Original article

Dexamethasone Cyclophosphamide Pulse Therapy in Dermatology

S. Parajuli, U. Paudel, D. B. Pokhrel

Department of Dermatology, Venereology and Leprology, Institute of Medicine, Maharajgung, Kathmandu, Nepal

Correspondence to: D. B. Pokhrel, Department of Dermatology, Venereology and Leprology, Institute of Medicine, Maharajgung, Kathmandu, Nepal

e-mail: dbpokh@healthnet.org.np

Introduction: The objectives of this study was to: study profile of dermatological disease treated with pulse therapy in TUTH , determine the clinical time to remission of diseases, duration of remission after withdrawal of treatment and determine the side effect profile of the treatment.

Materials and Methods: Demographic profile of the patients treated with pulse therapy for various dermatological conditions, the duration of diseases prior to treatment, the clinical time to remission of diseases, duration of remission after withdrawal of treatment and side effects of treatment.

Results: Pulse therapy was received by 12 patients, five patients were SLE (F: M-4:1) with mean age of onset 28.75yrs, six patients were of Pemphigus (F: M-1:1) with mean age of onset 30.6 yrs and there was one 40 yrs old female patient of scleromyxoedema.

The mean duration of disease prior to treatment was 2.8 yrs in SLE and 1.4 yrs in Pemphigus. The mean duration of clinical time to remission was 4 months for SLE while only one patient of Pemphigus had received clinical remission after 6 months. Duration of remission after withdrawal of treatment could not be ascertained because none of them had completed phase III. The main side effects observed in our study were flushing and secondary infection.

Conclusion: DC pulse therapy appears to be encouraging treatment in the treatment of dermatological conditions like SLE, Pemphigus and scleromyxoedema. However study involving a large number of patient and long duration of follow up is needed before considering it as best treatment available for treatment of these conditions.

Key word: Dexamethasone cyclophsophamide pulse; Pemphigus; SLE; Scleromyxoedema

Introduction

Dexamethasone cyclophosphamide therapy has been used in various dermatological conditions since 2 decades [1]. At that time, it represented a radical change in the approach to skin diseases as pulse therapy had previously been used mainly to prevent transplant rejection and in the treatment of lupus nephritis. [2,3]. Dexamethasone pulse therapy consists of the intravenous administration of 100 mg dexamethasone dissolved in 500 ml of 5% dextrose on 3 consecutive days. The pulses are repeated every 4 weeks. Cyclophosphamide 500 mg is given as an intravenous bolus on one day as part of dexamethasone-cyclophosphamide pulses (DCP) in Pemphigus and other diseases; these patients also receive 50 mg cyclophosphamide daily orally between the pulses which was withhold on the day of intravenous cyclophosphamide . In some patients, to achieve a quicker remission, daily/ twice weekly oral corticosteroids and/or 2-weekly boluses of dexamethasone are used in addition. Phase II of the regimen begins when complete clinical remission has been achieved. During this phase, the patient receives 9 more

DCPs along with 50 mg cyclophosphamide orally per day. In phase III, the pulses are discontinued and the patient receives only oral cyclophosphamide 50 mg a day for another 9 months. We present our clinico therapeutic experience of treating patients with DC pulse in our hospital.

Materials and Methods

We performed a retrospective analysis of patients admitted in dermatological ward for pulse therapy from 1st Baisakh 2063 to 1st Bhadra 2064(one and half years). Patients of Pemphigus, SLE and scleromyxoedema were found to be receiving pulse therapy. Pemphigus patients were diagnosed based on clinical finding, histopathology and direct immunofluorescense test. SLE patients were diagnosed based on ARA criteria. Histopathology was the basis of diagnosis in a patient of scleromyxoedema. Complete blood count , renal and liver function test, electrolytes, urine routine, chest X-ray, ECG were done before putting patients on pulse therapy. Clinical remission was considered when lesions were healed and there was no any new lesion in case of Pemphigus while in SLE remission was considered when the clinical criteria at the time of diagnosis had disappeared and ds DNA and lab parameters had returned to normal (except for ANA). Routine follow up to assess the response and complication of the therapy was done . Patients were described for demographic data, disease profile, time to clinical remission, clinical remission after withdrawal of treatment, side effects as a result of therapy , drop outs and mortality.

Results

It was found that pulse therapy was given to 12 patients during study period. (SLE-5, Pemphigus-6 and

Table: 1

Authors	Duration of study	Number of patients	Results
Pasricha JS et al. Int J Dermatol 1982	Total DCPs : 14-48	5 (16 -48 yrs)	All in remission for last 4- 9 yrs
Appelhans M et al. Haatartz1993 March	6 months	20(33-86 yrs) ;BP- 7, PV-6, PF-5, CP-2	65%- symptom free, 20%- improved,15%- no change
Pasricha JS et al, Int J Dermatol 1995 Dec	9 yrs	300	61- could not complete treatment,12- died, some due to unrelated cause,227 – completed treatment,84%- remission, 10%- remission not completed treatment schedule, 5% - active disease, 30% - relapse, responded with further course of DCP
Roy Renu, Kalla G. IJDVL 1997	2 years	37	13 – lost,4- died 40-remission 60% - active disease
Kanwar AJ et al, Dermatology 2002	12years	36	Partial remission: 5%- 22%,Complete remission : 22%- 88%
Masood Q et al, IJDVL 2003	3 yrs	30	40% - complete remission, 3% - relapse Others- different phases
Mahajan et al. Int. J Dermatol 2004	12 yrs	54	75%- DCP; 25%- other treatment 75%- phase I; 42%- phase II; 30%- phase III; 12% - phase IV Drop outs: 18% Number of patients shifted to other regimen: 6%
Rose E et al, J Desch Dermatol Ges 2005	2 yrs Multi centre prospective randomized study, DC pulse Vs methyl prednisolone-azathioprine therapy(M/A)	M/A: 11 pts DC pulse : 11 pts (total -22)	M/A : 9/11- remission, 1/11- progression,DC pulse : 5/11- remission, 6/11- progression More relapse, side effects in M/A group
Momeni Az et al, J Dermatol Treat 2007	15 years	50	38 finished the study,55%- remission,26%- healing stage,13%- partially healed,5%- died

scleromyxoedema-1) Table 1.

There were five patients of SLE (4- female, 1-male). Age of onset of disease ranged from21-37 yrs (mean age of onset-28.75 yrs). Duration of disease prior to pulse therapy ranged from 4mnths - 7 years (mean duration -2.8yrs) Most common presentation were photosensitivity and malar rash. ANA was positive in all cases while ds DNA was positive in 4 cases. One patients had thrombocytopenia (this patient received only dexamethasone pulse) none of the patients had serositis, renal and CNS involvement Pulse therapy was stopped in one patient because of development of cardiac ischemia. Out of three patients in remission, two are in phase II, one in phase III. Duration of time to clinical remission ranged from 3 – 5 months (mean 4 months). . Duration of clinical remission after withdrawal of treatment could not be ascertained as none of the patients had completed phase III. Methotrexate was added as an adjuvant in one patient of thrombocytopenia after 9 pulses as the disease was not responding to the treatment.

There were 6 patients of Pemphigus (3- male, 3- female) receiving pulse therapy. Age of onset ranged from 5 - 48yrs (mean age- 30.6yrs) with 2 cases of childhood Pemphigus (age 5 and 15 yrs). Duration of disease prior to treatment ranged from 3 mths to 4 yrs (mean-1.4 yrs). Most common presentation was P. vulgaris (total five; DIF proved in four patients: one was clinical diagnosis as he could not afford for DIF). One had P. foliaceous. One presented only with oral lesion. Out of six patients, one patient left treatment after 2nd pulse. One patient is in clinical remission after 6 pulses and is on phase II. Others are still in phase I and have received pulses ranging from two to seven. Table 2.

One patient with diagnosis of scleromyxoedema has received 9 pulses till now and her skin induration and papulation has decreased considerably (more than 25% percent).

Flushing on day of 2nd day of IV pulse(4, 33%) , headache(2,16%), erosive gastritis(1,8%), cardiac ischemia(1,8%) , nail pigmentation (2, 16%), herpes zoster(1,8%), secondary infection(4,33%), impairment of liver enzymes(1,8%) , hyperglycemia(1,8%), electrolyte imbalance(1, 8%), weakness(2, 16%), weight gain(1, 8%), amenorrhea (1, 8%)were the side effects observed during the therapy. No mortality was observed during the period of therapy. These side effects are summarized in Table 3.

	SLE	Pemphigus	Sclerom-yxoedema
Number of patients	5	6	1
M: F	1:4	1:1	F
Mean age of onset	28.75 yrs	30.6yrs	-
Mean duration of disease prior to treatment	2.8 yrs	1.4 yrs	-
Most common presentation	Photosensitivity (5) Malar rash (5)	P. vulgaris (5) P. foliaceous (1)	-
Number of patients in Remission	3	1	-
Mean duration of time to clinical remission	4 months	6 months	-
Drop out	1	1	-
Number of patients in phase II	2	none	-
Number of patients in phase III	1	none	-
Mortality	none	none	none

Table: 2 Side effects

Secondary infections	4 (33%)
Flushing	4 (33%)
Headache	2 (16%)
Nail pigmentation	2 (16%)
Weakness	2 (16%)
Herpes zoster	1 (8%)
Impairment of liver enzymes	1(8%)
Hyperglycemia	1(8%)
Electrolyte imbalance	1(8%)
Weight gain	1 (8%)
Amenorrhea	1(8%)

Discussion

DC pulse was used in our 12 patients. The pulse therapy was used for immunological diseases like SLE, Pemphigus and a mucinosis scleromyxoedema. The male to female ratio in SLE was 1:4. The commonest clinical presentation was photosensitivity and malar rash and duration of time to clinical remission for SLE was after 3-5 pulses which

was similar to that observed by Dhabai R et al in an Indian study [4]. The male to female ratio of 1:1 in Pemphigus is similar to that seen by Pasricha et al [5]. PV, 83.3% was the commonest presentation and corroborates with previously reported figure of 70% and 89 % [5, 6]. The time to clinical remission was after 2- 16 pulses (mean 6.5) in one study [7]. In our study only one patient had achieved clinical remission after 6 pulses. The difference could be due to the shorter duration of study period. Good result has been seen with our single patient of scleromyxoedema. Side effects mainly observed were secondary infection and flushing. Recurrent UTI, tuberculosis, dark complexion, hemorrhagic cystitis, and rise in body temperature after every pulse, anemia, cardiac arrest, hiccups and deaths as seen during other studies were not seen in our cases [4, 7]. Altogether clinical remission was seen in 4 of our patients, however none of the patient has been able to complete phase III of the treatment.

Dexamethasone cyclophosphamide therapy has recently emerged as an effective therapy for treatment of immunological diseases in dermatology. It has also been reported to be effective in treatment of scleromyxoedema [8]. Dexamethasone-cyclophosphamide pulse therapy is primarily used for Pemphigus. Literature available for the use of DC pulse in Pemphigus has been summarized in table 3. It was initially described as a treatment that produced quick control of the disease and reduced hospital stay in Pemphigus. Later, it was noted to lead to long lasting remissions even after stopping therapy, virtually amounting to "cure"[9]. However, we see that the therapy has been able to induce remission in more of our SLE patients than in Pemphigus.

After all the preliminary result of the treatment of our patient has been encouraging as seen by clinical remission in 4 out of 12(33.3%) patients However we need to have long term follow up of these patients before reaching to any conclusion.

Conclusion

DC pulse therapy is effective therapy for the treatment of immunological diseases in dermatology like SLE and Pemphigus. The long term effectiveness of therapy still needs to be explored. Side effects of the therapy looks less compared to conventional high dose long duration steroid therapy. However well designed randomized controlled study and long term follow up is necessary to confirm its effectiveness and minimal side effect profile.

References

1. Pasricha JS, Gupta R. Pulse therapy with dexamethasone in Reiter's disease. Indian J Dermatol Venereol Leprol 1982;48:358-61.
2. Feduska NJ, Turcotte JG, Gikas PW, Bacon GE, Penner JA. Reversal of renal allograft rejection with intravenous methylprednisolone "pulse" therapy. J Surg Res 1972;12:208-15
3. Cathcart ES, Scheinberg MA, Idelson BA, Couser WG. Beneficial effects of methylprednisolone 'pulse' therapy in diffuse proliferative lupus nephritis. Lancet 1976; 1:163-6.
4. Dhabhai R, Kalla G, Singh MK, Ghiya BC, Kachhawa D. Dexamethasone-cyclophosphamide pulse therapy in systemic lupus erythematosus. Indian J Dermatol Venereol Leprol 2005; 71:9-13.
5. Pasricha JS. Pulse therapy in Pemphigus and other diseases, 2nd edn. New Delhi: Pulse therapy & Pemphigus foundation,2000.
6. Bastuji-Garin S, Souissi R, Blum, et al. Comparative epidemiology of Pemphigus in Tunisia and France: unusual incidence of Pemphigus foliaceus in young Tunisian women. J Invest Dermatol 1995; 104:302-305.
7. Mahajan VK, Sharma NL, Sharma RC, Garg G. Twelve-year clinico- therapeutic experience in Pemphigus: A retrospective study of 54 cases. International journal of dermatology 2005; 44(10):821-7.
8. Kuldeep CM, Mittal AK, Gupta LK, Paliwal VK, Sharma P, Garg A. Successful treatment of scleromyxedema with dexamethasone cyclophosphamide pulse therapy. Indian J Dermatol Venereol Leprol 2005; 71:44-45.
9. Ramam M. Dexamethasone pulse therapy in dermatology. Indian J Dermatol Venereol Leprol 2003; 69:319-322.