

exposure. In addition, airborne food particles cause not only respiratory allergy, but also purely dermatologic symptoms (4).

Since positive reactions to uningested foods in RAST or skin prick tests predict cutaneous or respiratory symptoms after exposure to these foods (5), such tests performed on infants with early onset atopic dermatitis from high-risk families should routinely include the foods mainly causing allergic reactions, even though previously uningested, such as cereals, egg, and cow's milk.

Key words: dermatitis; atopic; food hypersensitivity; hypersensitivity; infant food.

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Comparison of three different oral corticosteroids in steroid-dependent asthma patients

CORTICOSTEROIDS represent the most potent treatment of asthma (1). Inhaled corticosteroids are highly effective in most patients, but, in a few

No significant differences were found in this pilot study.

patients, long-term oral steroids are required (2). The most commonly used oral corticosteroids are prednisone (P), prednisolone (PL), and methylprednisolone (MP) because they show the best efficacy/safety ratio. Several reports have

suggested some differences in the lung pharmacokinetics and bioavailability of these molecules (3, 4). Therefore, patients requiring long-term oral treatment with corticosteroids may present differences in the effectiveness of a given molecule.

To compare the effectiveness and the clinical side-effects of three different corticosteroids (P, PL, MP), we performed a randomized prospective trial in 10 severely asthmatic patients (six males, 38.4 ± 17.2 years of age) requiring long-term oral treatment with corticosteroids. All patients were classified as severe asthmatics according to the WHO/NHLBI workshop report (5) and had required at least 2 g of the equivalent dose of prednisolone during the last 12 months (mean $\pm$ SD: 18.0 ± 5.3 mg equivalent prednisolone per day). Many attempts to decrease their dose of oral steroid were unsuccessful, justifying the continuation of oral corticotherapy. All of them were receiving 1600–2000 μ g of inhaled budesonide or beclomethasone. No patient was taking salmeterol or formoterol. They had been instructed to measure their peak expiratory flow rate (PEFR) twice daily for at least 1 year. All the medications required to control the asthma symptoms remained unchanged throughout the study. The study was approved by the ethics committee of the clinic. Patients gave informed consent for the study.

The control of asthma was based on symptom score (0 = no symptoms, 1 = mild symptoms [symptoms which are easily tolerated], 2 = moderate symptoms [symptoms interfering with daily activity or sleep], 3 = severe symptoms [inability to perform usual duties or sleep]), physical examination of the patients, PEFR, and pulmonary function tests. The β_2 -agonist medication was recorded. A randomized prospective trial was performed. The study was preceded by a run-in period of 15 days. At entry to the study, the patients received the equipotent oral dose of glucocorticosteroid treatment that was previously required. The study was divided into three different periods of 21 days, during which the patients received the three molecules in a randomized order (three patients received P-PL-MP; three patients, PL-MP-P; four patients, MP-P-PL). No difference was observed according to the order of the different drug regimens. Side-effects were assessed at each visit by the eventual occurrence of a severe symptom associated with oral corticosteroids and the measurement of weight, blood pressure, and glycemia. Nonparametric tests were used, and paired data were analyzed by the Wilcoxon signed rank test.

All patients completed the study without side-effects. Patients did not experience clinical deterioration of asthma, and the three treatments were found to be similar in terms of efficacy (Table 1). The

Table 1. Clinical, pharmacologic, and pulmonary variables during baseline and three periods of treatment

Mean/periods	Baseline	Prednisone	Prednisolone	Methylprednisolone
Symptoms score	1.6 ± 0.5	1.4 ± 0.7	1.7 ± 0.5	1.5 ± 0.7
β ₂ Consumption [†]	9.2 ± 1.8	9.1 ± 1.8	9.0 ± 1.4	8.7 ± 1.2
PEFR morning	350.1 ± 64.2	367.6 ± 55.3	349.3 ± 77.0	351.9 ± 70.3
PEFR evening	402.2 ± 79.8	390.3 ± 83.5	389.1 ± 75.6	381.4 ± 72.9
PEFR variability* (last 7 days)	8.5 ± 4.7	6.5 ± 6.9	6.5 ± 7.5	10.2 ± 10.7
FEV ₁ (% pred.)	75.5 ± 10.3	75.5 ± 16.5	78.5 ± 20.1	76.3 ± 16.7
FEV ₁ (ml)	2415.0 ± 535.4	2411.0 ± 520.7	2490.0 ± 729.5	2410.0 ± 500.0
Blood pressure systolic	130.0 ± 8.2	130.0 ± 7.9	130.0 ± 14.2	129.0 ± 8.8
Blood pressure diastolic	72.0 ± 7.8	68.0 ± 7.8	69.0 ± 8.7	68.0 ± 7.8
Weight	67.3 ± 13.4	68.1 ± 13.4	66.0 ± 13.8	67.5 ± 13.3

[†] β₂ Consumption: number of inhalations of salbutamol per day.

* PEFR variability: (PEFR maximum) – (PEFR minimum)/PEFR maximum.

Results are expressed as mean and standard deviation.

lung function assessed by the measurement of the bronchial obstruction was not significantly modified, and the patients' FEV₁ and FEV₁/FVC remained stable during the study. Reversibility under β₂-agonists was unchanged. The variation in their self-reported measurement of PEFR was not significantly different, and the diurnal PEFR variability tended to be less important during the prednisone and prednisolone period than the methylprednisolone, but the differences did not achieve statistical significance.

The results of the present study show that the three drugs used were similar in clinical efficacy and safety. The change of molecule did not modify the control of asthma, the lung function, or the PEFR variability or symptom scores. We selected three molecules because of their wide use in asthma. Prednisone and prednisolone are closely related, and prednisone is converted in the body into prednisolone. Thus, the lack of difference between the two treatments might have been expected; however, 1) this had to be demonstrated *in vivo*, and 2) the formulation of the two drugs differed, prednisolone being supplied as an effervescent tablet in France, a feature which might have had a pharmacokinetic effect. To our surprise, although we gave equipotent doses of three oral corticosteroids, and although methylprednisolone has slightly greater anti-inflammatory properties and may have the best lung bioavailability (6), there was no difference in asthma control during the three treatment periods. The use of any washout period was impossible in such a study due to the steroid dependency of the patients. The absence of a washout period may introduce a possible bias into the study. In fact, the last molecule used may have a persistent effect. However, the randomization was done to reduce

this potential bias, and the absence of difference observed whatever the molecules or the order of the drug regimen argues against this bias.

Clinically, the results of the present study did not show any difference in the effectiveness and clinical side-effects among the three most common oral corticosteroids used in asthma. However, these results need to be confirmed by a larger study comparing a longer period of treatment for each of these molecules.

Key words: asthma; methylprednisolone; prednisolone; prednisone.

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