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SIDE EFFECTS AND PROGNOSIS WITH THE TREATMENT OF PEMPHIGUS VULGARIS

S. Pavlov, M. Slavova

Clinic of Dermatology and Venereology, Department of Infectious Diseases and Epidemiology, Prof. Paraskev Stoyanov Medical University of Varna

ABSTRACT

Pemphigus vulgaris is an autoimmune bullous dermatosis that affects between 0,1 and 0,5%000 of the population. The prognosis of the disease is determined by the severity of the side effects of corticosteroid therapy and their compensation. The present study covered 52 patients with pemphigus vulgaris treated in the Clinic of Dermatology and Venereology, Prof. P. Stoyanov Medical University of Varna, during a 10-year period (1990-2000). There were 20 males aged between 28 and 86 years and 32 females aged between 17 and 77 years. The adverse effects of the corticosteroids in the patients with pemphigus vulgaris and their influence on the course of the disease were described. The combination with a cytostatic drug (cyclophosphamide or imuran) proved to be effective in reducing the total course and maintenance dosage of the corticostteroids in these patients.

Key words: pemphigus vulgaris, corticosteoids, cytostatics, side effects, prognosis

Pemphigus vulgaris has been described by Wichmann in 1791. It is an autoimmune blistering disease presenting with acantholysis and bullous-erosive cutaneous and mucosal skin lesions (1,7). The natural course of the disease is progressive and leads to fatal outcome until the end of the first year in 75% of the patients. There is major progress in the understanding of its pathophysiology and in the development of new diagnostic techniques and therapeutic approaches (6). Incorporation of corticosteroids (CS) into the therapy since 1950 onwards sharply reduces the death rate down to approximately 30% (10). Recently, there is a continuous trend towards a lower mortality rate and nowadays it is below 10%. Although CS use remains the cornerstone of effective therapeutic regimens for pemphigus vulgaris, such a prolonged administration leads to unavoidable side effects determining the prognosis (2,8). Systemic immunosuppression makes use of CS such as azathioprine, dapsone, methotrexate, cyclophosphamide and gold as adjuvants or alternatives (9). Immunomodulation is widely applied, too (2,5,6). High-dose intravenous immunoglobulin is effective in 81% of the patients with pemphigus vulgaris which are more likely to respond to adjunctive therapy than to monotherapy (91% and 56% response rate, respectively) (4). Pulse intravenous cyclophosphamide is particularly efficacious and low toxic (3). Both cyclophosphamide and methylprednisolone "pulse therapy" are reserved for cases unresponsive to high doses of oral CS (8).

The purposes of the present study are to follow-up the therapeutic results from the treatment of the patients with pemphigus vulgaris, the adverse effects of the therapy with CS alone and in combination with cytostatic drugs and to suggest a model of therapeutic behaviour for minimization these unwanted effects.

MATERIAL AND METHODS

The study covered a total of 52 patients with pemphigus vulgaris treated in the Clinic of Dermatology and Venereology, Prof. P. Stoyanov Medical University of Varna, during a 10-year period (January 1, 1990 - January 1, 2000). They represented 0,95% of 5447 patients hospitalized in the Clinic of Dermatology and Venereology during this period. Their total hospital sojourn amounted to 4050 days (4,12% of the days of all the patients). There were 20 males (38,5%) aged between 28 and 86 years and 32 females (61,5%) aged between 17 and 77 years. Patients' records were analyzed by means of a special file card taking into consideration the following items:

i) from the anamnesis and status: gender, age, primary localization of lesions, accompanying diseases, duration of remissions, number of hospital days;

ii) from the paraclinical parameters: ESR, leukocyte count, blood sugar, urea, histologic examinations of skin and mucosal membranes,

iii) from the treatment: kind and initial dosage of CS, total weekly and average daily dosage for achieving the remission, and

Address for correspondence:
S. Pavlov, Clin. of Dermatology and Venereology, Dept. of Infectious Diseases and Epidemiology, Prof. P. Stoyanov Medical University of Varna, 55 Marin Drinov St, BG-9002 Varna, BULGARIA

ı complications from CS therapy and cause for death.

RESULTS AND DISCUSSION

l the patients were treated with CS such as hydrocorti-
ıe, prednisolone, methylprednisolone (MP), and dexa-
:thasone. The mean initial dose was equivalent to 57,5
ş of MP/24 hours. The mean daily dose of CS varied
m 54,31mg MP/24 hours in the first week down to
,03mg MP/24 hours in the fourth month. The average
iintenance dose was of 11,13mg MP/24 hours. A
ostatic drug such as cyclophosphamide or imuran was
ded to the therapy in one half of the patients admitted to
spital. The mean daily dosage for achieving the remis-
n was of 186,5mg/24 hours for cyclophosphamide and
3,5mg/24 hours for imuran. The hospital stay of the pa-
ıts treated with CS alone was on the average 30,2 hospi-
days long while that of the patients with accompanying
ostatic therapy was 48,6 hospital days long. The remis-
n occurred between the third and the eight week with
st patients. It is, therefore, accepted that the duration of
hospital treatment coincides with the time required for
ieving the remission.

mplications due to CS therapy were observed in 44 pa-
ıts (85% of the acses) treated longer than one year. Arte-
hypertension was most common - in 17 patients
,6%). Next came obesity and *facies lunata* - in 13 pa-
ıts (25%), steroid diabetes and disturbed glucose toler-
e as well as bacterial infections such as abscessus, pneu-
nia and sepsis - in 7 patients (13,4%) each, proximal
opathy - in 6 patients (11,5%), severe osteoporosis with
ological fractures - in 3 patients (5,7%), thromboses
embolisms - in 2 patients (3,8%). The sum was higher
ı 52 as there were more complications in one and the
ıe patient. Six patients (11,5% of the cases) died during a
year period from the onset of the disease. The death re-
ed from a progressive cardiovascular and respiratory
ure in 4 patients, from pulmonary thromboembolism
from cerebral stroke - in one patient each.

side effect of CS required cessation of the treatment as it
/ithout any alternative at all. The arterial hypertension
compensated by antihypertensive drugs in 32,6% of
patients. The course of the bacterial infections was pro-
ted and with relapses in 13,4% of the cases. As a rule,
· were managed with antibiotic combinations rather
ı by monotherapy alone. Increasing overweight and re-
ibution of fatty deposits in 25% of the patients tended
ormalization during the periods of longer remissions.
vever, the intake of Ca^{2+} preparations and the periodic
olic therapy failed to prevent the progressive osteopo-
; having provoked pathological bone fractures and a
imal neuropathy. The adverse effects of CS in the pa-
s with pemphigus vulgaris are in a direct dependence
he sum dosage and duration of treatment. One way to
ce this dosage is to combine the immunosuppressive
:t of CS with that of the cytostatics like in one half of
patients. The immunosuppressive effect of imuran in a dose of 3-4mg/kg b. w. occurred after 3-4 weeks and coincided with the reduction of CS dosage after achieving the morbistasis. Its relatively better tolerability has made it appropriate for a long-lasting maintenance therapy for 12-24 months. Cyclophosphamide was effective in a dosage of 2-3 mg/kg b. w. It was used in patients unresponsive to CS only because of its higher toxicity.

CONCLUSION

With a view to reduction of the total course and maintenance dosage of CS it seems reasonable to combine these drugs with cytostatic ones even in the slight forms of pemphigus vulgaris. The different therapeutic protocols should obligatorily be accompanied with a strict control of the arterial blood pressure and blood sugar. Additionally, use of prophylactic gastroscopy and bone densitometry is strongly recommended, particularly in menopausal women.

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