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Letter to the Editor on: Intravenous N-acetylcysteine in respiratory disease with abnormal mucus secretion

S.H. ADELI[1], K. JAZI[2]

[1]Department of Internal Medicine, School of Medicine, Qom University of Medical Sciences, Qom, Iran
[2]Student Research Committee, Faculty of Medicine, Qom University of Medical Sciences, Qom, Iran

Dear Editor,

We have read the review article entitled "Intravenous N-acetylcysteine in respiratory disease with abnormal mucus secretion" by Tang et al[1]. Gratefully admirable, this study was one of the leading clinical trials assessing the IV formula. In appreciation of publishing novel ideas in your journal, we want to congratulate the authors for this successful trial and make some contributions.

N-acetylcysteine (NAC), available in inhaled, parental, and oral formulations, has been used widely as a mucolytic in several lung disorders worldwide[2]. Besides its proven safety and tolerability, a meta-analysis also confirmed that 600 mg/day oral administration could significantly decrease acute exacerbation of chronic obstructive pulmonary disease (COPD) and improve forced expiratory volume in the first second/forced vital capacity (FEV_1/FVC) and FEV_1 among these patients[3].

Firstly, oral NAC as a mucolytic is indicated in patients with abnormal, viscid, or inspissated mucous secretions in respiratory diseases, such as chronic emphysema, chronic asthmatic bronchitis, and cystic fibrosis[4]. Importantly, there are certain circumstances, such as severely ill hospitalized, intubated patients that cannot tolerate oral agents, where NAC could promisingly improve their condition. Otherwise, the oral formula is the choice. Here, the indication of IV NAC among subjects is not clear. Moreover, authors have compared ambroxol hydrochloride with IV NAC, which showed the non-inferiority of IV NAC; however, the question of whether the superiority or non-inferiority of IV compared to oral formula remains so far.

Secondly, regarding the disposition of subjects, there is a significant amount of vague information. According to Figure 1, 111 patients were included in the NAC group. It was mentioned that 15 participants were excluded from the study, but only the reasons for excluding 12 of them were declared. Among the placebo control group, 95 subjects finally completed the study. However, 14 discontinued the treatment; the decision for patients remains unknown. Furthermore, IV administration of NAC has shown more significant adverse effects, such as anaphylactic reactions, as the result of high plasma concentrations, particularly after the infusion of the initial dose[5]. Therefore, we recommend that the authors focus more extensively on adverse events occurring during the treatment procedures in their study compared to previous trials that they have mentioned in manuscript[6-10]. Additionally, they should specifically mention any adverse events that resulted in discontinuation.

Table IV presents previous IV NAC studies and related key findings; however, it lacks adverse events mentioned in the caption. Besides adverse events, physician decisions and other reasons for discontinuation are not thoroughly discussed. In applying a novel administrative therapy for critical patients, as physicians, we attentively suggest further explanations of patients' status while discussing associated factors.

Corresponding Author: Kimia Jazi, MD; e-mail: kimiajazi@gmail.com

Conflict of Interest

The authors declare no conflict of interest.

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