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CDP-Choline Effect on Arthritis Model in Rat

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Mini Review

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Abstract

CDP-choline is a naturally occurring endogenous nucleotide, which after administration rapidly metabolizes to choline (which is a natural α7nAChR selective Agonist) and cytidine/uridine. In the body, Choline promotes several biological functions such as acting as a precursor of neurotransmitter Acetylcholine. As a result of choline availability, Ach synthesis will also increase. It is well known that nervous system under the cholinergic anti-inflammatory pathway concept has an important role in this inflammatory response mainly through α7 sub-unit of nicotinic acetylcholine receptor which is expressed by different types of immune cells, including macrophages. This pathway conducts its role mainly through stimulation of vagus nerve results in the production of Ach which is an α7nAChR Agonist. Therefore, in the light of above studies we can hypothesize that exogenously administration of CDP-Choline results in enhancement of Choline and subsequently Ach level in plasma that could antagonize α7nAChR present on various immune cells, such as macrophages and FLS; which may exert analgesic effect via decreasing pro-inflammatory cytokines production and decreasement of inflammation in arthritis pain model in rat.

Keywords: CDP-Choline; Choline; Arthritis; α7nAChR; Rheumatoid Pain

Mini Review

CDP-choline (citicholne, cytidine 5'-diphosphocholine) is a naturally occurring endogenous nucleotide, [1] which is mainly synthesized by CDP-choline pathway in the body [2]. CDP-choline beneficial role in improving mental performance among the Alzheimer disease patients [3], prevention of memory impairment [4], stroke and Other CNS Disorders [5] due to many studies has already been stablished.

CDP-choline following Orally, IV or intracerebroventricularly (i.c.v) administration rapidly metabolize to choline and cytidine/uridine [1,6] which leads to increased plasma and tissue concentration of these metabolites [6]. It has been shown that elevation in the plasma level of choline will also increase its level in the brain [7,8]. In the body Choline promote several biological functions such as acting as a precursor of neurotransmitter Acetylcholine [9] as a result of choline availability, Ach synthesis will also increase [6,7,10] subsequently increasing in Ach synthesis will also enhance the cholinergic neurotransmission activity [6,11] Centrally and peripherally enhanced cholinergic neurotransmission activity mediates many effects of CDP-choline [12,13].

Studies have discovered an anti-inflammatory role for the parasympathetic nervous system through inhibition of TNF-α release [6,14]. It is well known that nervous system under the concept of cholinergic anti-inflammatory pathway (CAP) has an important role in this inflammatory response [15]. This pathway conducts its role mainly through stimulation of vagus nerve results in production of Ach, the principle vagal neurotransmitter [14,16,17] that interacts with membrane of nicotinic acetylcholine receptor (nAChR) family; specifically the α7 sub-unit of nicotinic acetylcholine receptor (α7nAChR) [15,17] which is expressed by different types of immune cells, including macrophages (responsible for secreting pro-inflammatory cytokines including TNFa, IL-1[18], which both cytokines are actively produced at the local inflammation area [19]) [17,19] results in significantly and concentration-dependently decreasment of TNF production [20], and significantly attenuation of the releasement of other pro-inflammatory cytokines including interleukin (IL)-1beta, IL-6 and IL-18 [14].

Choline which is one of the hydrolism products of CDP-Choline is a natural α7nAChR selective Agonist [6,21–23] and from different researches we know that α7nAChR selective Agonists has been shown to have anti-inflammatory activity; [24-26] also choline is able to decrease TNF release dose dependently and this effect requires α7nAChR-mediated signaling [22] (TNF increase inflammation by activating the release of pro-inflammatory mediators such as IL-1, HMGB1, nitric oxide [20]).

Due to different studies we also know that intracerebroventricularly injection of CDP-choline dose and time dependently has antinociceptive effects which mainly mediated by activation of α7nAChR. [6,27,28].

So, in the light of the above studies we can hypothesize that exogenously administration of CDP-Choline dose and time dependently results in enhancement of Choline and subsequently Ach level in plasma that could antagonize α7nAChR present on various immune cells, including monocytes, macrophages, T and B lymphocytes, dendritic cells and FLS; which may exert analgesic effect via decreasing pro-inflammatory cytokines production and decreasement of inflammation.

According to our knowledge up on until now there is no research available which directly measure the levels of pro-inflammatory cytokines (such as TNFa, IL-1 and IL-6) and inflammation after exogenously injection of CDP-choline and investigate its possible role as an analgesic in arthritis pain model in rat.

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