

Phantom Limb Pain Treated with Duloxetine: A case series

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ABSTRACT:

Phantom limb pain treated with duloxetine: a case series

Phantom limb pain (PLP) is a general complaint after amputation which is usually described as burning, tingling, shooting, and cramping. Spontaneous recovery of phantom limb pain generally last many months or years. The pain gets chronic in most cases and impresses the life quality of the patient. Here we present four cases of PLP, treated with duloxetine.

Keywords: phantom limb pain, duloxetine, serotonin-noradrenalin re-uptake inhibitors

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INTRODUCTION

Phantom limb pain (PLP) is a general complaint after amputation which is usually described as 'burning, tingling, shooting and cramping'. Spontaneous recovery of phantom limb pain generally takes months to years. The pain gets chronic in most cases and impresses the life quality of the patients¹. There are three theoretical mechanisms suggested to explain PLP:

- (i) peripheral pathways that include neuromas,
- (ii) central neural mechanisms; sensitization of

spinal cord, cortical reorganization, body schema hypothesis, (iii) psychogenic mechanism^{2,3}.

Besides these theories no one separately explain the PLP and it believed that multiple mechanisms are potentially responsible². The serotonin-norepinephrine reuptake inhibitors (SNRIs) which may target central mechanisms³, are popular for neuropathic pain, migraines, and fibromyalgia due to efficacy and fewer side effects⁴.

Duloxetine, a SNRI, has been shown to be efficacious in several chronic pain conditions such as chronic musculoskeletal pain⁵, diabetic peripheral

neuropathic pain⁶, and chronic lower back pain⁷. Even though the efficacy of duloxetine in chronic pain was indicated, as far as we know there is only one case report of duloxetine use in PLP. Here we present four cases of PLP, treated with duloxetine.

CASE 1

A 19-year-old male who was referred to psychiatry outpatient clinic of Kahramanmaraş City Hospital from department of orthopedics with a complaint of PLP, 2 months after a traumatic below-knee amputation without prior psychiatric history. He described a sensation of shooting pain and itching in his right foot and toe. He initially rated the PLP a 9 on the visual analog scale (VAS) of 0 to 10. His pain was worse in the evenings and sometimes disrupted his sleep. Loss of appetite, irritability and sleep irregularity was present, so he was diagnosed as adjustment disorder according to DSM-IV-TR. We have initiated to duloxetine 30 mg/day for his pain, and olanzapine 2.5 mg/day for his self-mutilating behavior. Fifteen days after initiation, he scored 4 points on VAS, his appetite and sleep was better. He was still suffering from feeling anger about the accident almost all day. The treatment has been re-arranged as duloxetine 30 mg/day and risperidone 1 mg/day while olanzapine was quit. A month later, he reported feeling very well and he scored 1 on VAS. However, in the third month, recurrence of PLP was detected upon discontinuation of the drugs because of feeling very well. Since his main complaint was pain, he was started on only duloxetine and he was uneventful under the duloxetine treatment since two months.

CASE 2

A 20-year-old male, who underwent trans-tibial amputation of two legs secondary to bomb blast was admitted to Kahramanmaraş City hospital psychiatry outpatient clinic with the complaint of a sensation of intermittent pain and itching in his both feet for a month. He had no prior psychiatric history and had been taking mirtazapine 15 mg/day for a month for his sleeplessness however he

was still suffering from phantom limb pain-scored 8 on VAS. He did not complain neither depressive nor post-traumatic stress disorder symptoms according to DSM-IV TR. He scored 6 on Hamilton Depression scale. Duloxetine 30 mg/day was added. Follow-up visits over the next few months, the subject consistently reported his PLP symptoms to have improved by 60%, rating his pain as a 3 out of 10.

CASE 3

A 15-year-old female, with a left below-knee amputation due to combat wounding was referred to Kahramanmaraş City Hospital psychiatry outpatient clinic because of a complaint of PLP. Although she exposed to a blast a month ago and lost her family, unexpectedly she had no signs of depression or anxiety disorder according to DSM-IV-TR. We have started on 30 mg/day duloxetine treatment for her PLP and her VAS score was decreased 6 from 9 after 15 days later. She was subsequently lost to follow-up.

CASE 4

A 55-year-old male who underwent left trans-tibial amputation secondary to embolism. He had history of arrhythmia. A month after his amputation surgery, he maintained to report PLP in his left foot. He described it as “sharp” and “aching,” which occurs mostly in the evening. He rated his worst PLP as a 10 out of 10. He scored 8 on Hamilton Depression scale and 10 on Beck Anxiety Inventory. We have started on duloxetine 30 mg/day and his pain decreased gradually. In subsequent follow-up visits over the following 3 months, he reported a maximum 1–2 points out of 10 for pain on VAS, describing the pain as a tingling.

DISCUSSION

Various therapeutic approaches have been used in the treatment of PLP. Simple non-steroidal, anti-inflammatory and opioid drugs can be tried, but the mainstay of the pharmacological management

of PLP is the use of anti-neuropathic medication⁸. In spite of well-known side effects or intolerance to higher doses, tricyclic antidepressants are generally used medications for various neuropathic pains including PLP. The inhibition of serotonin-norepinephrine uptake blockade, NMDA receptor antagonism, and sodium channel blockade are the mechanisms that usually referred to analgesic effect of tricyclic antidepressants⁹.

The serotonin-norepinephrine reuptake inhibitors (SNRIs) are popular for neuropathic pain, migraines, and fibromyalgia due to fewer side effects contrary to tricyclic antidepressants (TCAs) and equal efficacy⁴. Milnacipran and duloxetine has already been approved by FDA for fibromyalgia due to its action on noradrenergic and serotonergic fibers in descending inhibitory pain pathways as noted by Barkin and Fawcett⁸. Duloxetine is a SNRI, sharing the class with other drugs like Milnacipran and Venlafaxine. Chalana argued that a molecule like Duloxetine, with analogous effectiveness to TCAs and unlikely less side effects will be efficient in PLP treatment¹⁰. In accordance with this study we used duloxetine effectively in our cases. In literature, there are case reports of successful use of milnacipran^{4,10} and mirtazapine¹¹ in PLP. In contrary to these cases,

our second case had been using mirtazapine and still suffering from PLP. After duloxetine combination, his pain reduced markedly. Additionally there is a case report of duloxetine and pregabalin combination¹².

In a recent review, it was mentioned that UK military pain management system recommended use pregabalin and amitriptyline in the shortest possible time after damage. The writers recommended up to 300 mg of pregabalin and up to 150 mg of amitriptyline. It was stated in the review that if PLP occurred comorbid with depression or pregabalin is ineffective, duloxetine can be used¹³.

Psychological factors, gender (PLP being more common in women), upper extremity amputation are some of the risk factors of PLP. A study reported that the patients with PLP were prone to describe their pain worse in the presence of concomitant depressive symptoms¹⁴. In contrast to arguments mentioned above, three of our cases were male, all of them had lower limb amputation and only one of our cases had depressive symptoms.

In conclusion, we proposed that duloxetine may display promising results and could have beneficial effects in treating PLP. More head-to-head comparison studies are needed in weighing its potential role in PLP.

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