

# Management of Post-surgical Peripheral Neuropathic Pain in Lumbar Degenerative Disease: Do Dietary Supplements have a Role?

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## Abstract

Neuropathic post-surgical pain occurs frequently in patients operated for degenerative spine disease, in particular when the arthrosic features have a direct compressive effect on one to more nerve roots. Surgical decompression is able to remove the cause of the pain and the possible neurological deficit. Notwithstanding, compression and subsequent surgical manipulation could establish an oxidative stress, which can promote a cellular and inflammatory cascade responsible for secondary damage. The oxidative stress have an important role in degenerative and painful pathological conditions of peripheral nerves. The different oxidative reactions seem to be involved in nociceptive signaling cascade and painful awareness typical of neuropathic pain. The analysis of the effectiveness of new active principles that can be suitable for neuropathic pain becomes imperative in order to define a therapeutic management that is more effective and tolerable for the patient. In this regard the Nutraceutical Science opens new horizons in the treatment of neuropathic pain; But is it possible that the synergistic action of the most active natural principles can also act on residual chronic neuropathic pain after surgery?

## Introduction

The analysis of the effectiveness of new active principles that can be suitable for neuropathic pain becomes imperative in order to define a therapeutic management that is more effective and tolerable for the patient. In this regard the Nutraceutical Science opens new horizons in the treatment of neuropathic pain. The nutraceutical is a discipline designed to define and apply the benefits of products as dietary supplements on organic chronic diseases; the therapeutic nutraceuticals dictates are widely known in the neurological field, in particular in respect of degenerative neuropathies or in the diabetic neuropathy, in which the active principles and the benefits associated therewith are well documented. But is it possible that the synergistic action of the most active natural principles can also act on residual chronic neuropathic pain after surgery?

**N-Acetyl-L-Carnitine:** ALC is a small water-soluble peptide involved in cellular metabolism; it can help increase energy production in the mitochondria (1). It contains a carnitine and acetyl moieties: carnitine is important in the beta-oxidation of fatty acids and the acetyl moiety can be used to maintain acetyl-CoA levels and can promote the production of the antioxidant called glutathione. Reducing lactic acidosis of tissues, ALC may be protective against oxidative stress, which leads to formation of ROS, through shifts in both the mitochondrial and cytosolic redox state, and/or through the induction of antioxidant genes. Oxidative stress is associated with a significant decrease in the effectiveness of antioxidant defenses, such as glutathione system (more specifically, they restored the ratio of reduced to oxidized glutathione) [1,2,3]. In addition, the amphiphilic structure of ALC may also affect membrane fluidity and may directly interact with the surface charges on cell membranes: the carboxylic group can interact with charges on membrane phospholipids, glycolipids, and proteins. Changes in neural phospholipid composition and further effects on signal transduction pathways seem to be characteristic of many neurological disorders, this is why the ALC regulation of lipids metabolism is important in neuroprotection. Essential is its role in the lumbar spinal nerves; in fact ALC has been shown to increase nerve growth factor (NGF) production and enhance NGF binding. NGF affects neuronal development and maintenance of neurons both in the peripheral and central nervous systems (CNS) [1-5]. Nonetheless, it is unclear if ALC's

biological effects are due to the acetylation of one or more amino acids of NGF or by increasing NGF gene transcription/translation (most likely by acetylation of histone H4) or by a combination of these effects. In the clinical practice, following sciatic nerve injury, ALC prevents structural changes and stimulates restoration of nerves by significantly increasing the density of regenerating myelinated fibers and axon diameter [4,5].

**Alpha Lipoic Acid:** the neuroprotective role of alpha lipoic acid is due to its antioxidant action. It improves the nervous conduction velocity and the nerve blood flow, reducing the pain and the hypoesthesia. The evidence that there is an involvement of oxidation processes in the onset and in the worsening of neuropathic pain, confirmed the important role of the oxidative stress in degenerative and painful pathological conditions of peripheral nerves [6-8]. The features that makes alpha lipoic acid effective in the treatment of neuropathic pain is its strong antioxidant activity capable to neutralize the oxidative reactions and to reduce oxidized forms resulting from other factors; among its features it is interesting to note that alpha-lipoic acid is water and fat soluble, a characteristic that makes it unique among antioxidants [7]. Numerous clinical studies have demonstrated the efficacy of alpha-lipoic acid in improving the parameters of signal conduction of peripheral nerves involved in neuropathy, with increase in nerve function [6,8,9].

**Curcumin:** Deriving from the rhizomes of *Curcuma longa* together with other two curcuminoids as desmethoxycurcumin and bis-desmethoxycurcumin [10-12]; Is currently used as anti-inflammatory drug in the ayurvedic medicine. It is water soluble but is stable in the pH of the stomach. Curcumin plays an important role in the inflammatory response [13]. It has been found to inhibit Phospholipase A2, COX-2, and 5-LOX (Arachidonate 5-lipoxygenase) activities. The limits in

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the use of curcumin are: the potential inhibition of chemotherapeutic drugs, and the reduced bioavailability in some tissues. moreover its availability is not high [11,14].

## Discussion

Neuropathic pain, in particular radicular post-surgical pain, commonly occurs after surgery for degenerative lumbar disease. Its management is currently quite controversial, both for diagnostic difficulties, either because the drugs available are not completely effective against a serious and annoying problem that can change the lifestyle. Probably the synergistic action of anti-inflammatory and neuroprotective drugs would be ideal to address the problem. Until now, the anti-inflammatory drugs available are poorly effective against this type of pain, and are burdened with considerable side effects and their use cannot be continued for long periods. Moreover the important role of neuroregeneration in post surgical period is often underestimated.

Neuromodulators proved fairly effectiveness in the control of these symptoms, but they are not neuroprotective against the oxidative damage generated by inflammation. The functional analysis of each natural principle most used in the treatment of neuropathic pain let assume that the synergistic use of the neuroprotective, anti-inflammatory and antioxidant action can be the cornerstone in the treatment of post-surgical neuropathies. However, there are some doubts: first of all the patterns of bio-distribution in tissues and the absorption capacity of each principle. In fact, the hydrophilic or lipophilic characteristics of the various principles do not seem to favor a combination of them in the formulation of a unique product containing all of them; likewise their obvious anti-inflammatory, analgesic and neuroprotective actions make a product containing all of these three principles, highly usable from the therapeutic point of view. Secondly, the timing of treatment. It is known that the inflammatory process and the secondary neurological damage start really fast, this is why an anti-inflammatory and neuroprotective therapy should be taken as early as possible compared to the beginning of the acute phase; this would bring to the reduction of inflammation itself and to the limitation of any secondary damage triggered by oxidative reaction, often responsible for the algo-paresthetic symptoms that secondarily appears. The use of these three active principles should therefore begin early in order to prevent the consequences. Furthermore, since those drugs have natural active principles (classified in the category of food supplements) ensure a pattern of risk very low compared to traditional drugs, and allow their use for longer periods. The technological evolutions in the pharmaceutical field, especially in the nutraceutical, helped in the development of systems for preparing natural composites able to meet the demands previously highlighted: there are in fact currently available formulations that provide for the simultaneous presence of N acetyl L carnitine, alpha- lipoic acid and curcumin associated with vitamin complexes. These compounds are able to bring together the hydrophilic or lipophilic characteristics of the various principles, allowing a controlled and active release continuous and constant. This seems to allow the synergistic action of the three principles while maintaining constant the level in the tissues and their concentration.

## Conclusion

Their use against nerve pain after surgery should be definitely investigated through randomized prospective clinical trials, but the results posted on their synergistic anti-inflammatory antioxidant and neuroprotective function seems to be very promising. Clearly, for

what concerns the degenerative spine disease, such formulations are not intended to replace drug therapy or surgery, since this remains the gold standard for the treatment of pain and neurological disorder, but it can take a significant role in helping the action of drugs both from the synergistic and alternative point of view.

## Competing Interests

The authors have declared that no competing interests exist.

## References

1. Pessoa BL, Escudeiro G, Nascimento OJ (2015) Emerging Treatments for Neuropathic Pain. *Curr Pain Headache Rep* 19: 56.
2. Baek SM, Zheng R, Seo EJ, Hwang DY, Kim BH (2015) Pharmacokinetic comparisons of two acetyl-L-carnitine formulations in healthy Korean volunteers. *Int J Clin Pharmacol Ther* 53: 980-986.
3. Sepand MR, Razavi-Azarkhiavi K, Omidi A, Zirak MR, Sabzevari S, et al. (2015) Effect of Acetyl-L-Carnitine on Antioxidant Status, Lipid Peroxidation, and Oxidative Damage of Arsenic in Rat. *Biol Trace Elem Res* .
4. Li S, Li Q, Li Y, Li L, Tian H, et al. (2015) Acetyl-L-carnitine in the treatment of peripheral neuropathic pain: a systematic review and meta-analysis of randomized controlled trials. *PLoS One* 10: e0119479.
5. Onofri M, Ciccocioppo F, Varanese S, di Muzio A, Calvani M, et al. (2013) Acetyl-L-carnitine: from a biological curiosity to a drug for the peripheral nervous system and beyond. *Expert Rev Neurother* 13: 925-936.
6. Javed S, Petropoulos IN, Alam U, Malik RA (2015) Treatment of painful diabetic neuropathy. *Ther Adv Chronic Dis* 6: 15-28.
7. Vasudevan D, Naik MM, Mukaddam QI (2014) Efficacy and safety of methylcobalamin, alpha-lipoic acid and pregabalin combination versus pregabalin monotherapy in improving pain and nerve conduction velocity in type 2 diabetes associated impaired peripheral neuropathic condition. [MAINTAIN]: Results of a pilot study. *Ann Indian Acad Neurol* 17: 480-481.
8. Papanas N, Ziegler D (2014) Efficacy of  $\alpha$ -lipoic acid in diabetic neuropathy. *Expert Opin Pharmacother* 15: 2721-2731.
9. Battisti E, Albanese A, Guerra L, Argenti L, Giordano N (2013) Alpha lipoic acid and superoxide dismutase in the treatment of chronic low back pain. *Eur J Phys Rehabil Med* 49: 659-664.
10. Snedecor SJ, Sudharshan L, Cappelleri JC, Sadosky A, Mehta S, et al. (2014) Systematic review and meta-analysis of pharmacological therapies for painful diabetic peripheral neuropathy. *Pain Pract* 14: 167-184.
11. Meng B, Shen LL, Shi XT, Gong YS, Fan XF, et al. (2015) Effects of curcumin on TTX-R sodium currents of dorsal root ganglion neurons in type 2 diabetic rats with diabetic neuropathic pain. *Neurosci Lett* 605: 59-64.
12. Babu A, Prasanth KG, Balaji B (2015) Effect of curcumin in mice model of vincristine-induced neuropathy. *Pharm Biol* 53: 838-848.
13. Di YX, Hong C, Jun L, Renshan G, Qinquan L (2014) Curcumin attenuates mechanical and thermal hyperalgesia in chronic constrictive injury model of neuropathic pain. *Pain Ther* 3: 59-69.
14. Moini Zanjani T, Ameli H, Labibi F, Sedaghat K, Sabetkasaei M (2014) The Attenuation of Pain Behavior and Serum COX-2 Concentration by Curcumin in a Rat Model of Neuropathic Pain. *Korean J Pain* 27: 246-252.