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# A RETROSPECTIVE STUDY OF EFFECTS OF DEXAMETHASONE CYCLOPHOSPHAMIDE PULSE (DCP) THERAPY ON AUTOIMMUNE VESICULOBULLOUS DISORDERS IN A TERTIARY CARE CENTER

Dermatology

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## ABSTRACT

**INTRODUCTION:** Traditional treatment for autoimmune vesiculobullous disorders is systemic corticosteroids, on daily basis, in continuous manner, associated with many side effects. Dexamethasone Cyclophosphamide Pulse (DCP) therapy is effective in inducing and maintaining remission.
**AIMS & OBJECTIVES:** To study the safety and efficacy of DCP therapy on Autoimmune Vesiculobullous Disorders.
**MATERIALS & METHODS:** A retrospective study to determine the safety and efficacy of DCP in autoimmune vesiculobullous diseases in tertiary care centre from January 2015 to December 2018.
**STUDY TOOLS:** Records and clinical photographs.
**STATISTICAL ANALYSIS:** Percentage.
**RESULTS:** In 30 patients-6 males and 24 females. 29 patients- Pemphigus Vulgaris, 1 patient Pemphigus Foliaceous. 11 patients were in phase I, 4 in phase II, 6 in phase III, 4 in phase IV.
2-Discontinued DCP, 3-defaulter. Immediate side effects were infections. Delayed side effects were metabolic and skeletal.
DCP is effective in achieving and maintaining remission in autoimmune vesiculobullous disorders for longer duration, with decreased steroid induced complications.

## KEYWORDS

Autoimmune Vesiculobullous Disorders, Dexamethasone Cyclophosphamide Pulse, Decreased Side Effects, Remission.

## INTRODUCTION

Autoimmune vesiculobullous disorders are due autoantibodies against structural elements of skin, which results in vesicles and bullae formation[1]. The target of these antibodies being Desmoglein 1 (Dsg 1) and Desmoglein 3 (Dsg 3) in Pemphigus Vulgaris and Desmoglein 1 (Dsg 1) in Pemphigus Foliaceus [2]. There are number of treatment available such as

a. Systemic corticosteroids on daily basis in high doses (1-2mg/kg/day of Prednisolone) in continuous manner.
**b. DCP** (Dexamethasone Cyclophosphamide Pulse)
First used in Pemphigus Vulgaris by Pasricha .[2]

(Pulse therapy has been defined as administration of large or suprapharmacological doses of drugs in a non continuous manner to increase their efficacy and decrease the side effects).[3]

c. Immunomodulators like Cyclophosphamide, Azathioprine, Mycophenolate Mofetil, Cyclosporine, Methotrexate, Dapsone, Tetracycline, Nicotanamide.
d. Biologicals like Rituximab.

As the systemic corticosteroids are associated with number of side effects and due to financial constraint of Rituximab, DCP is a balanced option taking into consideration the efficacy, side effect profile and the financial aspect.

## AIMS AND OBJECTIVES

AIM : To study the effects of dexamethasone cyclophosphamide pulse (DCP) therapy on autoimmune vesiculobullous disorders in a tertiary care center.

## OBJECTIVES:

1. To study age and gender wise distribution of various autoimmune vesiculobullous disorders.
2. To study effects of DCP on autoimmune vesiculobullous disorders.
3. To study the adverse effects of DCP.

## MATERIALS AND METHODS

After obtaining the permission from Institutional Ethical Committee, the data from the Vesiculobullous Disorder speciality clinic was taken. The duration of study was three years (January 2015 to December 2018). The clinical data and photographs of the patient from the record were taken and Statistical analysis was done. The age and gender wise distribution of the patients was studied. Their response to DCP was recorded and patients were also observed for the side effects.

Dcp Is Given In **4 Phases** [4]

### PHASE 1 INDUCTION PHASE

Injection Dexamethasone 100 mg in 500 ml of 5 % dextrose is given for 3 days with adding Injection Cyclophosphamide 500 mg on day 2 only. These cycles are repeated every 28 days. In between cycles daily oral steroids for maintenance are given and also oral Cyclopho sphamide 50 mg OD is given. This phase is continued till remission that is absence of fresh lesions and disappearance of existing lesions without need for oral corticosteroids in between pulses.

### PHASE 2 CONSOLIDATION PHASE

Injection Dexamethasone 100 mg in 500 ml of 5 % dextrose is given for 3 days with adding Injection Cyclophosphamide 500 mg on day 2 only. These cycles are repeated every 28 days. In between cycles daily oral Cyclophosphamide 50 mg is given.

Total of 9 cycles are given in phase 2.

### PHASE 3 MAINTENANCE PHASE

Only daily oral Cyclophosphamide 50 mg is given for nine months.

### PHASE 4 DISEASE FREE DRUG FREE PERIOD OF OBSE RVATION

Medications are stopped and patient is followed up and observed for adverse effects and relapses. Patients are generally followed up for at least 5 years.

**To summarize as shown in table 1 -[5]**
**Table 1**

| Phase | Lesions | DCP Monthly Pulses | Oral Cyclophosphamide 50 mg daily In between pulses | End Point |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| 1 | Present | Given | Given | Till no new lesion |
| 2 | Absent | Given | Given | 9 months |
| 3 | Absent | Stopped | Given | 9 months |
| 4 | Absent | Stopped | Stopped | 5 years |

Pulse therapy is used for achieving faster response and greater efficacy. With use of pulse therapy there is decreased need for systemic corticosteroids.

## RESULTS

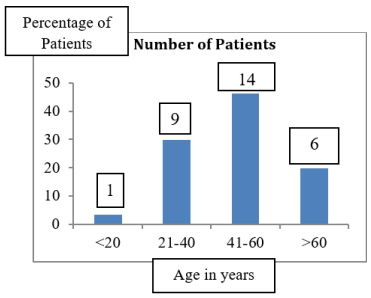
Total of 30 patient were enrolled in the study. Among these 24 (80%) were females and 6 (20%) were males.

### Gender wise distribution


29 patient had Pemphigus Vulgaris and 1 patient had Pemphigus Foliaceus.

## AGE WISE DISTRIBUTION

Most common age group involved was 41-60 years (46.2%), followed by 21-40 years (29.7%), then was patients above 60 years 19.8% and least common was less than 20 years which formed 3.3 %.

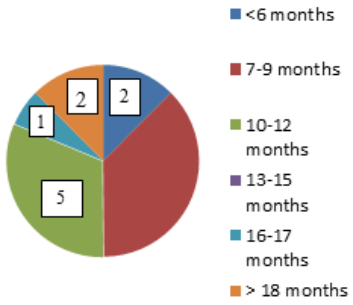



At the end of our study 11 patients were in Phase I, 4 in Phase II, 6 in Phase III and 4 patients in Phase IV.

In 2 of our patient we had to discontinue DCP due to side effects.

3 of our patient were defaulter, all 3 defaulted in Phase I.

As the duration of Phase II and III is fixed and Phase IV being an observational Phase duration of Phase I was studied- (16 patients had completed Phase I) Duration of Phase I Most of the patients that is 6 patients (37.5 %) required Phase I for 7-9 months, followed by 5 patients (31.5 %) in which Phase I was continued for 10-12 months, 2 patients (12.5%) achieved remission in less than 6 months , 1 patient (6.25%) responded in 16-17 months and 2 patients (12.5%) were non responders in whom we had to continue Phase I for 20 months and later were shifted to Phase II.




The **side effects** were classified as

a. Immediate – seen in first 6 months of initiation of DCP
b. Delayed – seen after 6 months of initiation of DCP

Among the **Immediate side effects** infections were seen most commonly. Activation of Herpes Zoster was seen in 3 patients.

In Bacterial infections, folliculitis and cellulitis was seen in 2 patients each. Furunculosis and abscess in 3 patient each. Among these one patient had Perineal abscess, who needed incision and drainage and one month later the DCP was continued. Superficial dermatophytosis and intertrigo was seen in 2 patients each. Oral candidiasis was observed in 3 patients, while one patient had Oro-oesophageal Candidiasis. One patient also had 4 th metatarsal fracture.

### IMMEDIATE SIDE EFFECTS -

| Side Effect | Number of Patients |
|---|---|
| VIRAL INFECTIONS | |
| Activation of Herpes Zoster | 3 |
| BACTERIAL INFECTIONS | |
| Folliculitis | 2 |
| Furunculosis | 3 |
| Cellulitis | 2 |
| Abscess | 3 |
| FUNGAL INFECTIONS | |
| Oral Candidiasis | 3 |
| Oro-oesophageal Candidiasis | 1 |
| Superficial Dermatophytosis | 2 |
| Intertrigo | 2 |
| **SKELETAL SYSTEM** | |
| 4th Metatarsal Fracture | 1 |

In **Delayed side effects**, Hypertension and Diabetes Mellitus were the most common seen in 7 and 5 patients respectively. Mooning of face that is Cushingoid facies seen in 2 patients. Osteoporosis and premature posterior subcapsular cataract were seen in 1 patient each. Delayed side effects - The delayed side effects which needed discontinuation of DCP were Gastric ulcer with impending perforation and Avascular necrosis of head of femur which were seen in Phase II and III respectively

### DELAYED SIDE EFFECTS -

| Side Effect | Number of Patients |
|---|---|
| **METABOLIC** | |
| Hypertension | 7 |
| Diabetes Mellitus | 5 |
| Cushingoid Facies | 2 |
| **SKELETAL** | |
| Avascular Necrosis of Head Femur | 1 |
| Osteoporosis | 1 |
| **OCULAR** | |
| Premature Posterior Subcapsular Cataract | 1 |
| **GASTRIC** | |
| Gastric Ulcer with Impending Perforation | 1 |

At the end of our study 17 patients achieved remission, which included all patients in Phase II, III and IV and also the patients in Phase I which were planned to be shifted in Phase II.

5 of the patients were with persistent lesions, all 5 in Phase I.

3 had recurrence of lesions, 2 in Phase II and 1 in Phase III, the recur rence was controlled on short course of oral corticosteroids in between pulses and the respective phases were continued.

## DISCUSSION

Pemphigus is chronic, autoimmune disease affecting skin, mucosa, or both, characteristic by autoantibodies against desmosomal adhesion proteins, causing intraepidermal blistering.[1] The worldwide incidence of Pemphigus is 0.5 to 2.7 cases per 1,00,000 and in India it varies from 90 to 1800 cases per 1,00,000 (0.09 to 1.8 %) [1,2]. Pemphigus Vulgaris is most common presentation of all autoimmune vesiculobullous diseases in India (88.8%), followed by Pemphigus Foliaceus (6.6%) [2]. The most common age group involved is 41-60 years [1]. Initially oral corticosteroid was the treatment of choice which later shifted to DCP,

and now being changing to Rituximab.

DCP is a good economical treatment option for treatment of autoimmune vesiculobullous disorders.

The most common age group in our study was 41-60 years, followed by 21-40 years ; in Sacchidanand et al [6] study it was 36-45 years, while Kandan and Thappa [7] study it was found to be 50-59 years.

In our study Pemphigus Vulgaris was most common disease (29 of 30 patients) similar to 88% Pemphigus Vulgaris patient in Sacchidanand et al [6] study; with one patient of Pemphigus Foliaceous, in Kandan and Thappa [7] study 75.4 % patients were Pemphigus Vulgaris, 16.92 % were Pemphigus Foliaceous, 4.6 % Pemphigus Erythematosus. 1.5 % Paraneoplastic Pemphigus and Pemphigus Vegetans.

In study by Kandan and Thappa [7] 46 of 65 patients had oral lesions , in contrary 28 of 30 patients had oral lesions in our study.

Remission was seen in most of our patients by 7-9 months similar to that of Kandan and Thappa [7] study. The duration between diagnosis and initiation of DCP in our study was 2-3 months, which was 6-9 months in Kandan and Thappa study.

In our study 2 of 16 patients discontinued in Phase I, whereas 6 of 50 patients discontinued in Sacchidanand et al [6] study and in Kandan and Thappa [7] study 8 of 33 patients discontinued in Phase I.

In Kandan and Thappa [7] study 7.7 % patient died during treatment, which was 0.5 % in Sacchidanand et al [6] study; though the number of patients were less in our study, no death was recorded.

As newer drugs like Rituximab are being useful in achieving remission early and also maintaining it but their cost is limiting factor. So taking cost effectiveness, side effect profile, efficacy all into consideration DCP is a good treatment option in autoimmune vesiculobullous disorders.

## CONCLUSION

DCP is a better treatment option than long term systemic corticost eroids alone. With DCP remission is achieved earlier and also maintained for longer duration, also the side effects with continuous corticosteroids are decreased.

And is another option in terms of economical consideration.

**CONFLICT OF INTEREST –** None.

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