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Challenges of Pain Medicine: The Stigma Associated with using Tri-Cyclical Anti-Depressants – It's not all in the Mind

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As anyone who is involved in chronic pain management would know, one of the most challenging aspects of treatment is convincing patients to take medication that are not conventional pain killers. Many patients living with chronic pain are aware that they may need long term or even permanent drug therapy. Their concerns regarding medication frequently stop them from trying or continuing with medication that may offer them a chance of some relief.

Drug therapy is just one aspect of a multi-modal approach to chronic pain management. Physical therapy (physiotherapy, acupuncture, Transcutaneous Electrical Nerve Stimulation (TENS), regional blocks (injection of drugs around nerves or other tissues) and psychological therapies (techniques which improve coping of pain) are also very important in a comprehensive chronic pain management program.

Before considering what medication to use, it is important to determine the type of pain. Pain can be described as nociceptive, neuropathic or "mixed". Nociceptive pain is pain that occurs as a result of tissue damage or a painful stimulus, such as mechanical low back pain and degenerative or inflammatory joint pain. These pains may begin as purely nociceptive, but over time there may be changes within the nervous system that result in a neuropathic component to the pain. Neuropathic pain occurs as a result of damage to the nervous system, resulting in the nerve becoming oversensitive. Patients describe this pain as sharp, stabbing, lacinating, burning and electric-shock like.

Conventional painkillers such as paracetamol, anti-inflammatory medication and narcotic analgesics are commonly used in chronic pain management and are useful for nociceptive pain. They are however often not effective for neuropathic pain. Medications effective for neuropathic pain work by stabilizing overactive nerves. These include drugs that are used in conditions where the nervous tissue is overactive or "excited" such as epilepsy or depression.

Unfortunately, according to the official FDA guidelines in the USA and the TGA in Australia, the indication for amitriptyline is for the relief of symptoms of depression [1]. In addition, most web-sites on amitriptyline indicate that they can help to treat symptoms of depression, obsessive-compulsive disorder, pain attacks, post-traumatic stress disorder and nocturnal enuresis but not pain [2].

As a result, when amitriptyline is prescribed, patients frequently do not commence this medication, despite it being prescribed by a Pain specialist [3]. Newer, more expensive medication, which now have an " indication" for treatment of neuropathic pain on their product information are being preferred, as first line treatment for neuropathic pain [4]. This is reflected in current guidelines from a number of Pain Society's around the world which conclude that following accurate diagnosis of neuropathic pain pregabalin, gabapentin, low-dose tricyclic antidepressants (e.g., amitriptyline) and serotonin noradrenaline reuptake inhibitors (duloxetine and venlafaxine) are all recommended as first-line options for the treatment of peripheral neuropathic pain [5]. In a result study comparing amitriptyline, duloxetine and pregabalin in diabeticc peripheral neuropathy, all medication reduced pain when compared to placebo, but no treatment was superior to any other. There were no significant safety findings; however, surprisingly there were a significantly higher number of adverse events in the pregabalin treatment group [6].

Amitriptyline inhibits the membrane pump mechanism responsible for uptake of noradrenaline and serotonin in adrenergic and serotonergic neurons. Pharmacologically, this action may potentiate or prolong neuronal activity, since reuptake of these biogenic amines is physiologically important in terminating its transmitting activity. This interference with the uptake of noradrenaline and/or serotonin is believed to underlie the antidepressant activity of amitriptyline. In addition, however, if these neurotransmitters are not reabsorbed they accumulate outside the nerve cell and the result is suppression of pain messages in the spinal cord.

The dose required for treating depression is much higher (often over 150 milligrams a day) than the doses used for pain (often 10 to 25 milligrams only at night) [7]. Also, there are many different antidepressant drugs available that are effective for treating depression, but only a small number are also effective in neuropathic pain [8].

Given this, it is very important to get across to the patient that medication, amitriptyline is being given for pain and not because the pain is "all in the mind". Depression can occur as a reaction to chronic pain and may improve as the chronic pain improves. However if severe, this may require specific antidepressant therapy.

The Numbers Needed to Treat (NNTs) for amitriptyline in neuropathic is 3.6, i.e., one in three people will get greater than 50% pain relief with amitriptyline, which is regarded as an excellent result for chronic pain conditions.

Although there are number of side effects associated with amitriptyline most of them are uncommon and usually occur at higher doses than those used in chronic pain. The most common experience by less than 10% of patients, include dizziness, daytime drowsiness, dry mouth, nausea and constipation. These side effects are generally harmless and do not require patients to cease the drug. If side effects are a problem, there are similar drugs (nortriptyline and imipramine), could be tried, which are less sedating. Amitriptyline is not addictive but if discontinued, should be withdrawn slowly over two to three weeks to avoid withdrawal symptoms of headache and malaise [2].

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Amitriptyline is a very effective and cheap treatment for chronic neuropathic pain that has been used since 1961. When dealing with a difficult problem such as chronic pain, it is worth giving a medication a chance rather than dismissing it just because of the stigma caused by the official "indication", as a medication such as amitriptyline has the potential to improve the pain and in doing so, improve function and quality of life.

The stigma associated with the use of low dose amitriptyline needs to be removed from the community, both general and medical, and also the misconception that it is only prescribed for depression. It is a very useful medication for the management of chronic pain.

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