The Point on N-acetylcysteine in Idiopathic Pulmonary Fibrosis Treatment

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Abstract

Idiopathic pulmonary fibrosis (IPF) is still a non-curable disease. The suggested therapy consists of Pirfenidone combined with other drugs like azathioprine, and acetylcysteine. The New England Journal of Medicine published a new study that goes against the common use of N-acetylcysteine (NAC) to treat IPF patient. There are other studies that went in favor of N-acetylcysteine. The present study reviews the entire developments and sums up the reality by affirming that new studies should be done to demonstrate whether the NAC should be administered in combination with Pirfenidone or not, as the last study did not clarify this point.

Keywords: Acetylcysteine; Idiopathic pulmonary fibrosis; Pirfenidone

Introduction

The idiopathic pulmonary fibrosis is a chronic, progressive, fibrosing interstitial pneumonia of unknown cause that mostly affects elder people. Major symptom is of this disorder is the onset of progressive worsening of dyspnea connected to the loss of lung function. This disease has a poor prognosis since the median survival is three years after the diagnosis [1-6].

Pirfenidone is the only drug approved worldwide to treat IPF because of its fibrosis inhibition and collagen production actions induced by TGF-beta2. It also shrinks the inflammatory process by reducing the production of TNF-alfa and IL-1beta [3-4].

However, this drug not free from side effects, mostly leading to gastrointestinal problems. The patients treated with Pirfenidone have an eight months median survival improvement: 3.8 years vs. 3 years. Efforts were on to improvise the case with other drugs. N-acetylcysteine is anumolyctic agent that acts both as precursor and reduced glutathione (GSH). It is a nucleophilic scavenger and an enzyme-catalyzed antioxidant. NAC regulates many cellular functions like apoptosis, cellular growth and the production of cytokine [5-8]. In humans NAC is used in some alveolitis and to avoid Paracetamoloverdose hepatotoxic effects. Therefore, GSH has a major role as a protector of biological structures and functions [9].

Overall, the anti-inflammatory action of NAC is well documented in vitro as well as in vivo.

Materials and Methods

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suppression in lung tissues of IPF patients at an early phase and while dexamethasone or pirfenidone showed no effects [17].

A multicenter, randomized and controlled clinical trial was conducted to evaluate the efficacy of NAC mono therapy among patients with early stage IPF. Seventy six patients were randomly divided in two groups: the NAC treatment group and the control group (no therapy). No significant differences in the FVC change were shown but with a post hoc exploratory analysis showed that NAC therapy was associated with stability of FVC among patients with initial FVC<95% or initial diffusing capacity of carbon monoxide <55% [18,19].

Sakamoto described the correlation between the uses of combined NAC therapy. His study described the difference between the two groups: one treated with Pirfenidone and NAC and the other without NAC. After six months the median change in FVC was 0 mL in the NAC group and -290 mL in the non NAC group and talking about the median survival period was 557 ± 66 days in the NAC group and 196 ± 57 days in the non NAC group (p=0.03) [20].

IFIGENIA is a very important study that compared the regimen consisting of azathioprine, prednisone, and acetylcysteine without NAC in the IPF therapy. They showed that the first one preserved the FVC and carbon monoxide diffusing capacity better than the second [21]. This study encouraged the researchers to evaluate the effects of NAC in treating IPF compared to the three drug regimen and this study was called PANTHER (Prednisone, Azathioprine, and N-Acetylcysteine: A Study That Evaluates Response in Idiopathic Pulmonary Fibrosis). PANTHER was interrupted because it was unsafe and the study continued with the NAC monotherapy and the placebo. The recent study concluded that acetylcysteine did not preserve IPF patients’ FVC and it would result in mild-to-moderate impairment in pulmonary function [22].

Conclusions

Although NAC mono therapy’s effects on IPF weren’t demonstrated in the only study conducted in comparison with placebo [22], the same journal published another article which demonstrated a major efficacy of the NAC combined therapy [21]. It is therefore essential to recap all these findings, as it indicates that NAC may have some beneficial effects, especially among early stage IPF patients. Discussion of these data highlights the importance of a further research in this area. Since the most important studies (IFIGENIA and PANTHER) gave us contrasting elements, an overview on N-acetylcysteine use is needed especially in the combined therapy of IPF. Nevertheless, considering the lack of differences in side effects, the common use of NAC-based therapy can be continued.

References