

## Pulse Corticosteroid Therapy with Methylprednisolone or Dexamethasone

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**Abstract :** Intravenous pulse steroid therapy consists of administration of supraphysiological doses of glucocorticoids. It is useful in conditions where rapid immunosuppression and anti-inflammatory effect is desired, as in systemic lupus erythematosus, pemphigus, renal transplantation, steroid resistant nephrotic syndrome and crescentic glomerulonephritis. This therapy may be associated with significant adverse reactions including hypertension, arrhythmias, hypokalemia, psychosis and infections. High dose steroid therapy should therefore be used in selected cases and under careful supervision. The drug most widely used for this treatment is methylprednisolone. However, in view of its easy availability and cost, dexamethasone has been often used in India for the above conditions. While there are no controlled studies comparing the two drugs, it appears that the two drugs may be similar in efficacy. Patients requiring high dose intravenous steroid therapy may be treated effectively with either methylprednisolone or dexamethasone. (*Indian J Pediatr 1998; 65 : 557-560*)

**Key words :** Pulse therapy; Adverse reactions; Methylprednisolone; Dexamethasone.

Corticosteroids are natural hormones synthesised by the adrenal cortex and are classified as mineralocorticoids and glucocorticoids. The former play an important role in water and electrolyte homeostasis, whereas the latter influence the metabolism of protein, fat and carbohydrates and also alter connective tissue response to injury. However, the most remarkable effect of glucocorticoids is the inhibition of inflammatory and immunologic responses.

Synthetic corticosteroids are available in both oral and injectable forms. Intravenous bolus steroid therapy is useful in situations where high levels of the drug are to be achieved rapidly. Those most often used

for bolus therapy include methylprednisolone and dexamethasone. Of these, the former has been most commonly used, whereas dexamethasone has been employed as an alternative, primarily because of its low cost and easy availability.

### BOLUS STEROID THERAPY

Glucocorticoids are often used in supraphysiological doses to suppress various disease processes through their effects on inflammation and immune response. Intravenous pulse therapy promptly achieves high blood levels of the drug quickly as is desired in emergency management of certain diseases like bronchial asthma, or whenever rapid immunosuppression is required for inducing remission in immune mediated illnesses like systemic lupus

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erythematosus and juvenile rheumatoid arthritis. The list of conditions that may be ameliorated by such therapy is given in Table 1. The desired anti-inflammatory and immunosuppressive effects of high dose corticosteroids are mediated by mechanisms, similar to those that mediate a myriad of other glucocorticoid effects in the body. However, there are limitations of pulse steroid therapy as glucocorticoids are rarely curative of the underlying disorder and usually only the immediate consequences of the body's inflammatory responses are reduced. In addition, excess glucocorticoids result in iatrogenic hypercortisolism which may prove to be

more disabling than the condition for which steroids were originally given.

### DOSAGE, ADMINISTRATION AND ADVERSE REACTIONS

The recommended dose of methylprednisolone for pulse therapy is 30 mg/kg, given I.V., over a period of 1-2 hours. Dexamethasone is used in a dose of 5 mg/kg as I.V. infusion. Steroid pulse therapy requires careful monitoring during its administration and after, in view of the side effects viz. :

#### (i) Hypertension

A sudden rise in blood pressure may occur particularly in patients with underlying renal disorder with hypertension. Therefore, the blood pressure should be carefully monitored during the infusion and thereafter for a few hours.

#### (ii) Cardiac arrhythmias

Pulse should be carefully monitored and EKG obtained whenever necessary. A defibrillator should be at disposal during the therapy.

#### (iii) Hypokalemia

Although both methylprednisolone and dexamethasone have negligible mineralocorticoid activity, sodium and fluid retention and hypokalemia may occur.

#### (iv) Neurological

Increased intracranial pressure (pseudotumor cerebri), seizures, depression and frank psychosis have been reported.

TABLE 1. Indications of Pulse Steroid Therapy in Children

Allergic states
Acute bronchial asthma
Collagen vascular diseases
Juvenile rheumatoid arthritis
Systemic lupus erythematosus
Dermatologic conditions
Atopic dermatitis
Pemphigus
Bullous pemphigoid
Gastrointestinal disorders
Crohn's disease
Neoplastic diseases
(as antiemetic)
Organ transplantation
Orthotopic cardiac transplantation
Renal transplantation
Neurologic disorders
Acute spinal cord injury
Hematologic condition
Idiopathic thrombocytopenic purpura
Renal disorders
Steroid resistant nephrotic syndrome
Crescentic nephritis
Lupus nephritis

**(v) Infections**

Superimposed opportunistic infection is an important side effect of pulse steroid therapy especially in immunocompromised patients with diseases like nephrotic syndrome and systemic lupus erythematosus. The patient should be rigorously screened for infection prior to starting pulse therapy.

Other side effects include hyperglycemia, gastrointestinal bleeding and muscle weakness. Rarely, hypersensitivity reaction including anaphylaxis may also occur.

#### METHYLPREDNISOLONE vs DEXAMETHASONE PULSE THERAPY

Methylprednisolone is a methylated prednisolone, whereas methylation at 16 alpha position of 9 alpha fluoro prednisolone produces dexamethasone (9  $\alpha$  fluoro 16  $\alpha$  methylprednisolone). These synthetic corticosteroids, in contrast to the natural steroids, have more potent glucocorticoid activity and negligible mineralocorticoid activity. The pharmacological aspects of methylprednisolone and dexamethasone are compared in Table 2.<sup>1</sup> Dexamethasone has more potent glucocorticoid and anti-inflammatory activity than methylprednisolone, because of its increased affinity

for glucocorticoid receptors and less protein binding (only unbound steroid has pharmacological effect). Dexamethasone has a comparatively longer half life which is due to its decreased hepatic metabolism despite low protein binding. Therefore, dexamethasone is a longer acting and a more potent glucocorticoid (more anti-inflammatory and immunosuppressive) than methylprednisolone. However, methylprednisolone may have an important advantage over dexamethasone as it penetrates cellular compartments more quickly than dexamethasone.<sup>2</sup> Dexamethasone has ten times less mineralocorticoid activity than methylprednisolone, which may become significant when the latter is being used for high dose pulse therapy. For this reason, dexamethasone has been preferred for the treatment of cerebral edema associated with cerebral tumors and head injury. However, both of them have been used in high doses in patients with head injury without any known advantage of one steroid over the other.<sup>3</sup>

The prolonged half life of dexamethasone may produce a greater degree of hypothalamic-pituitary axis suppression as compared to methylprednisolone. Also, prolonged immunosuppression may result in more superinfection following dexamethasone pulses than methylprednisolone

TABLE 2. Pharmacokinetics of Dexamethasone and Methylprednisolone

	Relative potency		Relative receptor affinity		Plasma half life (min.)	Biologic half life (hr)
	Glucocorticoid	Mineralocorticoid	Glucocorticoid	Mineralocorticoid		
Dexamethasone	30	0	7.1	0.2	150-270	24-72
Methylprednisolone	5	0.5	12	—	120-180	12-36

pulse therapy.

The therapeutic efficacy of methylprednisolone pulse therapy has been proved in several conditions where rapid anti-inflammatory and immunosuppressive effect is desired. However, very few studies have used dexamethasone for this purpose. A large trial using dexamethasone and cyclophosphamide pulse therapy has shown excellent results in patients with pemphigus.<sup>4</sup> In another study, oral dexamethasone pulse therapy was found to be useful in patients with idiopathic thrombocytopenic purpura (ITP).<sup>5</sup> Although studies comparing anti-inflammatory and immunosuppressive effects of dexamethasone and methylprednisolone are few, both these steroids have been found to be useful in pemphigus and ITP in separate trials.<sup>4,5</sup>

In earlier studies, in septic shock, high dose pulse steroid therapy was used for short duration.<sup>6</sup> A prospective trial compared the efficacy and complications of methylprednisolone and dexamethasone pulse therapy and failed to show any improvement in overall survival. However, it demonstrated that 30 mg/kg of methylprednisolone and 6 mg/kg of dexamethasone were similar in efficacy and side effects. In another study, Schummer demonstrated that methylprednisolone (30 mg/kg) and dexamethasone (3 mg/kg) were equally effective in reducing mortality among patients with septic shock. The complication rate did not differ in the two groups.<sup>7</sup>

In conclusion, pulse steroid therapy is useful in situations where a rapid anti-inflammatory effect or immunosuppression is desired. Because of the side effects, high dose therapy should be used selectively

and cautiously. Methylprednisolone is most widely used, particularly to treat acute cellular rejection in renal transplants. However, similar pharmacokinetics of dexamethasone and methylprednisolone, and studies using these steroids for pulse therapy suggest that the two may be similar in efficacy and side effects. In view of easy availability and low cost, dexamethasone may be preferred for pulse therapy in our country.

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