ORIGINAL RESEARCH

Heparin and Derivatives a New and Possible Treatment of Alzheimer's Disease

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Abstract: Our finding of the ability of heparin sulfate to control an psychiatric disorder as the onset of an acute myocardial infarction in elderly patients, led us to use this drug in Alzheimer's disease. A 78-year-old female patient with Alzheimer 's disease (AD) in moderate stage, was the first case that received heparin sulfate; initial dose of 10000 Uds, in 500 mls of 5% Dextrosa for IV inyection, weekly; demonstrating a significant improvement several hours after the initial treatment, in the cognitive impairment, especially in the memory and spatial orientation. Subsequently, five patients with AD received heparin having similar benefitial effect. We reported for the first time in the literature, both the atypical presentation of a myocardial infarction, controlled by heparin and, the effective response of Alzheimer's disease after received this drug [3, 4].

In conclusion, the initial results showed that the non-anticoagulant action of heparin and derivatives is effective for Alzheimer's disease which could be a targeted drug for this disease.

Keywords: Psychiatric disorder, heparin, non-anticoagulant properties, clinical response, targeted drug.

The central cause of Alzheimer's disease is unknown. However, valuable studies have been carried out and some pathogenic factors and the genetic contribution have been described. The neuro-pathological lesions are well established. Therefore, it is not possible to make treatment with curative purpose. On the other hand, the biomarkers that would serve to get the targeted drug have failed in AD because its development is hindered in this disease [1]. However, there has been progress in the development of blood-based biomarker [2], that help in the diagnosis and prognosis of AD. Direct evidence was the effective response with the use of heparin in patients with Alzheimer's disease. The purpose of this study is to demonstrate the consistent basis of the results, specifically by the non-anticoagulant properties of this drug.

DISCUSSION

This initial study, showed consistently the improvement of the Alzheimer's disease patients after receiving heparin sulfate, that could be a targeted drug for this disease. It is important emphasize that the improvement of the cognitive impairment of AD was rapid as the control of the psychiatric episode of the onset of the acute myocardial infarction (AMI). Also, both processes take place in elderly patients, being significative that the beneficial response of heparin in AMI has been confirmed.

We follow the clinical progression in patients with AD, and the assessment of the improvement after the use of heparin sulfate, with the clinical judgment essentially (clinical-based biomarker). It remains the mainstay of an accurate evaluation in any disease.

Fortunately, the beneficial effects of heparin obtained in AD are based on the non-anticoagulant properties of this glucosaminoglycan (GAG) which actions match for therapy with the pathogenic factors and the morphologic features of this disease. The anti-adhesive force is one of the hallmark of the non-anticoagulant properties of heparin. At the same time, amyloid beta peptide has an adhesive force that has even been measured using Surface Force Apparatus [5]. Also, experimental finding showed that heparin regulates chemokinesis cell migration and other adhesion-regulate processes [6] Thus, heparin inhibit melanoma cell adhesion and migration [7,8] with improvement of the outcome of this cancer patient (anti-adhesive therapy). Therefore, we consider that the anti-adhesive power of heparin sulfate and derivatives can act on the adhesion of the amyloid beta peptide removing the plaques in the brain of the Alzheimer's disease.

At the same time, with the disassembly of the plaques, the activation of AMP protein kinase (AMPK) by the amyloid beta peptide may be interfered or inhibited. This activation play an important role in the hyperphosphorilation of the tau protein [9,10] that is deposited in the neurofibril, forming the intracellular neurofibrillary tangles that lead to dysfunction and death of the neuron of the Alzheimer's brain.

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The inflammatory reaction in Alzheimer's disease is one of the basic factors of the pathogenesis and treatment, and has been considered a neurotoxic effect of amyloid beta and tau proteins. More recently, clinical research has demonstrated that an immune process has an important role in the inflammatory pathogenesis of AD. On the other hand, heparin and derivatives have efficacy and safe as anti-inflammatory agents [11]. Likewise, valuable studies showed that heparin and low molecular-weight heparin have anti-inflamatory activity [12]. This anti-inflammatory property has been used in several diseases as in asthma, inflammatory bowel disease, etc. Therefore, this anti-inflammatory effect used in AD may be a consistent indication.

Furthermore, heparin sulfate is a GAG found in the plasmatic membrane of the neuron where it acts as receptor, in the cellular growth and in the cell to cell communication. These functions could be of beneficial effect for the brain's neuron of AD.

In conclusion, the control of psychiatric disorder as the mode of onset an acute myocardial infarction in elderly patients with heparin is an incontrovertible fact. The beneficial effect of heparin for some patients with Alzheimer's disease was an objective evidence, with very strongly support of advanced and valuable experimental studies above referred. The heparin and derivatives due to its non-anticoagulant properties may represent an effective treatment for AD and so could be a targeted drug. We hope to be able to confirm the initial results in a next large-scale study.

CONSENT TO PUBLISH

Our method of research in human for clinical study arises from the outcome of the healthcare during their hospitalization. Thus, we do not select the patients for research "per se". Therefore the consent is unnecessary. However, we had the consent of the family and the LAR of the research Dept. of the School of Medicine in order to use this data for publication. Also, the patient is no longer alive.

Dr. Antonio Gomez-Valdes.

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