

phantom limb pain (PLP), the phantom limb sensation (PLS) and the stump pain (SP). These elements often coexist in each patient and may be difficult to separate. The PLS differs from PLP in being any sensation but pain. Numbness, feelings of posture and movement may be felt to varying degrees. A peculiar phenomenon, “telescoping” may occur rarely when the distal part of the phantom is gradually felt to approach the residual limb and in the end, may even be experienced within the stump. SP and PLP are interrelated phenomena and amputees with SP have a higher prevalence of PLP as compared with amputees without SP.^[2] PLP is primarily localized in distal parts of the missing limb. It is intermittent, variously described as shooting, stabbing, boring, squeezing, throbbing, or burning. Incidence of PLP is nearly 60-80% of all amputations. Estimations based on the patient’s request for pain relief grossly underestimates the incidence, with many patients not reporting for fear of being labeled mentally disturbed.^[2,3]

There has been a lot of research into the etiologies and factors affecting the incidence of PLP. There is now evidence for both peripheral and central contributions to PLP. Peripheral factors include novel expression or up-regulation of sodium channels, spontaneous activity and increased sensitivity of the dorsal root neurons to both mechanical and neurochemical stimulation as well as activation of the postganglionic sympathetic fibers. A central reorganization of the neurons of the primary somatosensory cortex, sub cortex and thalamus has also been seen in experimental studies.^[2,4,5]

An understanding of the mechanisms underlying PLP has led to new and rational types of treatments. There is a trend of transition from pharmacotherapy to more of behavioral techniques and psychotherapy. One such technique, “mirror therapy” has showed promise in the few studies and case reports where it has been described.^[4,6] Based on the common causes of amputation, two cases of different etiologies of PLP are described so as to highlight the hypothesis that the response to behavioral and adjuvant therapy differs as per the etiology of the amputation.

A 21-year-old male sustained a gunshot wound left knee with vascular injury (femoral and popliteal artery) and was evacuated to the closest secondary-care hospital after initial tactical field care. On evaluation by the surgeon, no pulses were detected in the left lower limb. With ongoing resuscitation, an end-to-end anastomotic repair of the arteries was performed. Postoperative (PO), adequate flow was present in the lower limb with palpable peripheral pulses. On 1st PO day, posterior tibial artery pulse was found to be feeble with absent anterior tibial artery pulsations. Clinically suspecting compartment syndrome, an emergency fasciotomy was undertaken and patient evacuated to this tertiary care

Mirror therapy: An adjunct to conventional pharmacotherapy in phantom limb pain

Sir,

As disturbing and distressing “phantom limb phenomenon” is for the patient, so has been the fascination of physicians since its early description in the 16th century.^[1] The phantom limb phenomenon includes three different elements, namely, the

center for re-exploration and revascularization. A reverse great saphenous vein graft was inserted. Intra-operative it was recorded that the muscles looked dusky with poor contractility. Postoperatively, peripheral pulses were absent on the table, but arterial signals were audible on the hand-held doppler.

Patient had persisting fever ($>101^{\circ}\text{F}$) with leukocytosis, not responding to appropriate antibiotics. Discoloration of the left leg was observed with no distal pulsations even with doppler. A left transfemoral amputation was performed on the 6th postinjury day. In view of sepsis, the amputation stump flap closure was delayed until the 15th PO day. During this period, his analgesic requirements were high and managed by the primary physician with NSAIDS and intermittent opioids.

On the 17th PO day following amputation (23rd day postinjury), patient started complaining of intermittent diffuse, vague pain in the distal part of the limb, below the stump, more while trying to walk with support. This was in addition to the preexisting continuous SP.

The primary physician increased the analgesics. There was a marginal decrease in SP, but no improvement in PLS/PLP. The case was then referred to the “acute pain service” team of this hospital.

After assessment and confirmation of diagnosis based on eliciting history typical of PLP, the patient was started on tablet gabapentin 300 mg at night and tablet nortriptyline 25 mg once a day in addition to tablet tramadol 50 mg 3 times a day. After 1 week of treatment, in the follow-up visit, there was improvement in visual analog scale (VAS) from 8/10 to 6/10.

In addition to the pharmacotherapy, he was also advised mirror therapy wherein the patient was advised to look at the reflection of his existing contralateral limb while trying to move both his limbs simultaneously. This was done 2-3 times/day.

By the 1st week, the patient reported a VAS for PLP of 4/10 as well as a decrease the PLS. The patient was motivated enough to continue with the mirror therapy and was discharged from hospital while continuing on the initial doses of gabapentin and nortriptyline. He was referred to an artificial limb center, for further management. Patient was followed-up telephonically for 3 months and reported a VAS for PLP of 2-3/10 with a positive feedback for mirror therapy.

We also report another known case of peripheral arterial occlusive disease (PAOD) right lower limb who had undergone a femoral-popliteal bypass at this hospital 2 years back with a polytetrafluoroethylene graft. This 65-year-old male was on regular antiplatelet medication. Two years later the graft

surgery was stormy with frequent procedures for repeated occlusions including catheter-directed thrombolysis and thrombectomy. He also had an episode of four-compartment syndrome, managed with fasciotomy and split skin graft. A reverse great saphenous vein femoral-popliteal bypass was offered, but the patient refused.

He developed a nonhealing ulcer in his left lower limb that progressed to irreversible ischemia of his calf muscles. After 2 years of the initial graft operation, a below knee amputation with flap closure in the same sitting was done.

Postoperative period was uneventful. SP was managed with routine NSAIDS, intravenous opioids and continuous epidural analgesia for 48 h.

On the 5th PO day following amputation, the patient complained of a discomforting pain sensation in the amputated limb suggestive of PLP. On detailed history, the patient was able to differentiate this from the SP that had mostly resolved by that time. It was typically described as a shooting pain in the “toes” of the amputated limb, which appeared intermittently, unrelated to any activity. It was not relieved with the ongoing pain medication.

As per the protocol of our acute pain service, he was started on tablet gabapentin 300 mg HS and tablet nortriptyline 25 mg OD. On evaluation after a week, VAS for pain came down from 7/10 to 5/10. The patient was satisfied with the pain relief and was then advised mirror therapy for a week. After 1 week, the patient showed tremendous improvement and virtually asymptomatic with VAS at 1-2/10. The patient was discharged with continuation of ongoing treatment and mirror therapy.

On follow-up visit after 3 months, the patient had no fresh complaints associated with phantom limb with VAS for pain at 1-2/10 and gave history of regularly utilizing mirror therapy.

The major causes of amputation in modern times have been traumatic, vascular disease related and malignancy. Two of these cases have been described here (traumatic and peripheral vascular disease). The term “phantom limb” was coined by Mitchell in 1871.^[1,7]

All three different elements of the phantom limb complex are usually observed in amputees though the PLS rarely causes discomfort in patients. Diagnosis of PLP is based on the classical description of the pain by the patients and is usually that of exclusion.^[2]

While there have been many studies which have established that there is no significant relationship between preexisting

diseases and incidence of PLP,^[2,8-10] there have been no studies correlating the preexisting condition and the response to treatment. Both our patients had different etiologies for amputation and both experienced PLP. However, we postulated that the preexisting condition might have a bearing on the response to treatment that is highlighted by the response of both patients. The 65 years old PAOD patient had a significant decrease in pain score with the medication and he was virtually pain free after mirror therapy at the time of discharge. He was also more satisfied in the follow-up visit. On interrogation, he had the peripheral vascular disease for the past 3 years, had undergone numerous operations and hospital admissions and had become somewhat used to the pain of ischemia. He had probably accepted his condition and the results to follow. The young traumatic amputee showed minimal improvement with the drugs and some relief with mirror therapy. He had a sudden loss of a limb, which was associated with emotional and social issues, which probably resulted in his more dramatic symptoms of PLP and unsatisfactory response to treatment.

Schug *et al.*^[11] in a randomized controlled trial (RCT) described the incidence of PLP to be significantly lower in patients who received preoperative, intraoperative and PO epidural analgesia thereby reinforcing the theory of preemptive analgesia in PLP. Many authors have postulated that the severity of preamputation pain has an effect on the occurrence of PLP.^[2,10-12] The PAOD patient here had received an epidural infusion of 0.125% bupivacaine perioperatively.

Numerous guidelines have been outlined for management of PLP, but no definitive treatment has yet been established, probably because of lack of significant study data. The main modalities of treatment being used up until now have been medical, nonmedical and surgical.^[2,13] Among the medical interventions, tricyclic antidepressants and sodium channel blockers are currently considered to be the drug treatments of choice for neuropathic pain. Nortriptyline and desipramine have been found to be equally effective with lesser side-effects compared with amitriptyline.^[14] There may be a role for the use of selective serotonin reuptake inhibitors (SSRI's) and serotonin-norepinephrine reuptake inhibitors (SNRI's) in the treatment of neuropathic pain, but the evidence is very limited and further research is needed.^[5] Carbamazepine, an anticonvulsant drug has been reported to be effective in anecdotal case reports. Novel anticonvulsants such as lamotrigine and gabapentin have shown mixed results in the control of PLP.^[2,13,14] In a RCT, 6 weeks of Gabapentin monotherapy was better than placebo in relieving PLP.^[15] Tramadol is an analgesic with both monoaminergic and opioid activity. Tolerance and dependence during long-term treatment with tramadol appears to be uncommon.

NSAIDs and paracetamol are considered to be ineffective in PLP.^[2,13,15] The protocol of the hospital's chronic pain services includes prescribing nortriptyline, gabapentin and tramadol as the first-line therapy for PLP. Both our patients received an initial trial of nortriptyline 25 mg OD and gabapentin 300 mg HS.

Recently, various non-invasive techniques such as transcutaneous electrical nerve stimulation, vibration therapy, acupuncture, hypnosis, biofeedback, and electroconvulsive therapy have gained popularity as adjuncts with medical therapy. However, despite the widespread use of some of these techniques clear evidence of effect is limited.^[2,13,16]

Ramachandran and Rogers-Ramachandran introduced mirror therapy, which is basically a nonpharmacological neurorehabilitation technique, in 1996. Under this therapy, the patient is allowed to feel the imaginary movement of the removed body part behaving as the normal movement through a mirror.^[4]

Rizzolatti *et al.* used a "mirror neuron" to explain the fundamentals of mirror therapy.^[14] Initially, found in monkey's premotor cortex, was later discovered in humans by Rossi.^[17] The mirror neuron provides observers with internally recognized experiences, making them understand and feel other's behaviors, intentions, and emotions.^[17,18] They are important for understanding the actions of other people, and for learning new skills by imitation. Using this principle, the phantom limb can feel the same sensation as the other normal body part by merely observing its mirror image. "Neurons that fire together wire together." Mirror therapy decreases pain by decreasing the conflict between motor system, proprioception, and visual system.

In the two described patients, mirror therapy had a significant impact on response to treatment. The young traumatic amputee who had virtually no improvement with medication showed a significant improvement with mirror therapy and was motivated enough to continue with it at home. On the other hand, the middle-aged patient showed a satisfactory response to medical therapy was virtually pain free at the time of discharge following mirror therapy.

Our experience with mirror therapy in these patients showed that irrespective of other modes of treatment, mirror therapy has a significant impact on the management of PLP.

The few studies/case reports, which have described mirror therapy, have all had positive responses. A study by MacLachlan *et al.*, described that during use of mirror therapy in a lower limb amputee, the patient reported an increased sense of motor control

over the phantom limb. He attributed this as a major contributing factor in producing relief in the discomforting PLS.^[19]

Kim and Kim in a case report^[20] mention a 30-year-old male patient who received an above-elbow amputation and suffered from PLP. He described his arm as being medially rotated along with having cramping electric like pain every few minutes. All pharmacological and nonpharmacological therapies gave only short-term benefits, but mirror therapy had a significant response with the patient stating that his phantom arm had rotated back to normal, with significant reductions in VAS for PLP.

The tantalizing advantage of using mirror therapy is the ease with which it can be performed by the patients, in the presence of the treating physician, or even at home.

The limitation of mirror therapy is that most of the evidence in favor of it is anecdotal and most studies have weak methodology, and quality of evidence. And lastly, the scientific basis for it is still evolving and being understood.

Phantom limb pain and PLS is a universal phenomenon in all amputation patients irrespective of the etiology, but the type and duration of the preexisting disease may have an impact on response to treatment and eventual satisfaction and acceptance of the condition. Mirror therapy is a new and exciting low cost neuromodulation technique, which has showed promise though it still needs research and further study to ascertain its role in the future management of PLP.

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