Phantom Limb Pain Management: Illustration of Two Cases

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The case series shows phantom limb pain (PLP) phenomenon in major lower limb amputation in early postoperative period in young patients. Phantom Limb Pain is the pain that develops over an amputated limb that no longer exists and has been described in a variety of ways and is characteristically localized in the distal area of the phantom limb. The pain may be constant and of varying intensity or intermittent episodes of high-intensity pain on a more or less frequent basis. Perioperative pain management of patients undergoing major limb amputation is indeed complex and challenging. The duration of symptoms is unpredictable and the management multimodal but the results of the methods are inconclusive.

Keywords: multimodal analgesia, phantom limb pain, phantom pain management.

A multidisciplinary as well as multimodal approach is often necessary to improve pain management and quality of life in patients with phantom pain. The term 'phantom sensation' describes any sensation excluding pain that is experienced in the absent part. Phantom pain normally occurs within the first week after amputation but may also develop months or years later. Phantom pain has been described in various terms (e.g. shooting, burning, cramping, and aching) and is typically in the distal area of the phantom limb. The episodes are intermittent, high-intensity pain on a daily, weekly, or less frequent basis. The duration of symptoms is unpredictable with some resolving in months in a few subjects to others persisting for years. Incidence, as per recent evidence, suggests rates of approximately 50-78%.[1] Four risk factors have been identified as: pre-amputation pain, presence of persistent stump pain, bilateral limb amputations, and lower limb amputations.[1] The incidence of phantom pain appears to be independent of age in

adults, gender and level, or side of amputation. It is less common in children and congenital amputees. Phantom pain might be a phenomenon of the CNS that is related to plastic changes at several levels of the neuraxis and especially the cortex.[2]

Case Series

Case 1

A 26-year-old male patient (70 kg) presented to the operation room for a left-sided below-the-knee amputation. The patient had presented to the emergency room 4 days back, sustaining a crush injury in the right leg with an open fracture of the shaft of tibia and fibula after a motor vehicle accident. He has no significant medical or surgical history (ASA I). There were no other injuries. During the pre-anesthetic checkup in the ICU, the patient looked ill. His vital parameters were normal. but had severe pain in the limb.

Figure 1: Right side below the knee amputation

Preoperatively, his systemic examination provided normal findings. He was receiving round-the-clock paracetamol 1 g IV TDS, ketorolac 30 mg IV TDS, fentanyl infusion 30 mcg/hr, pethidine im 50 mg SOS, tramadol IV 50 mg SOS, fentanyl IV 50 mg SOS preoperatively in the ICU. He had undergone multiple debridement prior to the planning of below-the-knee amputation as his limb was declared not viable. In the intraoperative period, the patient was pre-medicated with 2 mg IV midazolam, and 150 mcg IV fentanyl was given for analgesia and anesthesia was induced with 150 mg IV propofol, and 7 mg IV vecuronium for facilitation of tracheal intubation. For analgesia IV paracetamol 1 g, IV ketrorolac 30 mg and IV dexmedetomidine 50 mg were also given intraoperatively. The patient was hemodynamically stable and was easily ventilated and oxygenated. Maintenance of anesthesia was done with isoflurane, vecuronum, oxygen and IPPV. A total of 1300 ml lactated Ringer's solution and 1-pint whole blood was administered during the 1-hour 30mins surgical procedure. Reversal of NM blocker was done with 2.5 mg IV neostigmine and 0.6 mg IV glycopyrrolate. Suctioning of oropharynx was done and the patient was extubated.

Postoperatively (**Figure 1**), he developed a typical phantom limb sensation as well as Phantom Limb Pain in the first week of below-the-knee amputation. He had intermittent type of mild to severe pain in the distal part of the amputated limb, mostly

the toes. The pain was of pricking and burning type and it resembled the intensity of pain in the injured limb prior to the amputation. The patient was continued on fentanyl infusion 30 mcg/hr and titrated as demanded, IV paracetamol 1 g TDS, IV ketorolac 30 mg TDS, IV tramadol 50mg SOS and IV pethidine 50 mg SOS. Along with this tab pregabalin 75 mg BD, tab quitiapin 12.g mg IV HS and psychological counseling was done.

Case 2

A 32-year-old male patient (65 kg) had presented to the operation room for a left-sided below-the-knee amputation. The patient had presented to the emergency room 2 days back sustaining a crush injury in the left leg with an open shaft of tibia and fibula fracture, a left femur fracture and a left-side superior rami fracture, after a large rock fell on his leg at a construction site. He had no significant medical or surgical history. He was a smoker and consumed alcohol occasionally (ASAII.) He didn't sustain injury in other vital organs during the trauma. After multiple debridements and external fixator application in leg, the leg was not viable. Thus below-the-knee amputation was planned along with an external fixator application in the left femur. During pre-anesthetic checkup in the ICU, the patient looked ill. He had sustained vital parameters but had severe pain in the limb. Preoperatively, his systemic examinations were normal. He was receiving round-the-clock paracetamol 1 g IV TDS, Ketorolac 30 mg IV TDS, fentanyl infusion 20 mcg/hr,pethidine IM 50 mg SOS, preoperatively in the ICU. In the intraoperative period, patient was pre-medicated with 2 mg IV midazolam, and 150 mcg IV fentanyl was given for analgesia and anesthesia was induced with 150 mg IV propofol, and 7 mg IV vecuronium for facilitation of tracheal intubation. For analgesia IV paracetamol 1g, IV ketrorolac 30 mg and IV dexmedetomidine 50 mg was given intraoperatively. The patient was hemodynamically stable with some blood loss and was easily ventilated and oxygenated. Maintenance of anesthesia was done with isoflurane, vecuronum, oxygen and IPPV. A total of 1000 ml lactated Ringer's solution and 1 pint whole blood, 2 pint FFP was administered during the two-hour surgical procedure. Reversal of NM blocker was done with 2.5 mg IV neostigmine and 0.6 mg IV glycopyrrolate. Suctioning of oropharynx was done and patient was extubated.

Postoperatively, the patient developed typical phantom limb sensations and Phantom Limb Pain in the first week of amputation. The pain was intermittent, mild to severe pain in the distal part of the amputated limb, mostly the toes. The pain was of pricking and burning type and it resembeld the intensity of pain in the injured limb prior to the amputation the patient was continued on fentanyl infusion 20mcg/hr and titrated as demanded, IV paracetamol TDS, IV ketorolac TDS, IV tramadol 50mg SOS and IV pethidine 50mg SOS. Along with this tab pregabalin 75 mg BD, and psychological counseling was done.

Discussion

The patients' history, perioperative and in ICU/ hospital course of events and clinical examination were all consistent with the diagnosis of Phantom Limb Pain. This case description illustrates the most salient aspects of this type of pain. Both our cases are trauma-induced crush injury of leg and foot and developed Phantom Limb Pain. There were no any other organ injury or systemic derangement as the patients were under strict critical care protocol including maintenance of vital parameters, infection control, nutrition, pain management, etc. under a multidisciplinary team of intensivists, anesthesiologists and orthopaedic surgeon. Prior to amputation the management of pain was based on NSAIDs (ketorolac and paracetamol) and opiates (tramadol and pethidine). Our patients received General anesthesia and opiate based analgesia along with NSAIDs for the pain management intraoperatively and none of the regional techniques, neuraxial block, or peripheral nerve blocks were used. Postoperatively, the Phantom Limb Pain and stump pain was managed with multimodal analgesic techniques including fentanyl infusion in titrating doses along with NSAIDs, pregabalin, amitryptyline and counseling. Both the patients complain of inadequate analgesia despite the systemic analgesic approach.

In retrospective view of the cases the shortcomings in our management was not considering the use of regional anesthesia for pain management and aggressive use of opiates despite their notorious side effects. A recent study shows that optimized epidural or systemic analgesia initiated 48 hours preoperatively was indeed effective in reducing PLP at 6 months.[4] Although there remains a general controversy surrounding the issue of preemptive analgesia and its favourable effects on postoperative pain relief.[5] Patients experienced significantly less pain during the first week after their amputation if they received epidural or peripheral nerve block compared with patients who received general anesthesia or spinal anesthesia. Anesthetic technique might not affect Phantom Limb Pain at 14 to 17 months after. Further studies are needed to determine if such patients may benefit from epidural or peripheral blocks instead of general anesthesia or spinal blocks.[6]

Though the exact mechanism is still unknown, it is believed the Phantom Limb Pain is initiated by changes arising in the periphery that alter the afferent input that the brain and spinal cord receive which leads to central reorganization and changes that contribute to the development of phantom pain. The peripheral mechanisms include alterations in the afferent nerve supply to the central nervous system that arise as a result of ectopic discharge from afferent nerves at the amputation site and from any neuromas resulting from damaged nerves; increased sensitivity of any neuromas to mechanical and chemical stimuli; ectopic discharge from cells in the dorsal root ganglia, linked to the upregulation of voltage-gated sodium channels; or sympathetically maintained afferent input from the amputation site

secondary to coupling between the sympathetic system and the sensory nervous system. Two spinal cord mechanisms are proposed. The anatomical reorganization occurs within the spinal cord after peripheral nerve injury. Central sensitization of dorsal horn cells occurs in response to the increased barrage of painful stimuli from the amputation site. This state of hyperexcitability leads to the development of hyperalgesia, where the patient experiences an exaggerated response to noxious stimuli. Supraspinal mechanisms state that cortical reorganization has been demonstrated by magnetoencephalogram studies in both humans and monkeys after limb amputation. Phantom Limb Pain may arise from errors occurring in this cortical remapping process, leading to over-amplification of the pain experienced. There may also be errors in the sensory modalities, with touch being experienced as pain.[1-3]

The principle behind multimodal analgesia is the synergy between agents in interfering with pain pathways at multiple anatomic and pharmacologic sites and decreasing overall side effects, specifically through opioid-sparing effects.[3] Paracetamol is useful for treating initial postoperative pain, but is of little use in the treatment of Phantom Limb Pain. Opioids offer good pain relief for the immediate postoperative period. The use of opioids for the treatment of certain patients with chronic neuropathic pain is evidence based.[2] An observational study shows association between the pre-amputation use of opioids as a risk factor in the eventual development of Phantom Limb Pain.[7] There is some evidence that opioids may interrupt central cortical reorganization where Phantom Limb Pain is thought to originate. Morphine, given orally or intravenously, has been shown to reduce PLP in the short term.[8]

In the treatment of acute and chronic neuropathic pain after lower limb amputation, multiple drugs have shown beneficial effects including gabapentinoids, NMDA receptor antagonists, antidepressants, lidocaine, calcitonin, clonidine, and Botulinum neurotoxin. Nonopioid and nonsteroidal anti-inflammatory drugs (NSAIDs) are appropriate for alleviating postsurgical inflammatory pain but not for the prevention of neuropathic PLP**.** Gabapentin has opioid-sparing effects and prevent opioid tolerance but its efficacy in PLP management is inconclusive with side effects of somnolence, dizziness, headache, and nausea. Pregabalin, while showing some success in the treatment of neuropathic pain, also has dose-limiting side effects. The NMDA receptor antagonists, ketamine and dextromethorphan, have provided some benefit in reducing PLP in the short term. Use of ketamine has exhibited side effects of loss of consciousness, sedation, hallucinations, hearing and position impairment, and insobriety. Inconclusive results in reducing PLP were found with memantine therapy. Amitryptyline was determined to have inconsistent benefits in the treatment of PLP.[3] However, one article reported success in abolishing PLP with

amitriptyline and tramadol.[9] A case reported of four patients who exhibited a marked (>50%) reduction in PLP with the use of mirtazapine.[10]

Preemptive analgesia is an interesting concept where adequate and effective attenuation of peripheral and central sensitization to noxious stimuli is provided throughout the preoperative, intraoperative, and postoperative phases.[11] Multimodal analgesia, extending into the preoperative phase, is suggested to provide such preventative analgesia Opioid-sparing effect may be seen with the use of regional anesthesia.[12] Immediately following amputation, there is a continuous barrage of painful sensory input that results in inflammatory changes both peripherally and centrally. The transmission of painful stimuli along the pain pathway to the cerebral cortex is interfered by regional anesthesia.[13] Unlike continuous epidural or spinal anesthesia, continuous perineural analgesia is simple to administer, avoids risks and costs, and the complications of hemodynamic alterations in highly susceptible patients. Fisher and Meller pioneered the use of an intra-incision nerve block catheter, positioned at the distal end of the sciatic or posterior tibial nerve, inserted by the surgeon at the time of lower limb amputation. A bolus dose of local anesthetic is injected into the catheter by the anesthesiologist as per standard dosing to confirm placement prior to closure of the wound and to provide regional analgesia. This infusion is continued till the first dressing change on postoperative day five, when the stump catheter is removed. Patients did not complain of Phantom Limb Pain for approximately one year following amputation.[14] Non pharmacological strategies have shown limited efficacy (except for mirror therapy). Stress, anxiety, depression, and other emotional factors have been associated with the persistence and exacerbation of PLP.[3] A few case reports support the use of acupuncture in the treatment of Phantom Limb Pain in some patients with no strong evidence base. External heat and cold, ultrasound, transcutaneous electrical nerve stimulation, massage, adjustment of the prosthesis and manipulation of the stump have all been used with success. A mirror box has been used under these circumstances. A mirror is placed vertically in the centre of a wooden or cardboard box from which the top and front surfaces are removed. The patient places his normal hand on one side and looks into the mirror, thus creating the illusion that the amputated hand has returned and allowing the patient to visualize the unclenching of the phantom spasm. Most surgical procedures used for phantom pain have shown poor results. Stimulation of the spinal cord has been shown to decrease Phantom Limb Pain in some cases, but there are no randomized controlled trials.[1]

Conclusion

The mechanisms of pathophysiology of post amputation phenomena of pain remain incompletely understood. It is hoped that implementation of a strategy utilizing a multimodal analgesia protocol will address and enable pain control management at

these multiple complex levels and pathways. Pain following amputation may interfere with an individual's functioning, psychological well-being, and may even result in the development of chronic pain. It is important for health care practitioners to be aware of the various analgesic options and interventions available for an aggressive pain management plan promoting recovery and rehabilitation. Further inquiry is required for more effective ways to control pain in such patients.[1- 3]

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