ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN – POLONIA
VOL. LX, N 2, 158 SECTIO D 2005

Department of Allergology and Internal Diseases, Department of Pediatric Allergology
Medical University of Białystok, University Hospital in Białystok
Private Allergology Practice in Białystok

ALICJA TOMOROWICZ, EWA ŚWIEBOCKA, GRZEGORZ SIERGIEJKO,
AGNIESZKA ŚWIDNICKA-SIERGIEJKO, ZENON SIERGIEJKO

Comparison of clinical efficacy of two inhaled corticosteroids: budesonide and triamcinolone acetonide

Inhaled corticosteroids (ICS) are the first line therapy in asthma patients (4). Since the early seventies of the last century numerous ICS have appeared on the pharmaceutical market. First introduced to asthma therapy, Beclomethasone dipropionate (BDP) and budesonide (BUD) are regarded now as classic substances in this group. Most of new ICS are compared to them (5). A few years ago inhaled triamcinolone acetonide (TAA) appeared on the Polish market. Systemic formulations of TAA have been used since the seventies (1, 7, 12). The first attempts of asthma treatment with TAA aerosol were reported in the late seventies (16).

The aim of the study was to compare both clinical efficacy and effect on bronchial reactivity of two inhaled corticosteroids, TAA and BUD.

MATERIAL AND METHODS

Studies were carried out on a group of 50 mild to moderate adult asthma patients. They had to fulfill the following criteria: 1. Age 18–65 years. 2. Asthma diagnosed at least 6 months earlier. 3. On the first visit: $FEV_1 \geq 60\%$ of predicted values and $PC_{20}FEV_1$ histamine ≤ 8mg/ml, 4. before the study treated with ICS in daily dose of 400–800mcg of BUD or BDP or equivalent dose of other ICS, 5. Conscious consent. The study lasted 16 weeks. After two weeks of run-in period when the patients took earlier used treatment, they were divided into two equal groups: treated with BUD or TAA. For the next two weeks they inhaled placebo (looking as Pulmicort® turbuhaler or Azmacort®) instead of earlier used ICS. Since the visit 3 patients started the treatment with active drugs, BUD or TAA, and continued it for a period of 12 weeks (Fig. 1). For the whole period of the study patients noted in their diary cards morning and evening PEF values, asthma symptoms, salbutamol consumption (used as a rescue medication) and possible adverse events. On each of the five visits spirometry was performed. On the first and last visits bronchial challenges with histamine were performed according to Ryan's method (14). Characteristics of the patients are presented in Table 1. Statistical analysis was performed using software Statistica.

Table 1. Characteristics of the patients studied

	N	Sex	Age (years)	Height (cm)	FEV_1 (% PV)
Budesonide	25	F-12, M-13	28 ± 8	171 ± 8	78 ± 8
TAA	25	F-13, M-12	27 ± 10	171 ± 9	79 ± 9

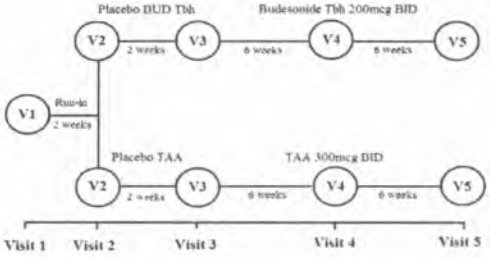

Fig. 1. Scheme of the study

RESULTS

After 2 weeks placebo using the values of FEV_1 decreased significantly in both, BUD and TAA groups, in comparison to the baseline values. After including active treatments, the FEV_1 came back to values earlier observed (Fig. 2). Morning and evening values of PEF are good indicator of asthma control. Changes in PEF during the study are presented in figure 3. Budesonide better than TAA improved morning PEF. The PEF values measured in the evenings did not differ in both groups. Budesonide and TAA comparably depressed intensity of asthma symptoms both night and daily (Fig. 4).

Requirement on salbutamol as a rescue medication can be used as another indicator of asthma control. Patients treated with BUD and TAA needed a similar number of salbutamol doses. Most patients in both groups after 12 weeks treatment increased the $PC_{20}FEV_1$ had in comparison to the baseline value. It proves that ICS can cause a decrease in bronchial reactivity. From the clinical point of view changes lower than 100% in comparison to the baseline value seem to be not important.

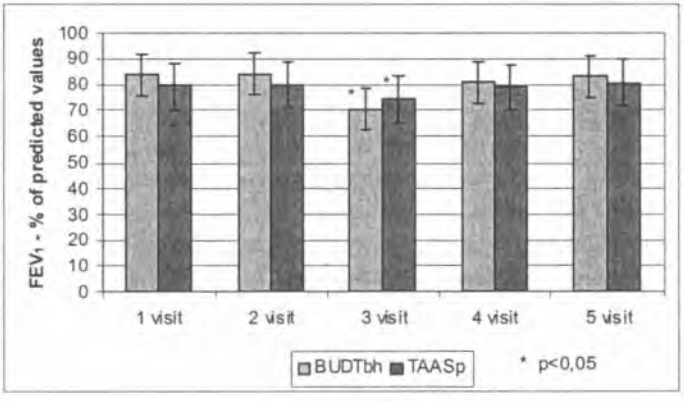

Fig. 2. Comparison of FEV_1 values on successive visits in both studied groups

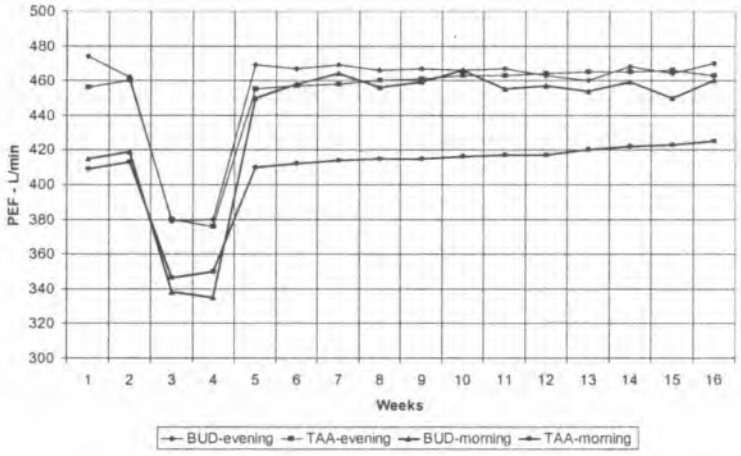

Fig. 3. Comparison of average values of morning and evening PEF in both groups during successive weeks of the study

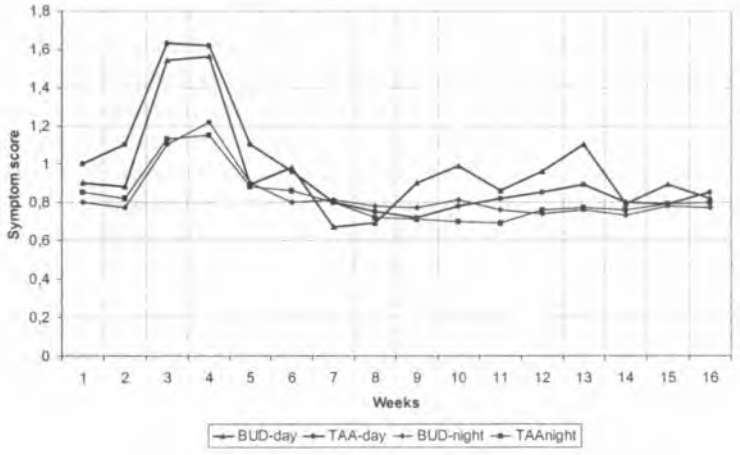

Fig. 4. Comparison of the effects of budesonide and acetonide triamcinolone on asthma symptoms during successive weeks of the study

DISCUSSION

The first two weeks of the study were needed to teach patients the correct measurement of PEF, and fulfill diary cards. The change of earlier used corticosteroids into placebo caused an increase in the intensity of asthma symptoms, salbutamol consumption and a decrease in PEF values in both groups. The degree of the changes in the above mentioned parameters was a surprise to us. On the basis of a paper by Berkovitz et al. before the study we forecast only a slight increase in daily sabutamol consumption (2). In our study we found a better effect of BUD than TAA on morning PEF. This phenomenon can be partially explained by esterfication of BUD in lung tissue and longer maintainance in higher concentration in lungs (8, 9, 10). Regular inhalation of BUD and TAA affected other evaluated

parameters in a comparable degree. Clinical efficacy of BUD is well documented (15).

In most earlier studies TAA was compared with placebo (3, 6). Berkovitz et al. performed studies comparing TAA with BDP. The efficacy of both ICS was comparable (2).

Treating asthmatics we expect a decrease in bronchial hyperreactivity. Our results indicate a slight improvement in BHR after 12 weeks of using both studied ICS. Ramsdell et al. observed a decrease in BHR after 6 weeks TAA inhaling in group of mild asthmatics (13). A significant increase in $PC_{20}FEV_1$ in patients treated with TAA in comparison to placebo was observed by Pincus et al. (11).

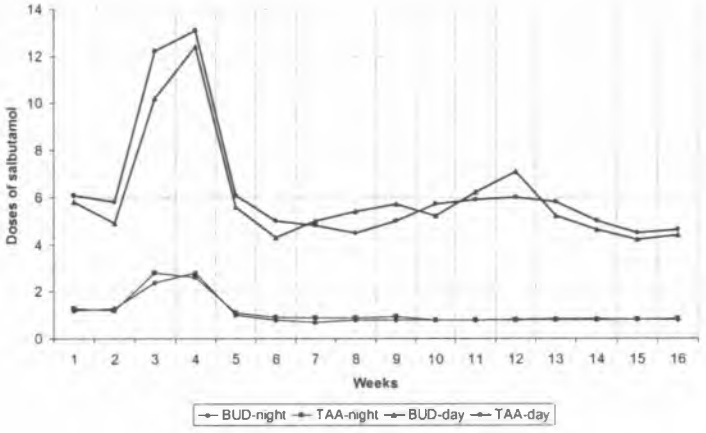

Fig. 5. Comparison of the effects of budesonide and acetonide triamcinolone on salbutamol consumption used as rescue medication

Table 2. The effect of 12-week treatment with budesonide and TAA on bronchial reactivity

	$PC_{20}FEV_1$ histamine [mg/ml]			
	BUD		TAA	
	baseline	after	baseline	after
1	2.50	2.80	2.00	2.80
2	0.045	0.50	3.00	2.50
3	0.20	0.38	0.03	0.08
4	4.00	5.00	0.50	1.00
5	1.00	2.20	0.06	0.21
6	5.00	8.00	7.00	8.00
7	0.03	0.20	3.00	3.50
8	5.50	6.80	6.0	8.00
9	6.00	4.00	5.00	4.00
10	0.08	0.05	0.03	0.05
11	0.20	1.50	1.20	2.50
12	2.80	4.20	1.80	2.20
13	1.30	1.80	3.30	1.80
14	3.40	6.00	7.00	8.00
15	5.60	7.20	6.00	10.00
16	0.55	0.60	0.25	0.60
17	7.00	9.00	0.18	0.25
18	1.18	3.20	7.00	8.00
19	2.30	4.40	3.20	4.40
20	1.80	2.60	0.18	0.60
21	0.40	1.30	0.50	1.00
22	2.10	1.80	1.10	1.00
23	1.00	2.00	2.00	3.00
24	0.18	0.30	0.13	0.30
25	0.25	0.80	0.10	0.80
Me X ± SD	1.30 2.17 ± 2.17	2.20 3.06 ± 2.60	1.80 2.42 ± 2.50	2.20 2.98 ± 3.04
	Z=3.618. p = 0.0002		Z=2.852 p = 0.004	

CONCLUSION

Inhaled TAA is as efficacious as BUD in the treatment of asthma patient.

REFERENCES

1. Ajewski Z. et al.: Zastosowanie Kenalogu® w przewlekłym leczeniu astmy oskrzelowej i przewlekłego nieżytu oskrzeli. Pneumonol. Pol., 44, 321, 1976.
2. Berkovitz R. et. al.: A comparison of triamcinolone acetonide MDI with a built-n tube extender and beclomethasone dipropionate MDI in adult asthmatics. Chest, 81, 20, 1982.
3. Bernstein D. I. et al.: A multicenter, placebo-controled study of twice daily triamcinolone acetonide (800mcg per day) for the treatment of patients with mild to moderate asthma. J. Allergy Clin. Immunol., 101, 433, 1998.
4. Global Strategy for Asthma Management and Prevention. Updated 2004. http://www.ginasthma.com
5. Gruvstad E., Bengtsson B.: A comparison of a new steroid budesonide, with other topical corticosteroids in the vasoconstriction test. Drugs Exp. Clin. Res., 6, 385, 1980.
6. Jacobson K. et al.: Placebo controlled, comparative study of the efficacy and safety of Triamcinolone acetonide inhalation aerosol with the non-CFC propellant HFA-134a in patients with asthma. Ann. Allergy Asthma Immun., 83, 327, 1999.
7. Mc Millian W. P.: Triamcinolone acetonide (Kenalog®) in treatment of case of hay fever and its effect on pituitary-adrenal axis. Ulster Med. J., 40, 76, 1974.
8. Miller-Larsson A. et al.: High capacity of airway (lung tissue for budesonide esterfication as compared to peripheral striated muscles. Eur. Respir. J., 14, Suppl. 30, 195s, 1999.
9. Miller-Larsson A. et al.: Glucocorticoid receptor occupancy modulates the formation of budesonide fatty acid esters *in vivo*. Am. J. Respir. Crit. Care Med., 159, (No 3 part 2), A628, 1999.
10. Miller-Larsson A. et al.: Prolonged airway activity and improved selectivity of budesonide possibly due to esterfication. Am. J. Respir. Crit. Care Med., 162, 1455, 2000.
11. Pincus D. J. et al.: Further studies on the chronotherapy of asthma with inhaled steroids: the effect of dosage timing on drug efficacy. J. Allergy Clin. Immunol., 100, 771, 1997.
12. Piotrowska B. et al.: Polcortolon 200® u chorych z astmą oskrzelową i zespołami astmatycznymi. Terapia i Leki, 9, 179, 1979.
13. Ramsdell J. W. et al.: A controlled trial of twice daily Triamcinolone oral inhaler in patients with mild-to-moderate asthma. Ann. Allergy Asthma Immunol., 80, 385, 1998.
14. Ryan G. et al.: Standardization of inhalation provocation tests: two techniques of aerosol generation and inhalation compared. Am. Rev. Respir. Dis., 123, 195, 1981.
15. Shaw M.: Pulmicort® – active where it matters. Astra Zeneca 2002.
16. Sly R. M. et al.: Treatment of asthma in children with triamcinolone acetonide aerosol. J. Allergy Clin. Immunol., 62, 76, 1978.

SUMMARY

Inhaled corticosteroids are thought to be the first line therapy in asthma patients. The aim of the study was to compare clinical efficacy and effect on bronchial reactivity of two inhaled corticosteroids, TAA and BUD. Studies were carried out on a group of 50 mild to moderate adult asthma patients. The study lasted 16 weeks. After two weeks of run-in period, when patients took earlier used treatment,

they were divided into two equal groups: treated with BUD or TAA. For the next two weeks they inhaled placebo instead of earlier used ICS. After the visit 3 patients started treatment with active drugs and continued it for a period of 12 weeks. For the whole period of the study they noted morning and evening PEF values, asthma symptoms, salbutamol consumption and possible adverse events in their diary cards. On each of the five visits spirometry was performed and furthermore on the first and last visits bronchial challenge with histamine. The change of earlier used corticosteroids into placebo caused an increase in intensity of asthma symptoms, salbutamol consumption and a decrease in PEF values in both groups. Clinical efficacy of BUD and TAA was similar. Both of them slightly affect bronchial reactivity. Inhaled TAA was as efficacious as BUD in the treatment of asthma patient.

Porównanie skuteczności klinicznej dwóch glikokortykosteroidów wziewnych: budezonidu i acetonidu triamcinolonu

Glikokortykosteroidy wziewne są uważane za leki pierwszego rzutu w leczeniu chorych na astmę. Celem pracy było porównanie skuteczności klinicznej i wpływu na reaktywność oskrzeli dwóch wziewnych glikokortykosteroidów: budezonidu i acetonidu triamcinolonu. Badanie przeprowadzono w grupie 50 dorosłych chorych na łagodną lub umiarkowaną postać astmy. Całe badanie trwało 16 tygodni. Po dwóch tygodniach okresu wstępnego, w którym badani przyjmowali wcześniej stosowane leki, podzielono ich losowo do grup leczonych budezonidem lub acetonidem triamcinolonu. Przez pierwsze dwa tygodnie otrzymywali placebo wyglądające jak porównywane leki, a potem w ciągu 12 tygodni stosowano leki czynne. Pacjenci przez cały okres badania prowadzili dzienniki samoobserwacji, w których notowali wartości porannych i wieczornych pomiarów PEF, nasilenie objawów, zużycie salbutamolu oraz ewentualne objawy niepożądane. Na każdej z pięciu wizyt przeprowadzano badanie spirometryczne, a na pierwszej i ostatniej także test prowokacji oskrzelowej z histaminą. Zamiana wcześniej stosowanych glikokortykosteroidów na placebo spowodowała obniżenie wartości zarówno porannych, jak i wieczornych wartości PEF, nasilenie objawów astmy, a także wzrost zużycia salbutamolu. Zastosowanie badanych leków doprowadziło do normalizacji obniżonych parametrów, a skuteczność obu leków była podobna. Acetonid triamcinolonu w leczeniu astmy jest lekiem tak skutecznym, jak budezonid.