ORIGINAL ARTICLE

CLINICAL EFFICACY OF MOMETASONE FUROATE INHALATION THERAPY IN ADULTS WITH POST-UPPER RESPIRATORY TRACT INFECTION COUGH

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Abstract

This study was designed to explore the curative effect of mometasone furoate inhalation therapy on adult patients with airway hyper-responsiveness (AHR) cough after having upper respiratory tract infection (URI). There were selected 56 patients who were diagnosed with AHR cough (still having dry cough after treatment of URI). They were randomly divided into treatment group and control group. Through chest radiography and nose endoscopy, the patients with chronic lung disease or perennial rhinitis were excluded. Among the included patients, the treatment group was treated with mometasone furoate inhalation therapy and oral administration of loratadine, while the control group was only treated with loratadine. Follow-up checkups were performed respectively after one-week and two-week treatment. Visual analogue scale (VAS) was used to evaluate the cough degree and cough duration of the patients. In the experimental group, cough duration was 11.60 ± 4.30 days; in the control group, it was 15.00 ± 4.85 days; the difference was statistically significant ($p < 0.05$). The VAS score of the experimental group was significantly lower than that of the control group ($p < 0.05$). In the early phase of the disease, the application of mometasone furoate inhalation therapy can shorten the duration of post-URI chronic cough and relieve AHR symptoms.

Rezumat

Prezentul studiu și-a propus să evalueze efectul terapiei inhalatorii cu mometazonă furoat la pacienții adulți ce prezintă tuse determinată de hiperreactivitatea bronșică după o infecție a căilor respiratorii superioare. Au fost selectați 56 de pacienți diagnosticați cu tuse cauzată de hiperreactivitatea bronșică (pacienți care prezintă tuse seacă după tratamentul pentru infecția tractului respirator superior). Pacienții au fost împărțiți în două loturi, lotul de studiu și lotul martor. După realizarea radiografiei pulmonare și a endoscopiei nazale, pacienții cu boli cronice pulmonare sau rinite perene au fost excluși. Pacienții incluși în studiu au fost împărțiți în două loturi: lotul de studiu tratat cu terapie inhalatorie cu mometazonă furoat și loratadină oral și lotul martor tratat numai cu loratadină oral. Evaluările au fost realizate la una și două săptămâni de tratament. Scara analog vizuală (SAV) a fost folosită pentru a evalua gradul și durata tusei pacienților. În lotul de studiu, durata tusei a fost de 11,60 ± 4,30 zile, iar în lotul martor de 15,00 ± 4,85 zile, diferența fiind semnificativă statistic ($p < 0,05$). Scorul SAV al lotului de studiu a fost semnificativ mai mic decât cel al lotului martor ($p < 0,05$). În prima fază a bolii, aplicarea terapiei inhalatorii cu mometazonă furoat poate scădea durata tusei cronice după infecții ale tractului respirator superior și ameliorează simptomele hiperreactivității bronșice.

Keywords: Mometasone furoate, inhalation therapy, upper respiratory tract infection, airway hyper-responsiveness, cough, visual analogue scale

Introduction

Patients who suffer dry cough after having upper respiratory tract infection received systemic medication, and antibiotics for more than two weeks. However, few doctors have paid attention to the local use of glucocorticoid and antihistaminic treatment in the early phase of the disease. In the few cases of such treatment, only budesonide liquid suspension was applied by oral atomization inhalation to treat the disease [14]. On the market, there are a lot of corticosteroid nasal sprays with different active substances as budesonide, triamcinolone acetonide, beclomethasone diproprionate, flunisolide, fluticasone proprionate, ciclesonide, fluticasone furoate and mometasone furoate. Many studies investigated their efficacy and side-effects profile and there is not a clear clinical evidence for any of these substances [15]. Mometasone furoate is a corticosteroid with rapid, powerful and nonspecific anti-inflammatory effects and anti-allergic effects [17], which can effectively relieve symptoms of inflammation by inhibiting the expansion of blood capillary and infiltration and phagocytosis of white blood cells [8]. Since

1998 when it was first introduced as nasal spray, it was been successfully used for the prophylactic treatment or for seasonal allergic rhinitis and perennial allergic rhinitis [2, 16], for relieving eye symptoms in allergic conjunctivitis [5, 20], for reducing polyp size and nasal congestion in nasal polyposis [1, 19], for reducing recurrence rate of acute rhinosinusitis when is used alone or in combination with antibiotics [9] and also in the treatment of daytime cough associated with rhinitis and rhinosinusitis [11]. Japanese researchers Yamasaki *et al*. [21] revealed that the longer the cough lasted, the more likely it was that the cough developed into cough variant asthma (CVA). Therefore, it is essential to explore a quick and effective therapy. Zhou [25] found that the method of treating cough with nasal spray had a high compliance rate and it greatly reduced the influence of long-term treatment on the work and personal life of patients. Gawchik *et al*. showed that the use of mometasone furoate nasal spray is effective in the treatment of daytime cough that can appear in seasonal allergic rhinitis [11].

Materials and Methods

Clinical design. We selected 56 patients, aged 18 - 72 years old, who were treated in outpatient service of the no. 2 hospital of Yinzhou in Ningbo, Zhejiang between August 2013 and August 2015. They were first clinically diagnosed (in the internal medicine department of this hospital) with airway hyper-responsiveness (AHR) - still having dry cough after upper respiratory tract infection for one to three weeks. Patients were transferred from internal medicine department to otolaryngological department. They were randomly divided into a treatment group (male: 12; female: 16) and a control group (male: 10; female: 18). The diagnosis of post-infection cough was performed in accordance with the Guidelines for Chronic Cough of 2006 [6] and the patients were selected according to the following criteria: no chronic lung diseases or history of chronic lung and bronchus diseases (chronic obstructive pulmonary disease, pulmonary heart disease, lung abscess, pleurisy); no perennial or seasonal rhinitis; nasal cavity was unobstructed, without evident secretions or neoplasm; with different degrees of cough symptoms, most of which having dry cough with little/without sputum; the above symptoms were secondary to URI and the duration was one to three weeks.

We used visual analogue scale (VAS) [4] to assess the patients cough degree and recorded the duration of cough for analysis and curative effect observation. Before case collection, all the patients and their families were informed of the detailed research process and the potential risks. With full respect for the right of informed consent of the patients and their families, we obtained the signed informed consent forms and kept them with the case history. This study has the approval of the medical ethics committee of the no. 2 hospital of Yinzhou.

Treatment method. According to the simple randomizing method, the patients were divided into two groups. In the control group, each patient received oral loratadine tablets (Merck & Co., Inc.), 10 mg, once a day. As for the treatment group, on the basis of taking loratadine (as the control group), each patient also applied mometasone furoate nasal spray (Merck & Co., Inc.) to both nostrils, 100 μg/spray, twice a day (in the morning and at night). None of the patients received other anti-tussive, expectorant drugs, nor antibiotics. In the first and second week of treatment, the patients were evaluated within the outpatient department; the further follow-ups were performed on the phone; their overall coughs and also the cough durations after taking drugs were recorded. VAS method was used to assess the coughing degree of the patients after taking one-week and two-week treatment.

Observation index. The time when cough appeared or disappeared was used as the index; overall coughs and the cough durations after taking drugs were recorded. Considering with the patients' main complaints, the subjective cough degrees of the patients after one-week/two-week treatment were evaluated using VAS method. The implementation steps of this method and log sheets of symptoms were printed and attached to the medical records for the patients to read and fill in. The procedures of the method was: a straight line (10 cm long, with 10 scales at an interval of 1 cm) was used as the standard, the patients with the most severe cough or suffocating asthma were in line with the scale 10, while the asymptomatic patients were in line with scale 0. The patients were asked to mark at the corresponding spots according to the severity of their symptoms so that their scores would be calculated; some patients were evaluated on the phone.

Statistical method. The statistical software SPSS 17.0 was applied; measurement data were expressed in the form of Mean ± standard deviation; independent samples t test was used ($p < 0.05$ revealed statistical significance).

Results and Discussion

Treatment results. The average age of the treatment group and the control group was 46.32 ± 17.15 and 46.00 ± 14.93 years old, respectively. Before the patients presented to the hospital for diagnosis and treatment, they have coughed for several days. We noted the number of cough days before and after the treatment (Table I). We used the total number of cough days only as reference. Also, the number

of evaluation days after treatment was in no obvious correlation with that before treatment. Among all the 56 patients, after 6 to 26 days of medication, cough disappeared completely or there were only occasional coughs. After combined medication, cough duration of the treatment group was 11.60 ± 4.30 days, which was a significantly decrease compared with that of the control group: 15.00 ± 4.85 days. As to the symptom scores of cough (score after seven-day medication/score after 14-day medication), the treatment group got 4.96 ± 1.83/2.03 ± 1.42, which was obviously lower than that of the control group 6.57 ± 1.19/3.21 ± 1.70. There was noted a significant difference in the cough grades of the two groups ($p < 0.01$); accordingly, the curative effect of the treatment group was better than that of the control group (Table I, Figure 1).

Table I

Symptoms of the two groups of patients before and after medication

Group	Average age (years)	Gender		Total cough duration (days)	Cough duration before medication (days)	Cough duration after medication (days)	Score after 7 days of medication	Score after 14 days of medication
		Male (no.)	Female (no.)					
Treatment group	46.32 ± 17.15	12	16	21.53 ± 7.16	9.92 ± 4.42	11.60 ± 4.30	4.96 ± 1.83	2.03 ± 1.42
Control group	46.00 ± 14.93	10	18	25.57 ± 5.74	10.57 ± 3.47	15.00 ± 4.85	6.57 ± 1.19	3.21 ± 1.70
t				-2.325	-0.605	-2.767	-3.878	-2.803
p				0.024	0.548	0.008	0.001	0.007

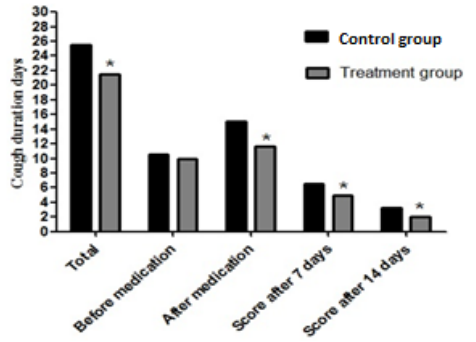

Figure 1.
Symptoms of the two groups of patients before and after medication

Adverse reactions. During the treatment, all the patients in the control group and treatment group had good tolerance for the drugs; there was not registered any severe adverse reaction; in the treatment group, there were occasional adverse reactions such as nasal cavity dryness, bleeding and a very few cases of exacerbation of cough after using the nasal spray; nevertheless, after 3 - 4 weeks of persistent medication, the disease outcome turned out to be the remission of cough.

The diagnosis of post-infection cough is exclusive in clinical diagnosis. The diagnosis criteria are: within a few days or a few weeks, the URI patients develop stubborn cough and suffocating asthma which last for a few weeks to a few months and cannot be controlled with normal medicines, excluding the possibilities that the patients have aggravated infection, chronic pharyngitis, gastroesophageal reflux, postnasal drip syndrome, cough variant asthma or allergic cough [12]. The pathogenesis of post-infection cough is still not determined. Currently, it is considered that post-infection cough results from the extensive damage to the integrity of the respiratory epithelium, widespread inflammation in upper airway and/or lower airway or short-term AHR [18]. Lai *et al.* showed that eosinophilic airway inflammation is common in subacute cough that follows acute upper respiratory tract infection and that in these patients the cough improves after corticosteroids treatment [13]. A few previous studies have shown that in the case of post-infection cough, without infiltration of oxyphilous granulocytes in the airway, infection-induced AHR could last for 6-8 weeks [7], which made it easy for the cough to evolve into CVA and subsequently progress to bronchial asthma [22]. Therefore, it is necessary to take early intervention by selecting an effective therapy with few side effects, which is contributively to cutting off the progressing deteriorating approach of post-infection cough.

The inflammatory factors/cytokines can stimulate afferent nerve endings in the nasal mucosa and reach *fasciculus solitarius* of *medulla oblongata*, further affecting the cough-related paths, thus cough sensitivity increases [23]. Inhaled corticosteroids can inhibit the release of airway inflammatory cytokines and attenuate airway hypersensitive reaction [24]; moreover, they can lead to the contraction and resistance of airway blood vessels, reduce mucosal oedema and mucus secretion [26]. Aerosol inhalation is a commonly used and effective method to relieve a cough in a short period of time [10]; however, it is relatively complex and time-consuming; in addition, its use is limited and patient compliance is unsatisfactory as the patients fail to persist in medication. Mometasone furoate nasal spray proved to be a highly effective glucocorticoid with local application; it is clinically superior as local anti-allergic, while its systemic side effects are subtle; under the therapeutic doses, it shows a low bioavailability (< 0.1%) [3]. The

therapy of nasally inhaled corticosteroids is not absolutely safe; however, as the drug dose is small and it does not enter directly into blood circulation, there are very few adverse reactions.

Conclusions

In this study, we found that the patients who used mometasone furoate nasal spray showed evident remission of cough symptoms and their cough durations shortened obviously, indicating that the therapy was apparently effective in treating post-infection AHR, which was consistent with previous research results.

So far, there are few studies related to treating post-infection cough with nasal sprays. The low number of patients included represents a limitation of the study, therefore, further evaluations regarding the treatment course and its mechanism of action need to be performed.

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