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Acetyl-L-Carnitine in Geriatric Care: A Review

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ABSTRACT

Acetyl-L-carnitine (ALC), a derivative of L-carnitine, has gained recognition as a potential therapeutic agent in geriatric care, attributed to its involvement in energy metabolism, mitochondrial function, and neuroprotection. ALC improves mitochondrial efficiency by facilitating the transport of fatty acids for energy production and minimising oxidative stress, both of which are essential for ageing cells. The neuroprotective effects encompass the promotion of synaptic plasticity, neurogenesis, and the safeguarding of neurones against age-related damage, presenting potential advantages in the management of cognitive decline, Alzheimer's disease, and vascular dementia. Furthermore, ALC has shown antidepressant effects through the modulation of neurotransmitters like acetylcholine and dopamine, which play a crucial role in mood regulation. In addition to cognitive and emotional well-being, ALC contributes to physical health by reducing fatigue, increasing muscle strength, and enhancing mobility, proving to be beneficial in addressing frailty and sarcopenia among older adults. While ALC is typically well-tolerated, its efficacy can differ from person to person, highlighting the need for additional clinical research to establish optimal dosing and long-term safety. ALC possesses considerable potential in geriatric care, providing a comprehensive strategy to enhance cognitive function, emotional well-being, and physical independence, ultimately leading to an improved quality of life for older adults.

Key-words: Acetyl-L-carnitine (ALC), Elderly, Cognitive Function, Neuroprotection

INTRODUCTION

Carnitine and its derivatives are endogenous compounds that participate in carbohydrate and fat metabolism. These chemicals may provide various therapeutic effects, likely due to their interaction with components of cellular membranes [1]. Diverse substances enhance the advantageous reservoir of carnitine derivatives. These comprise acetyl-l-carnitine, propionyl-l-carnitine, and isovaleryl-carnitine. Among these derivatives, the acetyl ester of carnitine, acetyl-l-carnitine, may constitute a chemical of significant interest due to its extensive clinical uses in numerous neurological illnesses [2,3]. Evidence indicates that ALC may serve as a crucial regulator of cellular stress response in both healthy and pathological conditions [4].

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It serves as a metabolic cofactor for the conversion of fatty acids into energy within the mitochondria of nerve cells, thus ensuring their energy supply. ALC may be suggested as a treatment drug for several neurodegenerative illnesses owing to its neurobiological effects [5].

Acetyl-L-Carnitine- Acetyl-L-carnitine (ALC) is an ester that originates from the trimethylated amino acid L-carnitine, produced in the human brain, liver, and kidney via the enzymatic activity of ALC-transferase. ALC facilitates the translocation of acetyl-CoA into the mitochondria during the process of fatty acid oxidation, enhances the synthesis of acetylcholine, and supports the production of proteins and membrane phospholipids [6,7].

L-carnitine and ALC can be delivered through oral, intravenous (IV), or intramuscular routes. The jejunum facilitates absorption through simple diffusion, followed by active transport into cellular tissue, achieving equilibrium in plasma concentrations via carnitine acetyl-transferase activity [8]. Both intravenous and oral

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administration leads to a corresponding increase in cerebrospinal fluid (CSF) concentrations of ALC, demonstrating its ability to effectively cross the blood-brain barrier (BBB). In a previous study conducted with healthy fasting males, the administration of a single 500 mg dose of ALC led to a peak plasma concentration of 1.19 µg/mL at 3.1 hours post-dose; the half-life of ALC was established at 4.2 hours, with an area under the curve quantified at 9.88 µg·h/mL [9]. L-carnitine and its esters undergo restricted metabolism and are subsequently excreted through the urine via renal tubular reabsorption, exhibiting a clearance rate that increases per their plasma concentration [10].

Although the exact mechanism by which ALC operates is not fully elucidated, studies indicate a potential link to its effects on cholinergic neural transmission and its ability to enhance neuronal metabolism within the mitochondria [11]. Some researchers ascribe the cholinergic effects of ALC to the inhibition of post-synaptic potentials, whereas others suggest a direct stimulation at the synaptic level [12,13]. Studies suggest that improved cellular energetics within the mitochondria enable ALC to maintain cell membrane fluidity through the regulation of sphingomyelin levels. Furthermore, it functions as a reservoir for substrates involved in cellular energy production, thereby aiding in the prevention of excessive neuronal degeneration [14]. ALC has been shown to improve the binding of glucocorticoids and nerve growth factors in the hippocampus, reduce oxidative stress, and inhibit excitotoxicity in brain tissue and cerebrospinal fluid, thus preventing cell death and neuronal damage induced by ischaemia. The implications for the peripheral nervous system suggest that ALC supplementation could provide advantages for individuals suffering from peripheral neuropathies. The benefits can be associated with its role in nerve regeneration and protection, as well as its properties that combat oxidative stress, prevent programmed cell death, and alleviate pain [18].

Cognitive Dysfunction and Depression- Acetyl-l-carnitine has been proposed to be of benefit in patients with a variety of conditions. However, in the elderly subjects, its use may help treat Alzheimer's dementia and depression, both of which are highly prevalent in the geriatric population [5]. The rationale for this application relates to the possible preferential effect of ALC on the brain tissue through which it offers major metabolic benefits to the brain. Herein, it may be important to mention that both carnitine and acetyl moieties of ALC may exert neurobiological properties. Carnitine plays a crucial role in the beta-oxidation of fatty acids, and the acetyl moiety serves to sustain acetyl-CoA levels [5]. Metabolic studies indicate that ALC assists the brain in sustaining a steady supply of energy essential for optimal homeostasis [2,19]. It can therefore mitigate various physiological and pathological changes characteristic of the brain ageing process. Experimental evidence has shown that ALC can mitigate the age-related decline of various receptors in the central nervous system (CNS), such as the NMDA receptor system, Nerve Growth Factor (NGF) receptors, glucocorticoid receptors, neurotransmitter receptors, among others. This action results in a trophic effect and improves the efficiency of synaptic transmission, which is significantly impaired by the ageing process [2,3].

Ischemic Brain Disease- ALC serves as a cognitive enhancer, offering partial protection against ischaemic brain damage, which may prove beneficial for individuals recovering from strokes. The molecule provides a means of survival for damaged neurones by engaging in cellular energy production, a critical process for neuronal function, and facilitating the elimination of toxic fatty acid accumulation [20]. Individuals experiencing neurological deficits due to cerebral infarcts necessitate rehabilitation therapy, and the administration of ALC alongside this rehabilitation may prove beneficial [21]. Related clinical evidence has been shown in patients with acute cerebral circulatory insufficiency. A double-blind cross-over study assessed the clinical efficacy of ALC in comparison to a placebo, involving 12 elderly participants engaged in rehabilitation for acute cerebral circulatory insufficiency. The findings indicated notable disparities between the drug and placebo concerning memory, numerical, and verbal assessments, as well as in reactions to basic stimuli and maze test performance [22].

Fatigue- Fatigue is a prevalent concern frequently reported within the elderly demographic. Nevertheless, there exists a limited array of treatment options that have demonstrated efficacy in individuals suffering from chronic fatigue syndrome. Clinical evidence in this

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context indicates that the administration of ALC may mitigate both physical and mental fatigue among the elderly population. Consequently, in addition to enhancing cognitive abilities, ALC also contributes to the improvement of physical functions. A research study examined 96 individuals aged 70 years and older (age range, 71-88; 50 females, 46 males) to assess the efficacy, tolerability, and effects on fatigue, alongside cognitive and functional status in elderly participants, with ALC [23]. The findings indicated that upon completion of the treatment, there was a reduction in both physical and mental fatigue, accompanied by enhancements in functional status and cognitive abilities. The findings indicated that the administration of ALC could potentially alleviate both physical and mental fatigue in the elderly, while also enhancing cognitive status and physical functioning [24-27].

Use of Acetyl-L-Carnitine in Gerontological Practice- Wang and Han *et al.* [28] conducted a thorough analysis of data derived from a series of in vivo and in vitro experiments. They proposed that ALC's effects, including its impact on neuroplasticity, modulation of membranes, and regulation of neurotransmitters, could significantly contribute to the treatment of depression. Consequently, ALC has emerged as a potential antidepressant, characterised by a novel mechanism of action linked to neuroplasticity. Pulvirenti *et al.* [29] demonstrated through experiments on rats that the administration of ALC resulted in a reduction of immobility duration during a forced swimming test. While the precise mechanism by which ALC exerts its effects on depression remains elusive, numerous scholars have posited that its impact may be linked to its capacity to engage the processes that activate neuroplasticity, modulate membrane dynamics, and affect neurotransmitter metabolism. Consequently, research conducted by Foreman et al. indicated that multiple administrations of ALC might inhibit the onset of stress and mitigate reductions in NGF levels within the brains of rats subjected to stress [30,31].

Findings from an additional investigation indicated that ALC exhibits antidepressant characteristics attributable to its capacity to elevate levels of brain-derived neurotrophic factor (BDNF) and enhance glutamate release. Furthermore, it promotes an increase in glial cell line-derived neurotrophic factors (ATN) and their corresponding ligands within the spinal cord, hippocampus, and prefrontal cortex. This phenomenon correlates with a dose-dependent antidepressant-like effect, evidenced by reduced immobility in the forced swimming test [32,33]. The influence of ALC in addressing depression may also stem from its capacity to modulate membrane functions. Experimental studies indicate that depression is associated with disruptions in membrane lipid metabolism, notably characterised by reduced cholesterol levels and a deficiency in omega-3 polyunsaturated fatty acids [34,35]. The extended use of ALC enhances cerebral energy metabolism through modifications in glucose and lactate processing, as well as an elevation in high-energy phosphates and myoinositol levels [36,37].

Another mechanism through which ALC may exert its influence on depression could be linked to its capacity to modulate neurotransmitter regulation. Extended use of ALC has been shown to elevate 5-HT levels in the cerebral cortex and enhance serotonin release in the mesocorticolimbic structures of the brain, thereby bolstering the development of protective mechanisms during acute stress in animal models [38].

CONCLUSIONS

Aging individuals have generally reduced tissue levels of carnitine and its derivatives, and may benefit from its supplementation during treatment for several neurobiological conditions. ALC is a natural substance that helps the nervous system maintain a constant supply of energy needed for effective homeostasis. In the elderly, it may be of particular benefit in treating Alzheimer's dementia and depression. Importantly, since ALC has a chemical structure like other essential compounds in the human body, its administration is supposed to be not harmful. Oral ALC may thus be recommended owing both to its efficacy and easier administration.

The future of acetyl-L-carnitine in geriatric care lies in its potential for personalized therapies, optimized dosing, and combined interventions to enhance cognitive, emotional, and physical health in aging populations.

CONTRIBUTION OF AUTHORS

One author has only contributed to this article.

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