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To Compare the Cost of Rituximab and DCP Therapy in Pemphigus in a Government Tertiary Hospital

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Abstract

Background: Pulsed corticosteroids are the mainstay in management of pemphigus but long term use is associated with numerous side effects. Biologics have shown promising results with minimal adverse effects but are expensive.

Aim: To compare the cost of DCP & low-dose Rituximab therapy in pemphigus in a government tertiary hospital.

Methods: We calculated the cost of DCP therapy (3 phases) and low dose Rituximab therapy in the treatment of pemphigus. These were considered under direct (medicines, usables for administering the medicines) and indirect costs (hospitalization, travel, loss of pay, the need for one attender) and a comparison were drawn.

Results: The cost of DCP therapy for 3 phases over 27 months totalled up to 87,800 while the cost of Rituximab therapy over 1 month was 49,594. Low dose Rituximab therapy was clearly more cost effective.

Limitations: We have not compared the efficacy of drugs, adverse effect profile or quality of life of patients in DCP and Rituximab group. Usables and steroids are free for patients in government hospital which partially reduces the cost of DCP further.

Conclusion: Low dose Rituximab therapy has a high upfront cost but still proves to be very cost effective compared to DCP. Going by the published data on efficacy and safety of low dose Rituximab, it can provide better quality of life due to fast and sustained remission, drastically reduce the duration of hospital stay, reduced burden of the disease on the family and medical fraternity. It is time to switch to safer, cheaper and more effective remedies.

Key messages: If the safety and efficacy of Rituximab can be clearly established, then it should be considered as a first line therapy for pemphigus.

Keywords: Pemphigus; Dexamethasone Cyclophosphamide Pulse therapy (DCP); Low dose rituximab

Introduction

Autoimmune blistering disorders are a group of chronic potentially life threatening disorders characterized by blisters in the skin and or mucous membrane [1]. The incidence among the dermatology outpatient attendees varies between 0.09 to 1.8% [2]. Its prevalence varies from 0.18 to 6.96 cases per 1,00,000 population worldwide [3]. Though corticosteroids are the mainstay of treatment, other modalities like Immunoadsorption techniques, intravenous immunoglobulin's and monoclonal antibodies have been tried.

Longer and larger doses of steroids are needed to treat these disorders which may lead to a host of adverse effects and even fatality. The commonly practiced Dexamethasone Cyclophosphamide (DCP) Pulse therapy is administered monthly, for more than 3 years. However, the newer drugs (biologicals) have been claimed to be comparatively safer, have shorter duration of therapy, provide faster remission and improved quality of life but at much higher costs.

Aims of the study

To assess the cost of Dexamethasone Cyclophosphamide Pulse therapy.

To assess the cost of low dose Rituximab therapy.

To compare the cost of Dexamethasone Cyclophosphamide Pulse therapy against low dose Rituximab therapy in pemphigus.

Materials and Methods

We analysed and calculated the cost of DCP for all 3 phases and cost of the low dose Rituximab therapy in the treatment of pemphigus. The prices were considered in the setting of a government tertiary hospital, where most drugs (except Rituximab and cyclophosphamide) and usables are available for free to the patients. However, we need to keep in mind that these drugs or usables were procured by payment from the government (Tables 1-4).

The parameters taken into account for calculating the cost of therapy were divided as direct costs and indirect costs. They are as follows:

DCP therapy comprises of IV phases of which first, usually is an arbitrary period of 9 pulses followed by II phase of 9 pulses DCP, III phase consists of only oral Cyclophosphamide for 9 months and phase IV is observation for 10 years.

Number of days of hospitalization during each pulse in DCP is 3 days. Total duration of hospital stay: 3 days per pulse × 18pulses=54 days III phase is oral medication, no hospitalization.

Cost of each investigation in government set up		
Sl. No	**Investigation**	**Cost (INR)**
1	Haemoglobin (Hb%)	20
2	Complete Blood Count (CBC)	70
3	Platelet Count (PLC)	50
4	Liver Function Tests (LFT)	200
5	Renal Function Tests (RFT)	110
6	Random Blood Sugar (RBS)	30
7	Urine Routine	30
8	Electro Cardio Gram (ECG)	30
9	Chest x ray(CXR)	60
10	Direct Immunofluoroscence (DIF)	1500
11	CD4 count	900

Table 1: List of prices under government setup.

Cost of drugs and usables		
Sl. No	**Drugs/Materials**	**Cost (INR)**
1	Injection Dexamethasone (1Vial)	6.25
2	Injection Cyclophosphamide (500 mg)	80
3	Each Tab cyclophosphamide (50 mg)	3.5
4	Each Tab prednisolone (10 mg)	1.5
6	Dextrose with Normal Saline (500 ml)	30
7	Intravenous (IV) drip set	75
8	IV cannula	75
9	5% Dextrose	29
10	Surgical gloves (1 pair)	50

Table 2: List of prices (Drugs and Usables).

Sl. No	Investigation Cost (INR)	Cost in each DCP pulse (INR)	Cost in each rituximab injection (INR)
1	CBC, PLC, LFT, RFT, RBS, Urine Routine, ECG, Chest X-Ray	600	600
2	Dexamethasone injection	244	-0-
3	Cyclophosphamide injection	80	-0-
4	5% Dextrose 500 ml	87	29
5	IV drip set.	225	75
6	IV Cannula.	75	75
7	Surgical Gloves.	350	150
8	Cost of Rituximab injection 500 mg	-0-	21,000 (subsidized cost)
9	Cost of each pulse/dose	1,661 per pulse	21,929 per dose
10	Direct cost of entire therapy(18 pulses in DCP and 2 doses in Rituximab)	29,898	43,858
11	Cost of routine investigation in Phase 3 of DCP(once in 3 months)	1800 (600 × 3)	
11	DIF*(3 in DCP and 2 In Rituximab Therapy)	4,500	3,000
12	CD4 count.	-0-	900
13	Inter pulse cyclophosphamide	2,750	-0-
14	Total Direct cost.	38,948	47,758

Table 3: Comparison of DIRECT COSTS, investigations, medicines in DCP and low dose Rituximab.

Sl No.	Parameters	Cost in each DCP pulse (INR)	Cost in each low dose Rituximab injection (INR)

1	ICU Charge	900 (300 per day × 3 days)	300
2	Minimum Wage Lost	1,764 (294 per day × 2 persons x 3days)	588 (294/day × 2 persons × one day)
3	Travelling charge.	50	30
4	Total indirect cost in entire therapy.	48,852 (2714 per pulse × 18 pulses)	1,836 (918 × 2 low dose injections)
5	Total expenditure	DCP therapy.	Rituximab therapy.
6	Total cost of therapy (Direct and Indirect)	87,800 (38,948+48,852)	49,594 (47,758+1,836)

Table 4: Comparison of expenditure in full phase of DCP therapy and full course of Rituximab injection in pemphigus.

DIF is done 3 times in DCP therapy; once for confirmation of diagnosis, 2nd time during the completion of phase one, and 3rd time after the completion of phase 2.

DIF is done twice in Rituximab therapy. Initially, for confirmation of the diagnosis and 2nd time after completion of the 2nd dose.

A patient needs complete work up of blood parameters before every DCP pulse therapy and at least once in 3 months during phase III. These investigations along with DIF add up to a whopping INR 87,800 for 3 phases of DCP over 27 months.

The indirect cost of DCP therapy is also to be taken into account. These include:

Loss of income of the patient

Loss of income of the attendant

Travelling expenditure of the patient and attendant.

Travel: In this city, the minimum cost of travel by public transport is INR 5. Hence if the patient has at least 1 attender by his side continuously and another shuffling between the house and hospital, that would make 4 trips in a day for 3 days which comes to INR 50. The same in case of Rituximab therapy is INR 30 because of shorter duration of hospital stay.

Usables: For each DCP there is usage of an average of 7 pairs of gloves and one IV cannula and 3 IV drip sets. So it costs about INR 650 for each DCP therapy whereas it costs only INR 300 for Rituximab therapy. Evaluating CD4 counts costs INR 900 and it's not free for HIV negative patients in our hospital.

Drugs: Though the cost of 1 vial of 500 mg of Rituximab is approximately INR 39,000, the same is provided at a subsidized cost of INR 21,000 for our institution. We have considered the subsidized price in calculating the cost of therapy.

Discussion

Pulse therapy means administering a drug at supra-pharmacological doses over a short period and then withdrawing it completely till next dose. DCP was introduced in the management of pemphigus vulgaris in the Department of Dermatology, All India Institute of Medical Sciences, New Delhi by Pasricha in 1982. The main objective of using DCP therapy was to achieve faster control of disease activity, reduction in total cumulative dose and to reduce the morbidity due to corticosteroid induced side effects. In the Indian scenario, it is the most commonly used treatment modality for pemphigus unlike in developed countries where it is uncommon [4].

Rituximab is an IgG type chimeric human mouse monoclonal antibody against transmembrane antigen CD20 expressed on B lymphocytes. It induces apoptosis of both circulating as well as tissue based B cells by complement dependent and antibody dependent cellular cytotoxicity. Both lymphoma regimen (four, weekly infusions of 375 mg/m^2) and rheumatologic dose (two infusions of one gram each separated by two weeks) have been successfully used to treat autoimmune blistering diseases including pemphigus [5]. Studies have shown that antibody producing B cells in the Pemphigus are not malignant and a single dose as low as 100 mg/m^2 can deplete B cells [6]. A recent prospective open case series reported that a low dose rituximab regimen consisting of two 500 mg infusions separated by two weeks was effective in pemphigus. This is just 39% of the hematological dose and yet more than 73% of the patients achieved complete remission [6].

Total duration of hospital stay is only two days in Rituximab therapy unlike 54 days in DCP (3 days per pulse × 18pulses=54 days) which is spread over 18 months. In Rituximab group follow up period is 2 years unlike the DCP group where it is about ten years [6-11].

From above analysis it is clear that the total expenditure for a patient to receive 3 phases of DCP over 27 months is about INR 87,800; whereas the total expenditure for two doses of Rituximab therapy is approximately INR 49,594.

The burden of the disease on the family members and medical fraternity is also more in case of DCP therapy when compared to Rituximab therapy.

Conclusion

Low dose Rituximab therapy is more cost effective when compared to 4 phases of DCP. The quality of life is obviously better in low dose Rituximab therapy because of early sustained remission, short duration of hospital stay and no complications of long term steroids. The above advantages also ease the burden of the disease on the family and medical fraternity. If the efficacy and safety profile of Rituximab can be clearly established, then it may be considered as a first line therapy for pemphigus.

Limitations of our study

We have not compared the efficacy of the drugs nor their adverse effects. We have not compared the change in quality of life of patients treated with DCP and Rituximab therapy.

We have considered the minimum travel charge in our state, but patients may be spending more than what we have calculated while travelling, which will be an additional burden.

In our institution we are getting Rituximab injection 500 mg at a subsidized cost of INR 21,000 while the retail price is approximately INR 40,000.

Larger studies and randomized controlled trials would be valuable to determine the long term safety and efficacy of Rituximab in Indian scenario.

Usables and steroids are free for the patients in a government hospital. Hence, DCP therapy may still remain the poor man's choice. Since the expenses in DCP are spread over 2 years they provide for a financial cushion, unlike low dose rituximab where patient has to spend entire amount in just 2 weeks.

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