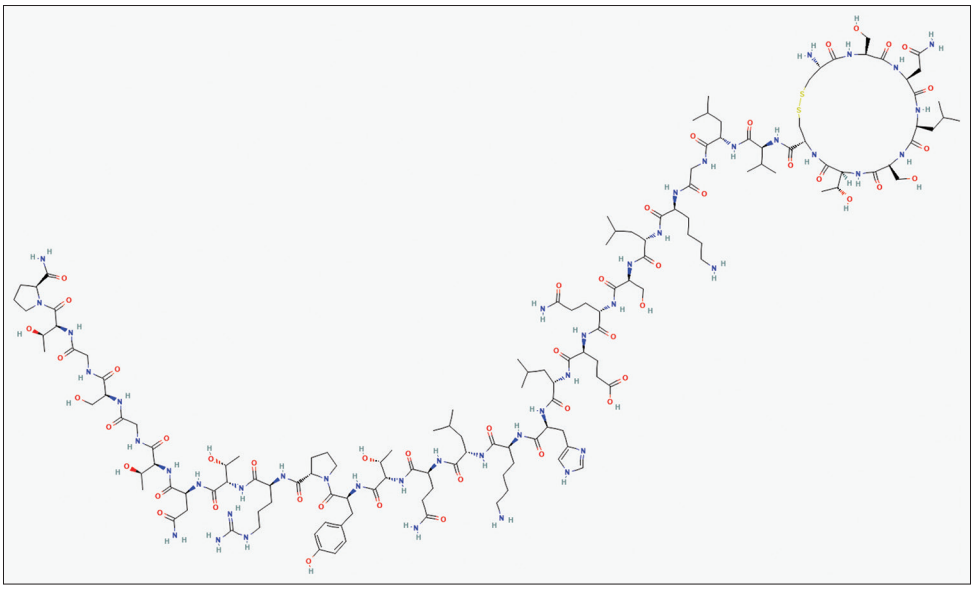

Figure 1: Chemical structure of Salmon Calcitonin. (Image source: National Center for Biotechnology Information (2022). PubChem Compound Summary for CID 16133812, Calcitonin salmon. Retrieved February 2, 2022 Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Calcitonin-salmon.)

At present salmon CT (molecular formula: C145H240N44O48S2, Figure 1) is commercially available in an injectable form (subcutaneous), which is 100-200 IU/ml, as a nasal spray (200 IU/actuation). Efforts are being made to manufacture CT that can be administered orally which can be resistant to gastric acid and is well tolerated by patients. CT can be considered as a viable alternative in patients with chronic pain in whom non-steroidal anti-inflammatory drugs are contraindicated, opioids are not effective, and other lines of drugs have failed to provide satisfactory relief. Further studies need to be conducted to establish the efficacy of CT in acute pain by comparing it with routinely used analgesics.

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Conflicts of interest

There are no conflicts of interest.

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