Biosafety
ISSN: 2167-0331

Pohanka, Biosafety 2012, 1:4
DOI: 10.4172/2167-0331.1000e115

Editorial Open Access

Could Inhibitors of Acetylcholinesterase Used in Alzheimer Disease Therapy Meet Immunity System and Alters Sensitivity to Pathogens?

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Keywords: Cholinergic anti-inflammatory pathway; Rivastigmine; galantamine; Donepezil; Acetylcholinesterase; Alzheimer disease

Alzheimer disease is a neurodegenerative disorder with a quite high incidence over the world. Currently available drugs for Alzheimer disease therapy contain one of the four compounds: memantine, galantamine, rivastigmine or donepezil [1]. The first, memantine is a non-competitive antagonist of NMDA (N-methyl D-aspartic acid) receptor. Rivastigmine is pseudoirreversible inhibitor of both acetylcholinesterase and butyrylcholinesterase. Galantamine and donepezil are reversible inhibitors of acetylcholinesterase. The enzyme acetylcholinestease plays a role in termination of neurotransmission. Inhibitors of acetylcholinesterase are used for Alzheimer disease therapy for the reason [2]. Beside central nervous system, acetylcholinesterase is widely presented in peripheral nervous system with dominant presence in parasympathicus. In the parasympathicus, regulation of immune system takes place. Mainly cholinergic anti-inflammatory pathway is the crucial part where nerve system meets immunity [3,4]. Owing to the link between acetylcholinesterase and immunity, therapy of Alzheimer disease by acetylcholinesterase could modulate immunity and alter sensitivity to pathogens in thus way.

Cholinergic anti-inflammatory pathway consists from three important parts. Termination of nerves releasing acetylcholine, acetylcholinesterase localized mainly on erythrocytes and macrophages having α7 Nicotinic Acetylcholine Receptor (AChR) are the parts. The α7 AChR can be directly influenced by many compounds as extensively reviewed previously [5]. The inhibitors of acetylcholinesterase used in Alzheimer disease therapy can affect central nervous system as well as blood acetylcholinesterase. The inhibited blood acetylcholinesterase does not split acetylcholine and cholinergic anti-inflammatory pathway is stimulated for the reason. Searching databases, there is evident lack of knowledge about link between the Alzheimer disease drugs and pathogens. Some conclusions can be made from the recently published works on other inhibitors of acetylcholinesterase aggravating progression of pathogen [6]. More extensive attention was given to galantamine which act not only as an inhibitor of acetylcholinesterase but can potentiate AChR as well [5]. Galantamine can ameliorate inflammation not only by inhibition of AChR but also potentiating acetylcholine [5,7] so its effect is probable more striking than the effect of rivastigmine and donepezil. An experimental comparison is, however, missing.

It can be concluded that inhibitors of acetylcholinesterase used in Alzheimer disease therapy or another drugs able to interact with acetylcholinesterase are able to modulate progression of an infection disease. Sufficient experiment assessing of the effect has not been done. The current data reported by several scientists confirms anti-inflammatory action of the drugs. It can be beneficial in some cases. Nevertheless, higher sensitivity to pathogens can be expected. Experiments aimed at the issue are needed to be finished before doing conclusions.

Acknowledgements

The Ministry of Education, Youth and Sports of the Czech Republic is kindly acknowledged for project LH11023.

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Received May 21, 2012; **Accepted** May 22, 2012; **Published** May 24, 2012

Citation: Pohanka M (2012) Could Inhibitors of Acetylcholinesterase Used in Alzheimer Disease Therapy Meet Immunity System and Alters Sensitivity to Pathogens? Biosafety 1:e115. doi:10.4172/2167-0331.1000e115