

N-Acetylcysteine: drug with clinical effectiveness during some respiratory tract diseases

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ABSTRACT

Mucolytic agents are well known and frequently prescribed drugs in children with different respiratory tract disorders. But their role in the treatment is still controversial. As it is proved that N-acetylcysteine reduces viscosity and adhesiveness of mucous sputum, facilitates expectoration of thick mucus as well as prevents accumulation and penetration of infection in sputum and hence, increases effectiveness of other agents, we carried out the study to find out whether N-acetylcysteine has some beneficial clinical effect in children with respiratory tract diseases. To evaluate the clinical effectiveness of N-acetylcysteine (ACC; HEXAL, Germany), an open type clinical observation study of 50 patients was carried out during 2002 – 2005 years period, from 22 months to 15 years old. Among them 15 (30%) [I group] were the patients with acute obstructive bronchitis, 15 (30%) [II group] with recurrent obstructive bronchitis and 20 (40%) [III group] with bronchial asthma. All patients received relevant treatment according to disease management. As an adjunctive drug for mucolytic capacity ACC was included for 8 ± 2 days, three times a day, after meal. After first signs of clinical improvement the dosage were reduced to half doses. All patients underwent routine laboratory testing; for bronchial asthma patients Lung Function Test was obligatory as well. In study groups, for children with ACC prescription, treatment was associated with adrenergic agents: Salbutamol (β -2 agonist) either per os, by Nebulizer (particularly, Fenoterol) or via dose inhaler, in relevant age and mass dosage. Control group consisted of 22 months – 15 years old children with the same diagnoses, which was compromised as a homogenous group according to the basic treatment, sex and age distribution in groups by disease. Inclusion of N-acetylcysteine in the complex treatment of some respiratory tract disorders have positive influence on general conditions of patients. Its effectiveness is expressed mainly toward: 1. Children did not refuse to take the medicine, due to its good taste and water solubility. 2. For patients was much more easy to expectorate less viscid sputum. 3. The relatively short period of acute phase of illness and increased effectiveness of other drugs. 4. Side effects of ACC were minimal when used in combination with adrenergic agents. 5. Wide availability and cost – effectiveness of the treatment.

KEYWORDS: *obstructive bronchitis, bronchial asthma, mucolytic agents and mucus plug*

Abnormalities in the production and transport of airway secretions play an important role in the pathophysiology of asthma, especially during acute exacerbations of the disease. The synthesis of mucus becomes disordered, and other constituents of airway contents, including eosinophils and shed bronchial epithelial cells, contributing to the abnormal sputum that is produced. Altered viscoelastic properties of asthmatic mucus lead to impaired mucus transport rates. In addition, ciliary function may be directly inhibited by factors within the secretions. The consequence of these derangements is often widespread plugging of small bronchi and bronchioles. Occasionally, segmental or subsegmental atelectasis develops, but in most series radiographically visible atelectasis is uncommon. A variety of pharmacological and other methods have been used in attempts to modify abnormal airway secretions and to promote their clearance, but none is not of proven benefit [2]. The process of chronic inflammation comprising mainly T – cells and eosinophils, and airway remodeling with goblet cell metaplasia and submucosal gland hyperplasia takes place as well. The matrix of airway sputum consists of high molecular glycoproteins and mucins, major gel – forming mucins MUC5AC and MUC5B [3]. Mucolytics are useful in adjunctive therapy of respiratory tracts disorders. Agents, such as Ambroxol and N – acetylcysteine are able to alter the secretion of mucus and its physical properties, which results in improvement of mucociliary clearance. Current evidence indicates that these drugs are effective, especially in chronic obstructive pulmonary disease, asthma and acute bronchitis. They produce modest improvements in symptom control and lung function. There is a synergism between mucolytics and antibiotics in the treatment of exacerbation of chronic bronchitis. Moreover, they act as scavengers of reactive oxygen species. As mucolytics are cheap and well –

tolerated they are beneficial in the therapy of patients suffering from respiratory tract disorders [4]. Acetylcysteine is a potent mucolytic agent. When utilized as a 10% solution with a bronchodilator by pressure machine, clearance of tracheobronchial secretions can be achieved in asthmatic subjects without inducing bronchospasm [5]. The relationship between markers of inflammation, adhesion and antioxidant capacity is significantly modulated by treatment with N – acetylcysteine or inhaled corticosteroids [6]. At the same time evidence shows that N – acetylcysteine is ineffective at prevention of deterioration in lung function and prevention of exacerbation in patients with chronic obstructive pulmonary disease [1].

MATERIAL AND STUDY DESIGN

To evaluate the clinical effectiveness of N – acetylcysteine (ACC; HEXAL, Germany), an open type clinical observation study of 50 patients was carried out during 2002 – 2005 years period, from 22 months to 15 years old. Among them 15 (30%) [I group] were the patients with acute obstructive bronchitis, 15 (30%) [II group] with recurrent obstructive bronchitis and 20 (40%) [III group] with bronchial asthma. All patients received relevant treatment according to disease management. As an adjunctive drug for mucolytic capacity ACC was included for 8 ± 2 days, three times a day, after meal. After first signs of clinical improvement the dosage were reduced to half doses. All patients underwent routine laboratory testing; for bronchial asthma patients Lung Function Test was obligatory as well. In study groups, for children with ACC prescription, treatment was associated with adrenergic agents: Salbutamol (β -2 agonist) either per os, by Nebulizer (particularly, Fenoterol) or via dose inhaler, in relevant age and mass dosage.

Control group consisted of 22 months-15 years old children with the same diagnoses, which was compromised as a homogenous group according to the basic treatment, sex and age distribution in groups by disease.

I group – 22 months-8 years old children. Most of them 12 (80%) received symptomatic agents for 3 ± 2 days before administration in the hospital. Due to disease duration deterioration, which expressed in excessive sputum, heavy breath and auscultation data, ACC was included in the general treatment.

II group – 2-8 years children. 10 patients (66,7%) of 15 (100%) due to recurrent cough, breathlessness, received agents of different groups, except ACC. Only to 5 (33,3%) patients was administered ACC at some times before, during previous exacerbation episodes of obstructive bronchitis.

III group – Mean age 10 ± 2 years children, patients with bronchial asthma of at least 1-year duration. Mean datum 3 ± 1 year. 11 (55%) of them did not attended regular hospital visits at all, received symptomatic treatment, different agents, with short term clinical effect. 9 (45%) received different pharmaceutical group agents, included mucolytics, prescribed by doctor either in polyclinic or in hospital. 2 (22,2%) of them ACC with clinical effect in acute period of bronchial asthma attack.

Patients' selection for study was done in accordance to diagnostic criteria of each disease. Criteria for exclusion from study population were side effects, contraindications and hypersensitivity to given drug. Patient's condition was appreciated by following items:

1. Cough – intensiveness, episodic, attack type, with/without sputum
2. Breathlessness
3. Chest tightness
4. Mucous sputum, its amount and viscosity, mucous plugs
5. General condition: mood, depression, low physical activity, anorexia
6. Lung Function Test

To appreciate symptoms for first five items score system was used: no symptoms (0), light symptoms (1), moderate manifestation (2), severe symptoms (3). Due to sleep disturbances during illness acute period (midnight, early in

the morning) and daily activities limitation, before ACC inclusion in the treatment and thereafter, patients estimated by above mentioned score system their quality of well – being. We took in to consideration estimation of general condition of patient, drug tolerance, its effectiveness and compliance. Results of clinical monitoring were calculated by score system for each item: excellent – 1, good – 2, moderate – 3, low – 4.

RESULTS

Acute phase episode in illness duration for each group reduced, and so, for I group it showed $4 \pm 1,0$ days (vs. $6 \pm 1,5$ days in control group). For II group $5 \pm 2,0$ days (vs. $7 \pm 3,0$ days in control group). For III group $4 \pm 2,0$ days (vs. $9 \pm 2,5$ days in control group).

As for first signs of clinical improvement 30 (60%) patients revealed in $1 \pm 0,5$ days (vs. $2 \pm 1,0$ days in control group) after starting ACC. 34 (68%) patients indicated the general effectiveness of ACC treatment as good, 10 (20%) as moderate and 6 (12%) as excellent. Compliance was excellent in 36 (72%) cases, 14 (28%) moderate. Drug tolerance was good in 32 (64%) cases, moderate in 16 (32%) cases and in 2 (4%) cases low. The letter revealed as discomfort while expectorate excessive mucous sputum.

In bronchial asthma group in addition to above-mentioned, an attention was paid to Lung Function Test. In severe cases the data were as follows: FVC $47 \pm 3\%$; FEV1 $38 \pm 4\%$; PEF $29 \pm 5\%$; FEF 75 – $22 \pm 2\%$, FEF50 – $25 \pm 3\%$, FEF25 – $30 \pm 4\%$. After complete treatment mean indices were: FVC $89 \pm 6\%$; FEV1 $97 \pm 4\%$; PEF $88 \pm 9\%$; FEF75 – $93 \pm 5\%$, FEF50 – $96 \pm 3\%$, FEF25 – $88 \pm 4\%$.

CONCLUSIONS

Inclusion of N – acetylcysteine in the complex treatment of some respiratory tract disorders have positive influence on general conditions of patients. Its effectiveness is expressed mainly toward: 1. Children did not refuse to take the medicine, due to its good taste and water solubility. 2. For patients was much more easy to expectorate less viscid sputum. 3. The relatively short period of acute phase of illness and increased effectiveness of other drugs. 4. Side effects of ACC were minimal when used in combination with adrenergic agents. 5. Wide availability and cost – effectiveness of the treatment.

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N – ацетилцистеин: препарат с клиническим эффектом при некоторых заболеваниях респираторного тракта у детей

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Р Е З Ю М Е

Муколитические средства хорошо известны и часто применяются при различных заболеваниях респираторного тракта у детей. Целью исследования являлось выявление облегчающего клинического эффекта ацетилцистеина (АСС, HEXAL, Германия) у детей с заболеваниями респираторного тракта. Под клиническим наблюдением находились 50 детей в возрасте до 15 лет. Среди них 15 - с острым обструктивным бронхитом, 15 - с рецидивирующим обструктивным бронхитом, 20 - бронхиальной астмой. Всем проводилось соответствующее лечение. В качестве вспомогательного средства применялся АСС в течение 8 ± 2 дней, три раза в день, после еды. При первых же признаках клинического улучшения доза препарата уменьшалась наполовину. Все пациенты проходили общепринятые лабораторные исследования. При бронхиальной астме обязательно исследовалась функция внешнего дыхания. Пациентам АСС назначался в комбинации с адренергическими препаратами: сальбутамол внутрь или с помощью небулайзера (в частности, фенотерол), или дозовый аэрозоль. Включение АСС в комплексное лечение некоторых заболеваний респираторного тракта вызывало положительный эффект, улучшалось общее состояние пациентов. Эффективность препарата выражалось в виде: 1. охотного приема детьми препарата вследствие растворимости и хорошего вкуса, 2. разжжения мокроты и облегчения ее отхождения, 3. относительного укорочения острой фазы болезни и увеличения эффективности других препаратов, 4. Минимальных побочных явлений при комбинации АСС с адренергическими препаратами, 5. общедоступности препарата и стоимости лечения.

Ключевые слова: *обструктивный бронхит, бронхиальная астма, муколитические средства, вязкая мокрота*