Tokai J Exp Clin Med., Vol. 27, No. 3, pp.79-84, 2002

Impact of Fluticasone Diskhaler on Health-related Quality of Life in Asthmatic Patients

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(Received June 10, 2002; Accepted August 14, 2002)

Objective: **To assess effect of a breath-actuated inhaled steroid, Fluticasone Diskhaler (Flutide™) on health-related quality of life in asthmatic patients using Hyland's living with asthma questionnaire (LWAQ).**
Subjects and Methods: **Randomly selected asthmatic patients filled out the LWAQ (the first study). Then, the eight physicians switched inhaled steroid from pressurelized metered-dose inhaler of beclomethasone (BDI) to Flutide according to their own decision. Consequently some patients were switched their prescriptions and others were not. In 12 weeks after the first study, all the patients again filled out the LWAQ (the second study).**
Results: **The patients treated with Flutide were 87 and without were 159. The scale scores of the Flutide group (mean, 1.900) were significantly higher than those of the BDI-group (mean, 1.789). In the second study, there was no significant difference between the scale scores in the two groups (mean, 1.782 vs. 1.705). Among the 8 domains, only medication score significantly decreased by Flutide therapy. More than 80 % of the patients favored easy handling of Flutide including no necessity of the spacer.**
Conclusions: **Flutide therapy significantly improved quality of life in asthmatic patients. The possible mechanisms are the stronger effectiveness of fluticasone propionate and improvement of adherence to inhaled steroid.**

Key words : health-related quality of life, bronchial asthma, Hyland's living with asthma questionnaire

INTRODUCTION

The Fluticasone Diskhaler (Flutide™) is a novel breath-actuated dry powder steroid which contains fluticasone propionate in the Diskhaler™. After the first introduction in Japan in November 1998, Flutide has been promptly distributed and it shared almost 40 % of the inhaled steroids in one year. Comparing with conventionally used beclomethasone dipropionate, fluticasone propionate has an extreme efficacy but less adrenal suppression [1]. The Diskhaler is also accepted as an easy-handling device [2]. One English literature [3] described that Flutide significantly improved the health-related quality of life (HQOL) in asthmatic patients. The similar tendency has also been reported in Japanese asthmatic patients [4, 5]. However, these Japanese reports were based on very small number of patients and the results were not compared with a BDI-group. There are yet controversies whether the international scale for HQOL is applicable to Japanese patients [6]. We have previously confirmed applicability of Hyland's living with asthma questionnaire (LWAQ) [7], one of the international scales for HQOL on asthmatic patients, to Japanese asthmatic patients [6] and found that LWAQ requires the BDI-group patients. In this study 93 out of the 275 subjects switched inhaled steroid from metered dose inhaler of beclomethasone dipropionate (BDI) to Flutide.

SUBJECTS AND METHODS

This study was conducted as a part of the previous study [6]. In December 1998,

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the asthmatic patients who regularly visited to Tokai University Hospital or Tokai University Oiso Hospital were randomly selected as potential subjects. Their mean BDP use was approximately 780 μg/day. The patients who accepted to be enrolled in the study filled out LWAQ (the first study) and returned it by mail. No criterion for patient-selection to prescribe Flutide was made. The eight responsible doctors switched inhaled steroid from BDI to Flutide (100 or 200 μg/blister) by their decisions. No other pharmacological intervention was done on the participated subjects. After 12 weeks, all the patients were again asked to fill out the LWAQ (the second study). Any physiological parameter such as peak expiratory flow rate or spirogram was not collected. In the Flutide-treated patients the mean daily use was approximately 420 μg/day.

To investigate patients' impression of Flutide use, additional five questions were asked to the patients who received Flutide in the second study. The questions were as follows. 1) I am bothered with changing Rotadisk. 2) Flutide inhalation induces coughing. 3) I favor no irritant smell of propellerant gas in Flutide use. 4) I feel handling the Flutide is easy. 5) I like no necessity of spacer. The responses were directed as three ranks; yes, maybe yes or no.

Precise description of the LWAQ was made previously [6]. In brief, the LWAQ composed of 68 items and each item allowed for four choices; "very true of me", "slightly true of me", "untrue of me", and "not applicable". We rated each question as 1, 2 or 3 with calculated scale scores between 1.00 and 3.00 (higher scores reflecting poorer HQOL). If the answers were "not applicable" or not completed in more than 23 items, the response was excluded from the study. Responses to each question were further classified into 11 domains [8, 9] and domain scores were calculated. Among the eleven domains "sex", "sleep" and "colds" have been eliminated from the analysis because they showed to be not reliable in our previous study [6]. As results the domain scores were compared in 8 domains: "social/leisure", "sport", "holidays", "work and other activities", "mobility", "effects on others", "medication usage" and "dysphoric states and attitudes".

All the statistical analyses were done with the Mann-Whitney or Wilcoxon's nonparametric test. A p value of less than 0.05 was considered significant.

RESULTS

Mean scale scores

In the first and second studies, 320 and 295 completed questionnaires were returned to us respectively (return rate 94 % in each study). Approximately 70 % of the patients were categorized as moderate severity of bronchial asthma according to their prescriptions. In the patients who completed two questionnaires, 87 patients received treatment with Fluticasone Diskhaler and 159 patients did not (Table 1). The mean ages and the male to female ratio were also shown.

Figure 1 shows frequency distributions of the scale scores in both groups in the first study. They were not normally distributed. The mean scale scores of the Fultide group and BDI group were 1.900 and 1.789 respectively. The scale scores of the Flutide group were significantly higher than those of the BDI-group.

Figure 2 shows frequency distributions of the scale scores in both groups in the second study. The mean scale scores of the Fultide group and BDI-group were 1.782 and 1.705 respectively. There was no significant difference in the scale scores in the two groups. In both the Flutide and BDI-groups, mean scale scores significantly decreased in the second study.

Domain Analysis

Figure 3 shows change in median of each

Table 1 Age and male to female ratio of the subjects

	Age (mean ± SD)	n	Male	Female
Not Flutide use (BDI-group)	52.4 ± 14.1	159	68	91
Flutide use (Flutide group)	54.2 ± 16.4	87	35	52

domain score in both groups in the first and second studies. In the first study, all the eight median scores in the Flutide group were higher than corresponding scores in BDI-group. The differences were significant in five ("holidays", "mobility", "social", "sport", and "work and other activities") domains. In the second study, four domain scores ("effects on others", "mobility", "sport" and "work and other activities") in the Flutide group were significantly higher than those of the BDI-group. Therefore, no statistical significance became obtained in holidays- and social-domains while effects on others-domain was newly appeared as disturbance after introduction of Flutide.

As we reported in our previous study [6], five domain scores, i.e., "social", "effects on others", "works and other activities", "holidays" and "dysphoric states and attitudes" significantly decreased in the second study in the BDI-group. When changes in domain scores between the first and second studies were compared in the Flutide group, the significant difference was recognized only in "medication" domain.

Patient's impression to Flutide

Figure 4 shows the responses to the questions about Flutide use. Only 5 % of the patients felt that procedure of changing Rotadisk bothered them and approximately 10 % of the patients felt that Flutide inhalation induced coughing. In contrast 65 % of the patients favored no irritant smell of propellant gas in Flutide use and more than 80 % of the patients favored easy handling the Flutide that requires no spacer.

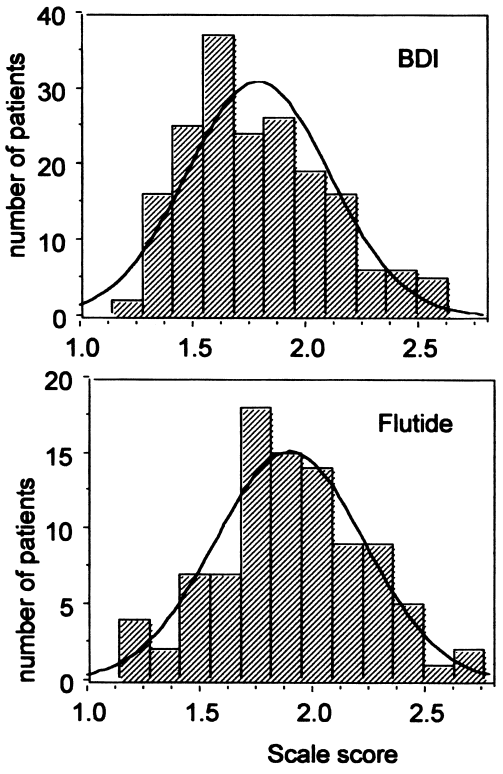

Fig. 1 Frequency distribution of scale scores in the first study. **BDI**: distribution in those who were not prescribed Flutide later. **Flutide**: distribution in those who were treated with Flutide later. Curves in the two panels represent normal distribution.

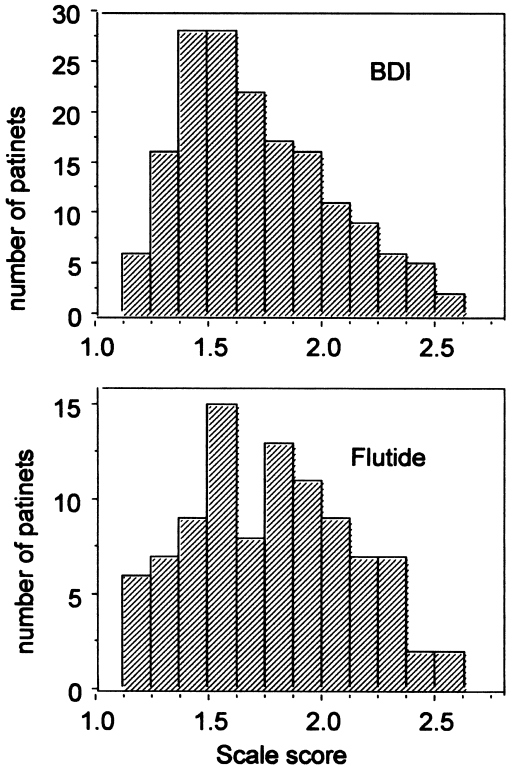

Fig. 2 Frequency distribution of scale scores in the second study. **BDI**: distribution in those who were not prescribed Flutide. **Flutide**: distribution in those who had been treated with Flutide.

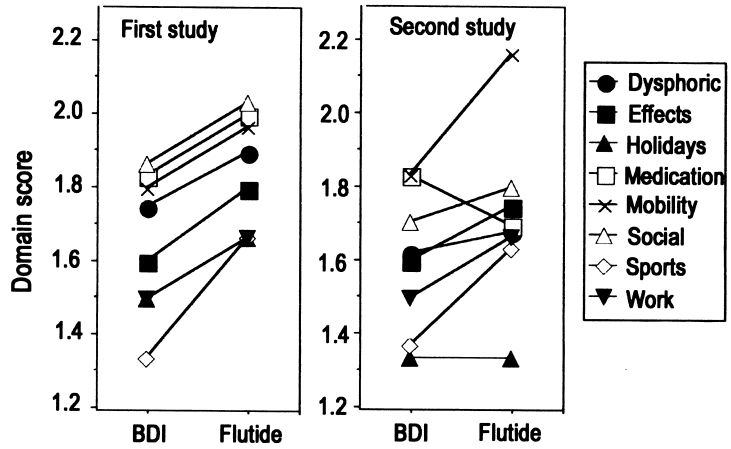

Fig. 3 Median scores in each domain at the first and second studies. In the first study, the differences were significant in "dysphoric states and attitudes", "holidays", "sport" and "work and other activities" domains. In the second study, the domain scores of "sport", "work and other activities" "mobility" in the Flutide group were significantly higher than those of the BDI-group.

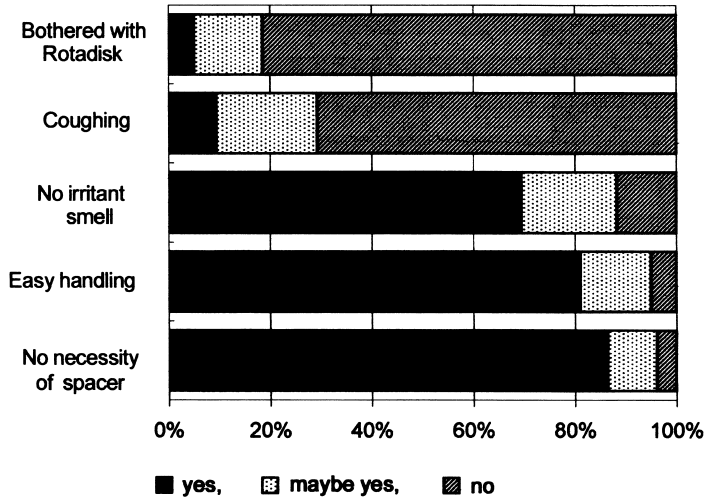

Fig. 4 The responses to the questions about Flutide usage.

DISCUSSION

This study revealed that 1) When no criterion for prescription was made, Flutide was tended to be prescribed to the asthmatics with poorer HQOL; 2) Flutide improved such poorer HQOL of these patients to the level of patients who continued to be treated with BDP; and 3) most of the patients accepted the Diskhaler as easy-handling device.

Though beclomethasone dipropionate with freon-actuated inhaler (BDI) is currently the most popular inhaled steroid in Japan, Flutide has two outstanding characteristics those BDI does not. One is a novel potent inhaled steroid, fluticasone propionate, and another is a new breath-actuated inhaler, Diskhaler. Therefore effects of Flutide on HQOL should be assessed from these two features.

There are several reports describing effect of inhaled steroid on asthma HQOL, how-

ever, nothing concerned the switching effect of inhaled steroid on HQOL. We should discuss why the Flutide-treated patients have had poorer HQOL at first. In the present study we did not make criterion to select patients to be treated with Flutide and also did not direct the physicians to prescribe dose of fluticasone equipotent to beclomethasone. Meanwhile, the physicians recognized that fluticasone propionate, either actuated by freon-gas or with breath-actuated inhaler, has twice potent effect of beclomethasone on asthma control [10, 11]. Only one breath-actuation of Flutide (100 or 200 μg/blister) has almost the equivalent effect of 4 or 8 puffs of BDI (100 μg/puff) as the result. Therefore, it appears to be reasonable that Flutide had tendency to be prescribed to the patients who were relatively poor controlled and who might have poor HQOL.

We consider the following two factors may have improved the HQOL in these patients who received Flutide. One is possibly increased dosage of inhaled steroid and the other is improved steroid adherence. In domain analysis, Flutide therapy significantly decreased a score only in the medication domain. This finding suggests that medical intervention contributed to improving HQOL. On the other hand, it is reported that increasing inhaled steroid dosage improved physiological parameters of bronchial asthma [12], but that HQOL score had weak correlation with physiological parameters in asthmatic patients [8, 10, 12, 13]. For example, Tsukino *et al*. [13] reported inhaled steroid-therapy significantly improved pulmonary function (FEV_1) and significantly decreased HQOL scores, however, their correlation was not good. Molen *et al*. [15] found in moderate asthmatic patients that formoterol treatment significantly improved both physiological parameters such as FEV_1 and PEF, and LWAQ scores after 6 months of regular inhalation. However, the correlation between pulmonary functions and LWAQ scores was poor. These reports suggest that stronger effect of fluticasone propionate may not be the only factor in improvement of HQOL in our patients.

Another important characteristics of Flutide is its easy-handling together with no necessity of spacer. The patients treated with BDI have to inhale slowly from a large volume (~700 mL) spacer. Daily conductance of this maneuver is time consuming and it is inconvenient to carry a large volume spacer to their working place. These disadvantages may disturb patient's adherence to the steroid inhalation therapy. However, there have been few studies on disadvantage of a spacer use. Shieh [15] reported that approximately 80-90 % of the asthmatic patients preferred Diskhaler to metered-dose inhaler though they did not describe the reason for the preference. In the present study, more than 80 % of our patients assessed Diskhaler as an easy-handling device and almost the same number of the patients favored no necessity of spacer. Thus, free from the spacer use may be one of reasons for Diskhaler favor. It is known that many patients receiving BDI have poor adherence with directed usage [16]. Switching inhaled steroid from BDI to Flutide relieved the patients from frequent actuation since one breath-actuation of Flutide is equipotent to 4 puffs of BDI. These may have provided better steroid adherence to steroid inhalation therapy that can contribute to the improvement of HQOL.

In conclusion, this study affirmed that Fluticasone Diskhaler significantly improved quality of life in Japanese asthmatic patients. This may be due to better adherence to steroid inhalation therapy as well as the higher clinical efficacy of fluticasone propionate than beclomethasone.

ACKNOWLEDGEMENT

We are grateful to Stanley M. Cassan, M.D., Ph.D. for his critical review of this manuscript.

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