ORIGINAL ARTICLE

COMPARISON OF EFFICACY OF HIGH DOSE DEXAMETHASONE WITH CONVENTIONAL PREDNISOLONE IN THE TREATMENT OF NEWLY DIAGNOSED ADULT PATIENTS OF IMMUNTHROMBOCYTOPENIC PURPURA

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Background: Immune thrombocytopenic purpura with multimodal incidence having peaks in each age groups is a chronic clinical syndrome in adults, with disease more predominant in females in adults. The aim of the study was to compare the efficacy (response rate) of high dose dexamethasone with conventional prednisolone in the treatment of newly diagnosed adult patients of Immune thrombocytopenic purpura. It was a prospective quasi-experimental study, conducted at the Department of Medicine of a tertiary care hospital from Jan to Dec 2019. Subjects and **Methods**: The sample population comprised of 130 cases of newly diagnosed ITP patients, having platelet count <30,000/ul with or without bleeding symptoms who received either dexamethasone (40 mg/day for 04 days) or prednisolone (0.5–1 mg/kg PSL for 01 week). Treatment response was measured at day 7. **Results:** Out of 130 patients 65 patients were treated with dexamethasone and 65 patients with prednisolone .83.08% (n=54) cases in Group-A and 33.85% (n=22) in Group-B had response while remaining 16.92% (n=11) in Group-A and 66.15% (n=43) in Group-B had no response. The *p* value was calculated as 0.000 which shows a significant difference. **Conclusion:** We concluded that high dose of dexamethasone shows a significantly higher response when compared with conventional prednisolone in the treatment of newly diagnosed adult patients of Immune thrombocytopenia purpura.

Keywords: Immune thrombocytopenic purpura; Conventional prednisolone; Dexamethasone

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INTRODUCTION

Immune thrombocytopenic purpura (ITP)with multimodal incidence having peaks in each age groups is a chronic clinical syndrome in adults, with disease more predominant in females in adults.[1] Its incidence is 3.3/100,000 adults/year and prevalence is 9.5/100,000 patients.[2] Primary ITP accounts for about 80% of cases and different therapeutic innovations have been developed so far and their response is variable but corticosteroids are the cornerstone of treatment in ITP.[3] Exact mechanism for increasing the platelet count remains a dilemma but one of the main hypothesis is increased platelet production and downregulating autoantibody production and phagocytic activity.[4,5]

The treatment paradigm with steroids improve platelet count early within a week in majority of patients, however long-term remission rates vary in different studies.[6,7] There is a necessity of long term of steroids for sustainability of remission but that is menace for the patients due to deleterious adverse effects. The American Society of Haematology (ASH) guidelines8 published in 2019 on ITP prefer shorter courses of corticosteroids over longer courses because longer courses are associated with more side effects.

Recently, studies have been conducted on dexamethasone with shorter exposure period and found to be effectual in durability of remission8 but no standard dose of dexamethasone can be recommended due to variability of treatment protocols and no head-head comparison trials available in the literature. The first single blind randomized prospective study conducted in Ali-Ebne-Abitaleb hospital in Zahedan, comparing between high dose dexamethasone and conventional prednisolone therapy demonstrated dexamethasone to be better in achieving remission at 01 week. (90% vs36.7%).[3] Another study conducted in Thailand demonstrate the remarkable impact of high-dose dexamethasone on platelet counts in the treatment of ITP over standard dose prednisolone. In addition, alternative analyses also found that the platelet counts were significantly higher after dexamethasone on

days 5 and 15.[8] Therefore, pulse dexamethasone is the drug-of-choice for severe ITP.[9]

The rationale of my study is to evaluate the response of single course of high dose dexamethasone comparing conventional prednisolone therapy in the treatment of newly diagnosed adult ITP patients as initial good response rate has been reported with dexamethasone compared with prednisolone and also literature review has revealed no published study addressing this issue in Pakistan in the last 05 yrs.

MATERIAL AND METHODS

This prospective quasi-experimental study was carried out at a tertiary care hospital and consecutive non-probability sampling technique was used with sample size of 130 cases (65 in each group) calculated via WHO sample size calculator (20.2b) After getting approval from the Hospital Ethical Committee, newly diagnosed ITP patients, male or female, aged 20–55 yrs., platelet count <30,000/ul with or without bleeding symptoms (grades 0–3) were enrolled in the study. Patients with major bleeds, i.e., grade 4 as defined in the operational definition, previously treated ITP, diabetes, liver and kidney dysfunction, infections including HIV, HCV, and HBV, pregnancy and SLE or autoimmune diseases were excluded.

The patients were divided into two groups by lottery method, group A was given dexamethasone (01 course, i.e., of 40 mg/day for four days) and group B was given prednisolone (daily administration of 0.5–1 mg/kg Prednsiolone for one week and at 7th day of treatment platelet count was checked manually by phase contrast microscopy. Results were measured in terms of complete response (CR) Platelet count >100,000u/l, partial response (Platelet count is between 30,000 and 100,000/microL) or no response (NR) platelet count <30,000 or no increase in platelet count with treatment) and results verified by a pathologist who were blinded to the patients. Data was collected on a *pro forma.*

Who Bleeding Scale 8

Grade	Type of bleeding
0	Absent
1	Petechiae
2	Ecchymoses and/or with moderate loss of blood
3	Major mucous haemorrhage with copious loss of blood without sequelae
4	Major mucous and/or parenchymal haemorrhage with copious loss of blood with sequelae or/and life threatening

Data was entered and analysed using SPSS version 20.0. Descriptive statistics were calculated for both qualitative and quantitative variables. Mean and Standard deviation (mean±SD) were calculated for quantitative variables like age, platelet count at presentation and after 01 week. Frequency and percentages were calculated for qualitative variables like gender, response rate. Qualitative variables were presented through charts and tables. For comparison of response rate of dexamethasone and prednisolone in ITP patients, chi-square was applied. *p*-value <0.05 was considered significant.

RESULTS

Table-1 showed the general characteristics of the patient. Mean platelet counts at presentation and after 01 week was calculated and represented in figure-1

Comparison of response in both groups was recorded in Figure-2. Table-5, *p*-value was calculated as 0.000 which shows a significant difference.

Table-1: General characteristics of patients in both groups

Characteristic of patients	Group A n (%)	Group B n (%)
Sex		
Male	44 (67.69)	36 (55.38)
Female	21 (32.31)	29 (44.62)
Age (years)		
20–40	38 (58.46)	42 (64.62)
41–55	27 (41.54)	23 (35.38)
Mean ± SD	37.78 ± 9.17	37.89 ± 8.74

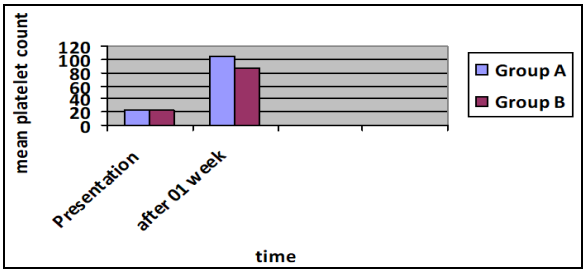

Figure-1: Mean Platelet count at presentation and after 01 week

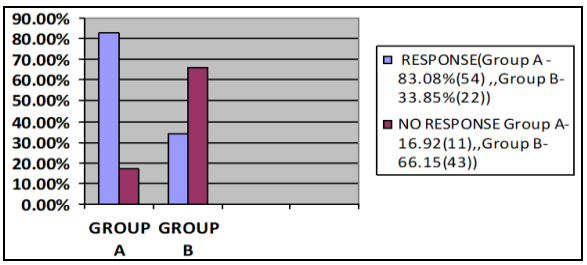

Figure-2: Comparison of response in both groups (n=130)

DISCUSSION

Corticosteroids as the primary treatment for adult primary immune thrombocytopenia (ITP) with weak durability of remission and untoward long-term consequences indelibly remains a subject of

controversy,[10,11] and no consensus has been made even on the exact protocol. There is always an exigency for the execution of large scale randomized studies on this topic to reach to a solid conclusion and include it in guidelines .Many studies have been conducted up till now at international level on this topic as well on different steroid dosing regimen for ITP but representative data at national level is exiguous .Our study highlights and advocate the previous reports that High Dose dexamethasone is the potential replacement for the classical prednisolone (PSL) therapy for newly diagnosed ITP patients.[12,13] Johannes Matschke in 2016 and Banhe Din in 2015 also substantiated that Dexamethasone mounted a better and sustained response.[11,14] Indeed, the latest international consensus report and practice guideline for ITP proposed HD-Dexa therapy as one of the front-line options for ITP.[5,15]

Complete long-term remissions with steroids have been reported in approximately 20 percent of individuals. Short term remissions with different steroids have been tried in various international studies1 Our study showed complete response in 83.08% in group A and 33.31% (n=22) in group B. This is in accordance with first randomized prospective study conducted in Ali-Ebne-Abitaleb hospital in Zahedan, about comparison between high dose dexamethasone and conventional prednisolone therapy, which showed 90% complete response in dexamethasone group at 1wk and 36.7% in prednisolone group2. Another study demonstrated 77% response with dexamethasone maintaining remission (median follow-up was 46 months with a range of 17–148) 11 but contrary to the study conducted in Japan which proved standard classical prednisolone regimen to be superior to HD-dexamethasone in sustainability of remission.[11]

Different dosing regimens /protocol of steroids have been tried in antecedent studies for ITP patients .Few studies recommend repeated dosing of steroids in order to achieve long term remission.[16] Our protocol is based on the study with little modification conducted by Dr. Yu Wei and colleagues who compared high dose dexamethasone (40 mg) for four days with four weeks of 1mg/kg of prednisone followed by a taper.[8,17,18] There was no difference observed in our study in response rates between the different age groups, however, few differences can occur in side effect profile due to long term use but that was not studied. This is in contrast to the multicenter study which showed more favourable response in younger populace compared to adults.[2]

Our study had few constraints—firstly it is a single blind study with limited sample size in both groups. Secondly it also lacks the adverse effects observed in both groups and long term follow up data of both groups required for sustainability of remission. However, the higher response rate with dexamethasone bodes well for future long-term outcomes. Thus, more alacrity in conducting future muticenter prospective trials on this topic addressing all the constraints and to vindicate the results of our study is necessitated

CONCLUSION

High dose dexamethasone to be better in achieving response when compared with conventional prednisolone in the treatment of newly diagnosed adult patients of Immune thrombocytopenia.

AUTHORS' CONTRIBUTION

BB, UQ: Conceptualization of the study design, data interpretation and analysis. HB, OA: Data collection, data interpretation. F, HE, JK: Data collection, analysis, proof reding.

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