(50 mg/kg) intravenously to induce suppression of a clonal population of B cells followed by administration of granulocyte colony stimulating factor (G-CSF). A high dose of cyclophosphamide spares the progenitor hematopoietic stem cells in the bone marrow which express high levels of aldehyde dehydrogenase, an enzyme causing resistance to cyclophosphamide. However, peripheral lymphoid tissue, being susceptible, is suppressed, with apparent clearing of pre-existing autoimmunity. After a nadir of leucopenia at 8-12 days, there is a repopulation by division of stem cells from the bone marrow which have been spared. G-CSF given during this period hastens this process. Obviously, this approach has to be reserved for severe cases unresponsive to conventional DCP and has to be carried out in institutional settings under cover of broad spectrum antibiotics and anti-candidal drugs. As G-CSF is now available in India (Grastim®) this approach can be tried in selected cases.

7. Persistent oral ulcers are usually treated with topical steroids in a gel/orabase. An alternative approach may be to spray these lesions directly with a steroid inhaler (budesonide or fluocinolone acetonide) used in asthma. Apart from a rapid effect, an additional advantage is that palatal and pharyngeal ulcers that are not accessible to topical steroids can be treated effectively.

I hope that the practicability of these suggestions can be tried in different centers in order to further improve the efficacy of pulse therapy.

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REFERENCES


Response by Dr. Rao and Dr. Laxmi

Sir,

We thank Dr Navin Modi for his comments and for the interest shown in our article. In response to the points raised in his letter, I would like to make the following remarks.

1. Duration of infusion time of cyclophosphamide pulse:

Cyclophosphamide is a pro-drug that is converted by hepatic microsomal enzymes into 4-hydroxy cyclophosphamide. The concentration of 4-hydroxycyclophosphamide is 5 to 10% of the concentration of cyclophosphamide at peak steady state.1 The half life of 4-hydroxycyclophosphamide is about the same as that of cyclophosphamide ranging between 3-10 hours.2 Cyclophosphamide is supplied in 50 mg tablets and vials containing powder for injection. Solution for injection is prepared by adding
5 ml. of sterile water. Unlike mechlorethamine, solution remains stable for 3 hours. By above reasons it is all right if it is administered over 2 hours in an intravenous infusion as its pharmacological activity is not affected. Moreover, cyclophosphamide is added to the same solution wherein dexamethasone is present and it is advisable to administer it over 2-4 hours to avoid the adverse effects associated with pulse steroid therapy.

2. Prevention of cyclophosphamide induced sterile hemorrhagic cystitis

The rationale behind the additional infusion of 500ml of 5% dextrose on the day of intravenous cyclophosphamide is to wash out any retained drug in the urinary tract to prevent urinary complications of cyclophosphamide. We have made this a part of the protocol so that adequate hydration become a fixed routine on the day of administration of cyclophosphamide. We chose 5% dextrose to the normal saline to avoid the sodium load. This was well accepted by the patients and none of our patients had any complications associated with such an administration. Adequate oral supplementation of fluids definitely will suffice. However, such instruction which cannot be incorporated in protocol are frequently neglected / over looked.

The use of MESNA in these patients is an accepted practice. However studies have shown that subclinical renal toxicity has been observed in children receiving ifosfamide, which is an oxazophosphorine like cyclophosphamide, despite MESNA administration and that administration of MESNA does not eliminate the need for adequate hydration and careful observation of the patient.

3. The early morning administration of steroids to avoid HPA axis suppression is only relevant when short or intermediate acting corticosteroids are used for therapy. In pulse therapy for pemphigus, we are administering high dose of dexamethasone which is a long acting corticosteroid, (action for 24 to 36 hours). Hence, irrespective of the time of administration, the drug is in circulation for the whole day. More importantly it is administered only for 3 days in a month. Adrenal suppression occurs only when corticosteroids are administered for more than 2 weeks which is not the case in pulse therapy for pemphigus.

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REFERENCES

2. Cyclophosphamide in cancer chemotherapy, Book section of www.pubmed.com

Response by Dr. Ramam

Sir,

The suggestions made by Gandhi et al will have to be considered by centers administering pulse therapy and implemented if considered beneficial and feasible. It would be ideal to compare the proposed changes to the original schedule in a randomised, controlled trial. Carefully kept records will be needed to document the