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How Should Glucocorticoids Be Used?

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Glucocorticoids (GCs) have been used successfully for over 60 years in hematologic and non-hematologic disorders. They were first used in the treatment of a patient with adrenal insufficiency so were administered every 6 to 8 hours to substitute for its deficiency. From this start, GCs were given in divided dose without considering that with the exception of surrenal insufficiency, substitution was not necessary. Actually, the pharmacologic effects of GCs do not require substitution therapy. Different from conventional GC (2 mg/kg in divided doses), in pulse methylprednisolone (MP), 1000 mg MP is infused within 4 hours intravenously (iv). Bacigalupo and colleagues successfully used for the first time 30 mg/kg MP, as pulse MP in 4 hours infusion (iv), for the treatment of acquired aplastic anemia cases (1).

We also started to use 30-100 mg/kg MP treatment in acquired aplastic anemia cases, and the dose was given 10-15 minutes iv before 9 a.m. with excellent response (2). Thereafter, this megadose (MD) MP administration was applied in different hematologic and non-hematologic disorders (3).

Following aplastic anemia, MDMP was also used in the treatment of steroid refractory or resistant Diamond-Blackfan anemia patients, which has hereditary background, with extraordinary response (4,5). This was verified by Dr. George Buchanon et al., president of the American Pediatric Hematology Society (5,6).

The results of MDMP treatment in acute and chronic idiopathic thrombocytopenic purpura (ITP) cases were somewhat surprising. Conventional corticosteroid (2 mg/kg) seemed to delay the platelet response compared to the untreated group. Anti-platelet antibodies decreased much faster with MDMP treatment and resulted in much earlier platelet response (7-10).

Remission induction with MDMP in different types of leukemia was also shown to be much faster (11-14), as in autoimmune hemolytic anemias, myelofibrosis, hemangiomas and other hematologic disorders (3,15-17).

MDMP response was also found to be quicker in several non-hematological diseases (18), such as rheumatoid arthritis, acute rheumatic fever, juvenile rheumatoid arthritis, systemic lupus erythematosus, polyarteritis nodosa, nephrotic syndrome and other diseases with immunologic base such as alopecia totalis. Therefore, we believe whenever corticosteroid treatment is indicated, MDMP should be used, given once a day around 5-6 a.m., except in adrenal insufficiency.

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Although MDMP administration is a kind of corticosteroid treatment, it is different from pulse methylprednisolone in which 1000 mg MP is administered iv within 4 hours, anytime of the day, and from conventional prednisone, which is given 2 mg/kg/day, in divided doses. MDMP treatment starts with daily 30-100 mg/kg MP dose for 3 days given around 6 a.m. when corticosteroid level is physiologically the highest and ACTH the lowest. It was given initially iv within 10-15 minutes and recently orally by us at once (19). Daily MP dose was halved gradually 20-50 mg/kg for 4 days and then 10-30, 5-20, 2-10, and 1-5 mg/kg, with each dose continuing for a week. Oral MDMP was found as effective as iv administration. A daily dose of MP is placed in a tablespoon covered by honey (since MP is extremely bitter), and given at once, and a glass of milk is given thereafter. This early administration of MP is less disturbing to ACTH-corticosteroid homeostasis, which is important for steroid side effect, mostly related to suppression of ACTH secretion.

During MDMP administration, adrenal suppression is not expected (20); therefore, it could be discontinued anytime, without gradually decreasing corticosteroid doses. In MDMP administration, strict salt restriction is also not necessary. With these explanations, MDMP could be used whenever corticosteroid treatment is required, with the exception of adrenal insufficiency.

With the exception of mild Cushingoid appearance, other side effects of corticosteroids, such as hyperglycemia, hypertension, and sodium retention, etc. are rarely observed.

In patients who receive MDMP, extra salt should be omitted and they should ingest more foods containing potassium, such as orange, carrots, and banana. With the exception of extra calories and salt, they can consume normal diets.

We advise that patients on MDMP treatment should apply saline nasal washing as previously described by us for the prevention of upper respiratory infections (21,22). They should also walk as fast as possible to prevent muscle atrophy.

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