MULTIDRUG THERAPY IN PEMPHIGUS VULGARIS

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Twenty four patients having pemphigus vulgaris were treated with combined drug therapy consisting of oral prednisolone 1 mg per Kg body weight, cyclophosphamide 2.5 mg per Kg body weight and methotrexate 2.5 mg biweekly. The drugs were gradually tapered off to achieve a minimum maintenance dose of 10-15 mg prednisolone on alternate days at the end of 2 years of observation. The age groups of patients varied from 15 to 78 years. Maximum cases were between 31 to 50 years. There were 15 males and 9 females. The duration of disease varied from 4 months to over 36 months at the time of reporting. Number of episodes recorded at the time of first presentation were one episode in 6 (25%) and multiple episodes in 18 (75%). The period of observation varied from 6 months to 27 months. Two patients relapsed during the period of observation. There has been remarkable response to treatment in the form of quick recovery from lesions without any significant side effects.

Key words : Pemphigus, Treatment, Multidrug.

Pemphigus vulgaris is an autoimmune disease[1] and corticosteroids remain the mainstay of treatment, though often, fairly large doses of the drug are required to control the disease. The maintenance therapy invariably has to be continued for an indefinite period. The mortality of pemphigus vulgaris has markedly fallen following use of corticosteroids. However, the long-term side effects of corticosteroids cannot be overlooked. Under these circumstances pemphigus continues to be an extremely serious disease with high morbidity.

In view of the relationship of the disease with immunological disorders, a rational alternative is the use of immuno-suppressive drugs. From all accounts, immunosuppressive drugs act relatively slowly. Hence, the initial treatment of choice is corticosteroids as soon as the diagnosis is confirmed.[2] Successful results have been claimed with combination of corticosteroids with azathioprine,[3] cyclophosphamide[4] and methotrexate.[5] We treated our patients with a combination of corticosteroids, cyclophosphamide and methotrexate. The aims of the study were to administer lower doses of corticosteroids, to have minimum side effects if any, to withdraw the drugs one by one, to have minimum maintenance doses of corticosteroids and finally to withdraw all drugs.

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Materials and Methods

The material for this study included 24 patients of pemphigus vulgaris, 15 males and 9 females, seen from March 1984 to July 1986. The diagnosis of pemphigus vulgaris was made on clinical grounds, demonstration of Tzanck's cells and typical histopathological features.

Detailed clinical findings of individual patients were recorded. Each patient underwent investigations like haemoglobin estimation, total and differential white cell counts, platelet count, estimation of serum proteins, electrolytes, calcium, blood urea, serum creatinine, liver function tests, blood sugar fasting and postprandial, immunoglobulin profile, urine examination, X-ray lumbo-sacral spine and ECG examination prior to and during treatment and follow-up of cases.

All the patients were initially treated with prednisolone 1 mg/Kg/day, cyclophosphamide

2.5 mg/Kg/day, and methotrexate 2.5 mg biweekly for 4 to 6 weeks. Depending on the response, prednisolone was reduced every 15 days by 5 mg till a two-third of the dose of corticosteroids was reached. This was continued for three months. After 6 months of first reporting, prednisolone was reduced to 30 mg daily, cyclophosphamide 50 mg daily and methotrexate 2.5 mg weekly. The patients were reassessed after another three months. All the parameters being normal, the treatment was continued for another three months.

After one year of first reporting, prednisolone was reduced to 15-20 mg, cyclophosphamide was discontinued and methotrexate 2.5 mg was continued once a week.

After 18 months, methotrexate was discontinued, prednisolone was continued 10-15 mg daily for 6 months, and after 24 months prednisolone was reduced to 10-15 mg on alternate days.

Results

The age group affected maximum was 31 to 50 years in 15 (62.5%) patients. Seventeen (70.8%) patients had already had the disease for more than one year. Six (25%) patients reported with the first episode and the remaining 18 (75%) reported with multiple episodes. Site of onset in 23 (95.8%) patients was skin, in one (4.2%) patient it was buccal mucosa, while 18 (7%) had involvement of both skin and mucous membranes at the time of presentation. In 19 (79.2%) patients, almost the entire body was involved. None of the patients had any other associated autoimmune disease. During the course of treatment, only 2 (8.3%) patients relapsed. Side effects of treatment were pyoderma 5 (20.9%) cases, candidiasis 3 (12.5%) cases, lung infection 1 (4.2%), diabetes mellitus 3 cases (12.5%) and trunkal obesity 2 (8.3%) cases.

Comments

Before corticosteroids, little could be offered for pemphigus cases other than supportive symptomatic therapy with the hope that a spontaneous remission might occur. A rather ineffective array of measures including arsenic, germanin and gentian violet as well as antibiotics were used. None of them proved effective in stemming the relentless progress of the disease or postponing death. The characteristic remission of pemphigus had always suggested the possibility of effective therapy. After the advent of corticosteroids, the treatment was anchored upon this hormone. Pemphigus has been considered one of the few diseases in which the steroids therapy is justified as soon as the diagnosis is established even when the presenting symptoms are mild. Because of the gravity of the disease the ordinary contra-indications to corticosteroid therapy may have to be disregarded.[6]

Systemic corticosteroid therapy provides the disease control at the expense of long-term complications, necessitating care in balancing risks and benefits.[7,9] Hence, the search for alternative drugs. Till todate alternative drugs to corticosteroids have not been recorded for the treatment of pemphigus, however, some workers have successfully used immunotherapeutic agents. Among the combination of drugs claimed effective with steroids are azathioprine,[3] cyclophosphamide,[4] methotrexate.[5] Pulse therapy with dexamethasone-cyclophosphamide in pemphigus vulgaris has been reported by Indian workers.[10] Gold therapy and plasmapheresis have also been used as supplement procedures, as well as sulphones and sulphapyridines.[11] However, the combination of corticosteroids with cyclophosphamide and methotrexate in pemphigus vulgaris has not been reported in the literature. The aim of the multidrug regimen was to use minimum steroids both initially and for maintenance, to achieve maximum benefit

with insignificant side effects as already cited earlier. The additional advantage recorded was to withdraw the drugs one by one without relapse of the disease. Only two (8.3%) patients relapsed.

There were no significant side effects recorded with the combined drug therapy in the present series. This regimen achieved immunosuppression in six to eight months, giving the patients subsequently a relatively healthy span of life with least medication.

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