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Bridging the gap in neuropathic pain treatment: The potential role of astaxanthin

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ABSTRACT

Neuropathic pain is a challenging condition to treat. It is heterogeneous in nature and could be resistant to treatment with commonly prescribed analgesics. Current management strategies fail to achieve adequate or satisfactory pain relief in a high proportion of patients. The previous review mentioned that only less than 50% of patients can achieve good pain control with standard treatment. The available treatment only focuses in the symptom control, and does not interfere with the progressing damage of the nerve. Astaxanthin is a very potent anti-oxidant. In this review, we discuss about the potential use of astaxanthin for the add-on treatment of painful neuropathy.

Keywords: neuropathic pain, astaxanthin, treatment

INTRODUCTION

Neuropathic pain is the leading cause of physical disability and impairment in the elderly [1]. Effective management for certain neuropathic pain conditions (for example: central post-stroke pain and chemotherapy-induced peripheral neuropathic pain) remains inconclusive. Typically, this chronic pain condition is managed with palliative measures that focus on pain reduction [2,3]. There were a significant group of patients in whom these treatments do not provide adequate pain relief [4]. The previous studies of treatments that proven can stop or reversing the progressing process are limited [5,6].

Modification of disease progression and symptom reduction are the ultimate goal for chronic pain treatment. The most common agents for the treatment of this condition are tricyclic anti-depressant and gabapentinoid. This medication have been associated with serious adverse effects [4]. The previous review showed that many patients cannot tolerate with the side effects [2].

There is still an unmet need for chronic pain treatment in terms of pain reduction [2]. It is, therefore, apparent that there are unmet needs in neuropathic pain management. The unmet needs especially in either the safety of treatment options and the ability of therapies to disease modification. The insufficient management of comorbid conditions; incorrect understanding or selection of treatment options; and the use of inappropriate outcomes measures are the common reasons for inadequate pain control [2].

Astaxanthin is ubiquitous in marine organisms. Recent review have uncovered the contribution of different astaxanthin isomers to antioxidant activities, both in vitro and in vivo [7]. The previous review discusses that the effects of astaxanthin on oxido-inflammatory and NMDA receptor down-regulation pathway by using in-silico, in-vitro and in-vivo models of neuropathic pain showed promising results [8].

This narrative review aimed to discuss the unmet needs in the pharmacological management of neuropathic pain. We discuss the potential role of astaxanthin as an add-on pharmacological treatment for painful neuropathy.

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METHODS

We systematically search the studies about astaxanthin for the treatment of the various neuropathic condition. The keywords: neuropathic pain, oxidative stress, astaxanthin, neuropathy. We mainly focus on the studies with either in an animal model of painful neuropathic pain condition and randomized controlled trial design. The studies with the available full text and published in English/ Indonesian language will be review further. We make a systematic table to explain our review.

NEUROPATHIC PAIN AND ASTAXANTHIN

Painful neuropathic condition refers to pain that originates from a lesion or dysfunction of the peripheral or central nervous system [1]. Despite recent advances and understanding in the identification of pain-generating mechanisms, patients with neuropathic pain are challenging to manage. The currently available systemic pharmacological therapies provide only about half of the affected patients with meaningful pain relief and are further limited by unwanted adverse effects, such as drowsiness and dizziness, and the need for multiple daily dosing [2].

The physical, emotional, and economic impact of poorly controlled neuropathic pain is well documented [9,10,11]. Patients with inadequately managed centralized (neuropathic) pain often exhibit a common behaviour problem. Patients with chronic pain who are not receiving adequate pain control often will present ahead of their scheduled appointments, frequent emergency rooms, and see more than one physician [9,11]. These patients often lose their jobs, social contacts, and former way of life [10].

Recent reviews on neuropathic pain indicate that only a minority of patients have an adequate response to drug therapy [4]. Only one-third of painful neuropathic pain patients experience satisfying pain relief [2]. Mostly, complete freedom of pain cannot be achieved; however, improvement of life quality, sleep, social activities, and ability to work is possible [2,4]. The treatment that can interfere with the progressing damage of the nerve is very limited.

Astaxanthin is a very potent anti-oxidant [12]. Astaxanthin is found mostly in marine organisms. Our review showed that the add-on therapy with astaxanthin is very promising for relieving certain neuropathic pain conditions. The previous studies mainly focus in the painful diabetic neuropathy model.

Previous studies found that astaxanthin reduces the oxidative stress caused by hyperglycaemia in pancreatic β-cells and improves glucose and serum insulin levels in diabetes [12]. Furthermore, it has been suggested that astaxanthin is a potential therapeutic agent against atherosclerotic cardiovascular disease [13].

In human mesangial cells, astaxanthin prevented the high-glucose exposure-induced elevated ROS production in the mitochondria. Astaxanthin may have a protective effect against diabetic neuropathy by modulating oxidative stress, inflammation, and apoptosis by quenching free radicals [14]. Astaxanthin can interfere with the elevated concentrations of plasma glucose and oxidative stress, inflammation, and advanced glycation end products (AGEs) [14,15].

TABLE 1. Astaxanthin in the treatment model of neuropathic pain

Author	Model	Dosage	Biomarker	Finding
Sharma [8]	Rat C6 glial cells; Adult male Sprague Dawley rats	5 and 10 mg/kg	ROS	Significantly attenuate biochemical alterations with the decreased oxidative stress
Jiang [17]	Chronic constriction injury (CCI) mice	80 mg/kg	IL-1β, IL-6 and TNF-α	Exert therapeutic effects on thermal hyperalgesia
Fakhri [18]	Adult male Wistar rats	10 µL of 0.2 mM	NR2B, p-p38MAPK and TNF-α	Decrease the expression of inflammatory mediators (NR2B and p-p38MAPK) and inflammatory cytokine TNF-α
Fakhri [19]	Spinal cord injury (SCI) rats	–	ERK1/2, AKT	Decrease mechanical and thermal pain through the inhibition of ERK1/2 and the activation of AKT

TABLE 2. The clinical studies of astaxanthin for neuropathic pain

Author	Method	Subjects	Finding
MacDermid [20]	Randomized Controlled Trial	63 patients with Carpal Tunnel Syndrome	No difference in pain reduction with add-on astaxanthin
Latumahina [21]	Randomized Controlled Trial	36 subjects with painful diabetic neuropathy	There was a significant reduction in pain on both therapy groups (p= 0,000), where the pain scale reduction in the astaxanthin group was higher but not significant (2.45 ± 2.02 vs 2.37 ± 2.38, p>0.05)

A recent review that focuses on the studies that conducted on type 1 and type 2 DM animal models showed that either orally or parenterally administrated astaxanthin improves insulin resistance and insulin secretion; reduces hyperglycaemia; and exerts protective effects against neuropathy [15]. Astaxanthin could significantly attenuate behavioural and biochemical alterations with the decreased oxidative stress. It was also found that astaxanthin attenuated neuroinflammation and mechanical allodynia via decreasing the expression of inflammatory signaling mediators (NR2B and p-p38MAPK) and inflammatory cytokine TNF-α [15,16].

In the study of 63 patients with carpal tunnel syndrome (CTS), astaxanthin as an adjunct in conservative management of CTS has not been proven beneficial. There was a reduction in symptoms as measured by the SSS over the course of treatment in both groups (p = 0.002), but no differences between the groups (p = 0.18). The disability of arm, shoulder, and hand questionnaire and the short form 36-item health survey showed no effects over time or between treatment groups [20].

The study from Latumahina [21] is a randomized, open-label, controlled group with 8 weeks of follow-up that conducted on 36 subjects with painful diabetic neuropathy. This study showed that there was a significant reduction in pain in both therapy groups (p= 0.000), where the pain scale reduction in the intervention group was higher than the control group (2.45 ± 2.02 vs 2.37 ± 2.38), but there was no significant difference on the statistical analysis between the two treatment groups (p= 0.692).

Further trials with larger study subjects are needed to confirm the beneficial effects of astaxanthin. Astaxanthin showed promising effects in neuropathy and pain in the animal model, but were not confirmed in the clinical studies yet. Future trials that consist of larger, higher-quality RCTs that specifically examine the role of astaxanthin as an adjunctive treatment for neuropathic pain patients are warranted.

CONCLUSIONS

The results of our review showed that there are gap in the pharmacological treatment in neuropathic pain. Astaxanthin showed very promisingly in the animal models for treating neuropathy conditions. Future research should consist of larger, higher-quality RCTs that specifically examine the role of astaxanthin as an adjunctive treatment for neuropathic pain patients.

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