Original Article

Dexamethasone Cyclophosphamide Pulse Therapy in Immunobullous Diseases: Our Experience

S Parajuli, U Paudel

Department of Dermatology and Venereology, Maharajgunj Medical Campus, Institute of Medicine, Kathmandu, Nepal

Abstract

Background: Dexamethasone cyclophosphamide (DC) pulse therapy seems to be emerging affordable modality of treatment in immunobullous disorders. The objective of this study was to describe the effectiveness of DC pulse therapy in immunobullous disease in our setting.

Methods: This was a retrospective study carried out in the Department of Dermatology of a tertiary referral centre by reviewing the medical records of all the patients of immunobullous diseases receiving DC pulse therapy from January 2010 through January 2014.

Results: There were a total of 10 patients of immunobullous disease receiving the therapy during above mentioned period (7- Pemphigus Vulgaris, 2- Pemhigus foliaceus, 1- Bullous Pemphigoid). There were 5 males and 5 females receiving the therapy, with the mean age of the diseased at presentation being 47.4 years. Out of 10 patients, 2 patients were lost to follow up after the 1st pulse. Out of 8 patients, 6 patients (75%) achieved clinical remission. The mean time to remission was 10.6 months (Range: 3 months to 23 months). The major adverse effects seen during therapy were diabetes (50%) and leucopenia (20%).

Conclusions: DC pulse therapy seems to be effective treatment modality in the management of immunobullous disorder in our setting with good safety profile.

Keywords: DC Pulse therapy, immunobullous diseases

Introduction

Immunobullous diseases are difficult to manage conditions in Dermatological practice and are associated with high morbidity and mortality.[1] Dexamethasone - cyclophosphamide pulse (DCP) therapy is one of the treatment modalities used for these diseases and consists of three days pulsed regimen (Table 1) which is administered for three consecutive days every 28 days.

Address of correspondence
Dr. Upama Paudel
Department of Dermatology and Venereology
Maharajgunj Medical Campus, Institute of Medicine, Kathmandu, Nepal
E-mail: upama_ups@yahoo.com

Table 1: DC pulse therapy regimen

Day 1	100mg Dexamethasone IV in 500ml of 5% Dextrose, in 2 hours
Day 2	100mg Dexamethasone IV + 500mg of Cyclophosphamide in 500ml of 5% Dextrose, in 2 hours
Day 3	100mg Dexamethasone IV in 500ml of 5% Dextrose in 2 hours + Cyclophosphamide 50mg oral daily except on day of IV Cyclophosphamide

There are certain modifications in this regimen which is driven as per patients' conditions on

follow-up, which includes Dexamethasone Azathioprine pulse (DAP), Dexamethasone only pulse and DCP therapy along with Prednisolone oral mini pulse (OMP) used mostly in our patients depending on the severity of disease not controlled by DCP alone and patients of reproductive age group.[2] Patient with side effects of Cyclophosphamide therapy are given Dexamethasone only pulse or changed to Azathioprine or Methotrexate in order to minimize the side effects while maintaining its efficacy. Though there are several recent studies on the treatment of these diseases including Rituximab as first line therapy[3], the information on optimal therapy available so far are inadequate. Dexamethasone Cyclophosphamide pulse appears to be associated with good success rate and low side effect profile at an affordable price, especially in a country like ours where expensive therapy like Rituximab is still out of reach to majority of the population. The main objective of this study was to describe the effectiveness and side effect profile of DC pulse therapy in immunobullous diseases in our centre.

Methods

This was retrospective study carried out in department of dermatology by reviewing the records of patients of immunobullous diseases who received DC pulse therapy between 2010 and 2014. The study variables included were demographic details of the patients, the time to remission of disease after starting DC pulse therapy, duration of remission after receiving the therapy and side effects seen during the therapy. The study was approved by Institutional review committee of our Institute.

Results

A total of ten patients received DC pulse therapy during this time period with five males and five females (Male to female patient ratio 1:1). The mean age of presentation of immunobullous disease in our centre was 47.4 (+/- 17.7) years. There were seven patients of Pemphigus Vulgaris, two patients of Pemphigus Foliaceus and one patient of Bullous Pemphigoid. Out of all these patients, two patients were lost to follow-up after 1st pulse whereas eight patients received pulse therapy at different points of time (Table 2).

Table 2: Details of the patients

S.N.	Age (yrs.)	Sex	Diagnosis	Time to remission (months)	Number of Pulse received
1	76	Male	Bullous Pemphigoid	None (lost to follow-up)	1
2	56	Female	Pemphigus Vulgaris	9	18
3	38	Male	Pemphigus Foliaceus	None	27
4	48	Female	Pemphigus Vulgaris	None	3
5	69	Male	Pemphigus Vulgaris	11	20
6	25	Female	Pemphigus Foliaceus	3	12
7	49	Female	Pemphigus Vulgaris	15	24
8	55	Male	Pemphigus Vulgaris	23	32
9	20	Female	Pemphigus Vulgaris	3	12
10	38	Male	Pemphigus Vulgaris	None (lost to follow-up)	1

Total (in months) of DC Pulse therapy received by patients ranged from 3 months to 32 months (mean 18.5 months +/- 9.35). Six out of eight patients (75%) achieved clinical remission. The mean time to remission was 10.6 months (Range

3 months to 23 months) and the duration of remission after withdrawal of the 1st phase of treatment was 9.3 months with no relapse during follow up till the date of data evaluation. The major side effects (Table 3) seen during therapy were diabetes and leucopenia (Total count less than 4000/cu mm), which was corrected after modifying the DC pulse regimen and instituting the appropriate treatment.

Table 3: Side effects of DC Pulse therapy

Side effects	Number (Percentage)
Diabetes	5 (50)
Hypertension	1 (10)
Leukopenia	2 (20))
Others	1 (10)
None	1 (10)
Total	10 (100)

Discussion

DC Pulse therapy is effective in the treatment of immunobullous diseases as per our experience and probably with less number of side effects. No serious adverse effects were seen so far in this analysis of 4 years of the data on the use of this therapy. It was also seen that Pemphigus Vulgaris responded more effectively to the therapy than Pemphigus Foliaceous. The remission rate of 75% seen in our centre was comparable with remission rate seen in other large case series.[4]

The major adverse effects seen in this study were diabetes (5 patients) and leucopenia (2 patients). However, it was seen that in patients with preexisting diabetes, no major fluctuation in blood sugar was seen after starting the therapy. Diabetes and leucopenia were managed by appropriate treatment and modification of treatment regimen.

The effectiveness of DC pulse therapy was first described in a large series of patients by Pasricha et al.[4] It is believed that when supra pharmacologic dose of steroid is used in pulsed regimen, the efficacy is maintained while reducing its side effects. Cyclophosphamide is a cytotoxic agent which reduces the population of lymphocytes, thus, destroying antibody producing B-cells. There are large number of case series published on efficacy and side effect profile of DC pulse therapy in past.[5-8] All these studies showed a large group of patients achieving remission (22- 88%). However, there were significant numbers of dropouts because of prolonged duration of therapy.

In our centre, we have recently switched over to Rituximab therapy for immunobullous diseases. However, there are many patients who cannot afford it. This study was an attempt to assess the effectiveness and acceptability of DC pulse therapy given the socioeconomic limitations in our part of the world. This study shows that DC pulse therapy is beneficial for the patients and justifies its use in patients who cannot afford or are not suitable candidates for Rituximab. Limitations of this study include relatively small sample size, retrospective nature of the study and lack of controls. A comparative study with a larger sample size is recommended in the future.

Conclusion

DC pulse therapy is an effective therapy for patients of immunobullous diseases with a relatively safe adverse effects profile. This therapy can be used for those patients who develop adverse effects of prolonged use of oral corticosteroids and can be used effectively in economically resource poor setting like ours.

References

1. Martin LK, Agero AL, Werth V, Villanueva E, Segall J, Murrell DF. Interventions for pemphigus vulgaris and pemphigus foliaceus. Cochrane Database of Systematic Reviews 2009, Issue 1. Art. No.: CD006263. DOI: 10.1002/14651858.CD006263.pub2
2. Parajuli S, Paudel U, Pokhrel DB. Dexamethasone cyclophosphamide pulse therapy in Dermatology. JIOM 2008; 30(1): 51-4.
3. Schimdt E. Rituximab as first-line treatment of Pemphigus. Lancet 2017; 389(10083): 1956-8. doi: 10.1016/S0140-6736(17)30787-0. Epub 2017 Mar 22.
4. Pasricha JS, Khaitan BK, Raman SR, Chandra M. Dexamethasone-cyclophosphamide pulse therapy for pemphigus. Int J Dermatol 1995; 34: 875-82.
5. Roy R, Kalla G. Dexamethasone - Cyclophosphamide pulse (DCP) therapy in Pemphigus. Indian J Dermatol Venereol Leprol [serial online] 1997 [cited 2020 Jan 3]; 63: 354-6. Available from: http://www.ijdvl.com/text.asp?1997/63/6/354/4616.
6. Kanwar AJ, Kaur S, Thami GP. Long-Term Efficacy of Dexamethasone-Cyclophosphamide Pulse Therapy in Pemphigus. Dermatology 2002; 204: 228-31. doi: 10.1159/000057886.
7. Masood Q, Hassan I, Majid I, Khan D, Manzooi S, Qayoom S, Singh G, Sameem F. Dexamethasone cyclophosphamide pulse therapy in pemphigus: experience in Kashmir valley. Indian J Dermatol Venereol Leprol [serial online] 2003 [cited 2020 Jan 3]; 69: 97-9. Available from: http://www.ijdvl.com/text.asp?2003/69/2/97/5886.
8. Mahajan VK, Sharma NL, Sharma RC, Garg G. Twelve-year clinico-therapeutic experience in pemphigus: a retrospective study of 54 cases. Int J Dermatol. 2005 Oct; 44(10): 821-7.