

Methylprednisolone pulse therapy in severe acute asthma

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In a group comparative double blind pilot study six asthmatic patients with an acute exacerbation of their disease were randomly treated with either methylprednisolone pulse therapy (MPPT) (1000 mg daily for 3 days) ($n = 2$) followed by placebo tablets, or standard doses of methylprednisolone (MP) (50 mg daily gradually decreased to zero over 3 weeks) ($n = 4$). The results showed that the effect of MPPT did not differ from that of standard doses of MP. MPPT has, however, the potential of being preferable to standard treatment with MP, because of easy administration and optimal patient compliance.

Key words: asthma; corticosteroid; pulse therapy

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There has been widespread agreement that glucocorticosteroids are of value in the treatment of acute episodes of asthma refractory to standard bronchodilator therapy (2, 4, 8). The recommended initial dose of methylprednisolone (MP) varied considerably (3). In our department the initial dose is 50 mg MP intravenously followed by oral administration of MP over 3 weeks in declining doses dependent on the clinical response.

Methylprednisolone pulse therapy (MPPT) (1000 mg MP intravenously on 3 or 4 consecutive days) is one of the therapeutic possibilities available in patients with rheumatoid arthritis (RA) and other chronic inflammatory connective tissue diseases, and there are several reports of a marked clinical improvement and a fall in the acute phase reactants during and after MPPT (3, 6, 7, 10). Recently we reported results indicating that high doses of MP in patients with RA induced strong irreversible immunosuppressive effect on natural killer (NK) cells (5).

Acute severe asthma is dominated by oedema

and inflammation of the bronchial mucosa, and inflammatory processes might play a role in the pathogenesis of bronchial asthma. It was therefore obvious to examine the effect of MPPT in acute severe asthma. The present pilot study was designed in order to evaluate whether MPPT was preferable to our standard dose of MP in the treatment of acute severe asthma.

PATIENTS AND METHODS

Six asthmatic patients (2 males and 4 females) between the ages of 21 and 60 years with an acute exacerbation of their illness, and who failed to respond to 1 h of intensive bronchodilator therapy, were eligible for entry into the study. The initial bronchodilator therapy consisted of terbutaline (Bricanyl) inhalations, intravenous infusions of terbutaline (5 mg of terbutaline in 1000 ml isotonic glucose, 300 drops/min) and intravenous injection of aminophyllines (Theophylline) (6 mg/kg).

All patients met the asthma criteria of the American Thoracic Society (1) and were free

from other complicating cardiopulmonary diseases, hypertension or insulin-dependent diabetes mellitus. On admission to hospital, each person underwent a complete medical history and physical examination. Chest radiograph, electrocardiogram and blood pressure were normal. First-second expiratory volume (FEV₁) and forced vital capacity (FVC) were performed (Table 1).

The study was double blind and controlled. The patients were randomly assigned to receive either 1000 mg MP intravenously on 3 consecutive days followed by placebo tablets, or 50 mg MP intravenously on 3 consecutive days

followed by MP tablets in declining doses to zero over 2 weeks.

Concurrently with the MP and MPPT administration each subject inhaled terbutaline (5 mg every 4 h) during the initial 3 days - the following days only when needed. Intravenous terbutaline (5 mg in 1000 ml isotonic glucose, 30 drops/min) was given as long as needed. Terbutaline aerosol, 2 puffs (500 µg), was given when needed. Budesonide aerosol 800 µg twice daily, Theodur 300 mg twice daily and Bricanyl Retard 7.5 mg twice daily were given throughout the study period of 3 months.

The patients were examined by the same

Table 1
Characteristics of patients at admission to hospital

Patient Nos.	1	2	3	4	5	6
Weight (kg)	70	85	63	24	20	57
Height (cm)	170	168	165	165	168	161
Age (years)	36	50	56	75	60	59
Sex	♂	♂	♀	♀	♀	♀
FEV ₁ (l/sec)	0.3	0.5	0.5	1.1	0.5	0.7
FVC (l/sec)	0.5	1.4	1.3	1.0	1.3	1.2
PEF (l/min)	0	120	0	0	0	120
Heart rate (beats/min)	170	124	132	140	120	124
Respiratory rate (per min)	32	34	36	32	32	30
pH	n.d.	7.3	7.4	7.6	n.d.	7.7
pO ₂ (kPa)	n.d.	7.8	6.0	6.4	n.d.	6.2
pCO ₂ (kPa)	n.d.	13.3	8.0	5.5	n.d.	5.8

*n.d. = not determined

Table 2
Clinical course of the six patients evaluated by seven asthma criteria

Patient Nos.	1	2	3	4	5	6
Treated with MPPT	+	-	-	+	-	-
Day when patients fulfilled no criteria for asthma	7	2	14	4	2	3
Day at which PEF was at least 80 % of maximum	14	3	7	7	14	4
Day at which FEV ₁ was at least 80 % of maximum	7	7	7	7	1	7
Day of lowest subjective score	14	28	7	10	7	8
Day of lowest use of terbutaline aerosol	14	27	7	4	7	4
Day at which i.v. terbutaline stopped	3	4	4	3	3	3
Study months left when patients dropped out	2	2	0	1	0	0

doctor 1, 3, 6, and 12 h, 2, 3, 4, 7, and 14 days as well as 1, 2, and 3 months after receiving the first injection of MP. Record was made of pulse, respiratory rate and peak expiratory flow (PEF). The presence of the following seven criteria of asthma was recorded: 1) PEF < 120 l/min, 2) heart rate > 120/min, 3) respiratory rate > 30/min, 4) pulsus paradoxus > 18 mmHg, 5) use of accessory respiratory muscles, 6) moderate to severe dyspnoea and 7) wheezing.

Measurement of the following blood tests was made before, during and after treatment with the test solutions of MP: serum-potassium, serum-sodium, serum-creatinin, ESR, peripheral blood eosinophils, IgG, IgA, IgM, IgE, leucocytes, hemoglobin, blood-glucose and theophylline levels.

Patients recorded PEF before and 15 min after 2 puffs of terbutaline aerosol in the first 14 days four times daily, in the rest of the study period only twice daily. Asthma symptoms (breathlessness, cough, wheezing) were graded from 0-5: 0 = no symptoms; 1 = slight symptoms; 2 = somewhat moderate symptoms; 3 = moderate symptoms; 4 = somewhat severe symptoms; 5 = severe symptoms.

Furthermore, patients recorded number of extra terbutaline puffs. On day 4 the patients were queried for the presence of medication side effects.

The clinical course of the six patients was evaluated by the following criteria: 1) day at which the patient had none of the seven asthma criteria, 2) day at which PEF was 80% of the maximum reached in the study period, 3) day at which FEV₁ was 80% of the maximum, 4) day of lowest subjective score of asthma, 5) day of lowest use of terbutaline aerosol, 6) day at which intravenous terbutaline stopped, and 7) months left of the study when the patient dropped out.

RESULTS

Patient characteristics at admission to hospital are given in Table 1. In Table 2 the clinical data show that there was no remarkable difference between the effect of MPPT and that of

standard doses of methylprednisolone. Patient No. 1 dropped out because of bad patient compliance, patient No. 2 because the clinical course of his asthma indicated open treatment with prednisone, and patient No. 3 because of hyper eosinophilia indicating open treatment with corticosteroids.

No side effect was reported, in particular no bradycardia, on any of the treatments. Apart from a fall in eosinophil count for all patients during the first week, no remarkable changes in blood tests were observed.

DISCUSSION

Our results indicate that it is possible to treat severe acute asthma with high-dose methylprednisolone pulse therapy. However, more data are necessary in order to evaluate this new form of administering MP to patients suffering from severe asthma. Recently it has been reported from our department that patients with rheumatoid arthritis treated with MPPT, 2-3 g of MP, developed bradycardia (9). Although none of our patients developed this side effect, we discontinued our study and reduced the dose of MP to 1 g in a new prospective study evaluating the effect of MPPT in patients with severe asthma. The study is now in progress. If future studies confirm that there is a comparable effect between MPPT and standard doses of methylprednisolone, treatment with MPPT would be preferable to standard doses, because of easy administration and better patient compliance.

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