

Serotonin and noradrenaline reuptake inhibitor (SNRI) for chronic musculoskeletal pain may be a red herring?

Dysfunction in the central serotonin and noradrenaline systems cause not only depression but also increased pain sensitivity. Many animal studies indicated that lumbar-intrathecal administration of serotonin and noradrenaline reuptake inhibitor (SNRI) could ameliorate the pain sensitivity which might be mediated by affecting the descending pain inhibitory pathway in the spinal cord, not via its antidepressant effects. Recently, duloxetine, a SNRI, is indicated for the management of chronic musculoskeletal pain and is increasingly being prescribed by many doctors who are not familiar with psychopharmacology.

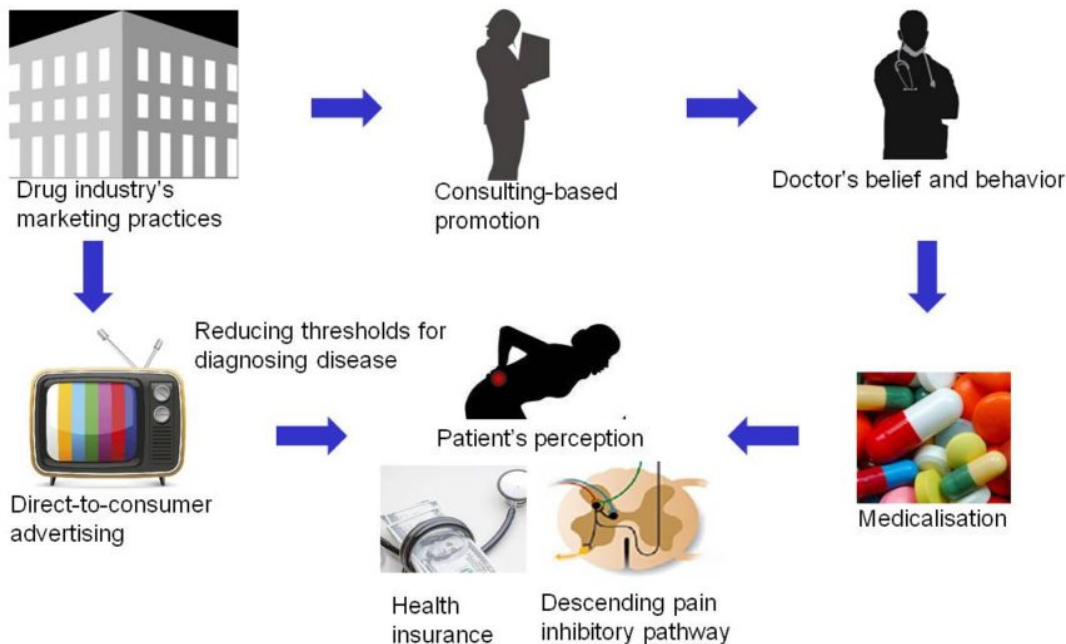


Fig. 1. Bio-psycho-socioeconomic factors of the SNRI prescription for chronic musculoskeletal pain.

The effect on chronic pain of SNRI, however, is not so great. Duloxetine trials for chronic pain utilized changes in pain intensity as their primary efficacy outcome variable. This numerical rating scale is based on an 11-point Likert scale (an ordinal scale with 0 = 'no pain' and 10 = 'worst pain imaginable'). The mean change from baseline to end-point in the average pain score showed a statistically significant difference in favor of duloxetine (duloxetine=?2.92 vs placebo=?2.08) by the representative study. This small statistical difference between duloxetine and placebo does not always have an effective meaning clinically. Moreover, duloxetine has some severe side effects at

the same level as other SNRIs. Syncope and orthostatic hypotension can occur at any time during duloxetine treatment, particularly after dose increases. Duloxetine, as well as selective serotonin reuptake inhibitors (SSRIs), is well known to have side effects of syndrome of inappropriate antidiuretic hormone secretion (SIADH), resulted in hyponatremia that is the most commonly encountered electrolyte abnormality in clinical practice. Following abrupt discontinuation of duloxetine, discontinuation symptoms such as dizziness, headache, irritability, insomnia, and fatigue may occur.

Duloxetine has become a popular prescription drug for several chronic pain conditions, which include neuropathic pain associated with diabetic peripheral neuropathy, chronic low back pain, chronic osteoarthritis knee pain, and chronic musculoskeletal pain, even so it has a small effect size with some severe side effects. In those circumstances, pharmaceutical companies emphasize the effectiveness and safety of duloxetine for chronic pain conditions. Now come to think of it, after the introduction of SSRI or SNRI for mood disorders pharmaceutical companies initiated educational campaigns. Thanks to these marketing practices, SSRI and SNRI sales have achieved a tremendous increase, resulted in an increase in severe side effects. Some pharmaceutical industries are shifting their focus of the SNRI marketing from mood disorders to chronic pain conditions, which are common illness and provide a huge marketing. Many doctors who prescribe duloxetine for chronic musculoskeletal pain say that it is unthinkable that severe accidents will occur with a systematic review of published double-blind randomized controlled trials, but who can be so sure? Because the majority of patients with chronic musculoskeletal pain are elderly, who tend to have a higher underlying risk for falls such as use of multiple medications, medical comorbidities. The doctor who prescribes duloxetine must weigh the benefits against the side effects. Once prescribing duloxetine, patients should be carefully monitored against side effects.

Over-medication arguably did more harm than good. Marketing actions of the pharmaceutical industries, patient's expectations for the drugs, the physician's interaction with pharmaceutical industries, the physician's interaction with the patient, and health care systems should influence the SNRI sales beyond its pharmacological characteristics. We should analyze the prescription pattern of SNRI for chronic musculoskeletal pain from bio-psycho-socioeconomic aspects (Figure 1). We can learn a great deal from the experience with the aggressive marketing of SSRI and SNRI for mood disorders as a kind of disease mongering. The same risk exists with other conditions, including chronic pain conditions. More research is needed to elucidate the true effectiveness of SNRI for chronic musculoskeletal pain.

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Publication

[Responsibility of the doctor who prescribes serotonin and noradrenaline reuptake inhibitors for patients with chronic musculoskeletal pain.](#)

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