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A COMPARATIVE STUDY TO KNOW THE EFFICACY OF DEXAMETHASONE VERSUS PLACEBO FOR THE BACTERIAL MENINGITIS TREATMENT

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Abstract:

Objective: *To compare the dexamethasone versus placebo efficacy in reducing hospital mortality in addition to antibiotics used to treat patients with bacterial meningitis.*

Study Design: *A randomized control trial.*

Place and Duration: *In the Medicine Unit 1 of DHQ Hospital Rawalpindi for six months duration from February 2019 to July 2019.*

Methods: *In this study, non-probability purposive sampling technique was used. Informed consent forms were taken from all patients. All patients received a Cefotaxime combination at a dose of 2gramIV for 8 hours and Vancomycin 1g IV for 12 hours. The volunteers were then distributed randomly into 2 groups using the lottery method. In group D, 10 mg of dexamethasone IV was given to patients for 4 days every 6-hourly and group P patients were not treated with dexamethasone with standard regimens. The patients were followed up during the hospital stay due to mortality. The data were classified according to age, sex, disease duration, and TLC at the time of admission to deal with the impact modifier. Chi-square test was performed after stratification. A value of <0.05 was measured significant.*

Results: *A total of 480 patients were selected for this analysis. The 40.98 ± 14.28 years was the patients mean age. The M/F ratio of the patients was 2: 1. In our study, mortality was seen in 55 patients (11.5%). There was a statistically substantial variation between the study and placebo groups in relations of mortality.*

Conclusion: *Our study results concluded that dexamethasone was more effective in reducing hospital mortality in bacterial meningitis patients than in the placebo group.*

Keywords: *antibiotic therapy, bacterial meningitis, dexamethasone, placebo, mortality.*

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INTRODUCTION:

Bacterial meningitis (BM) consists of pyogenic inflammation of meninges and underlying subarachnoid CSF. If left untreated, it can cause life-time disability or death[1-2]. The 3 membrane layers surrounding the brain and spinal cord is a clinical syndrome characterized by inflammation of meninges[3]. Meningitis patients presenting with a changed level of consciousness increase the risk of neurological sequelae or death. A seizure during a meningitis attack is also a risk factor for death or neurological sequelae, if the seizure is prolonged or difficult to control[4]. The outcomes are better if antibiotics given at early stage, but the efficacy of commonly accessible antibiotics is endangered by the global emergence of multidrug-resistant bacteria[5]. In addition, if adjuvant anti-inflammatory treatments (e.g, dexamethasone) progress to better results in bacterial meningitis patients, the discussion continues; in the Netherlands a national cohort observational study, if dexamethasone use adjunctively it reduced pneumococcal meningitis death from 31% to 22%. Also the van de Beek et al meta-analysis of individual patient data could not determine which patients would benefit most from dexamethasone treatment; In fact, there is no significant reduction in death or neurological disability[6]. The reason for this study is to compare the mortality rate with dexamethasone and placebo in the management of patients presenting with BM. The literature is clear that dexamethasone is effective in preventing high mortality, but due to controversy, doctors do not recommend routine dexamethasone for BM management[7]. In this study, we would like to confirm whether dexamethasone can help prevent mortality. In addition, no local studies have yet been conducted. We will also obtain local size with this study and the results of this study will help us to recommend the use of dexamethasone with standard treatment for BM.

MATERIALS AND METHODS:

In this study, deliberate improbable sampling technique was used. Informed consent forms were obtained from all patients. Your demographic information (name, age, gender, address and contact) was also noted. All patients received a Cefotaxime combination at a dose of 2 gram IV for 8 hours and Vancomycin 1g IV for 12 hours. Into 2 groups; patients were divided randomly using the lottery method. In group D, 10 mg of dexamethasone IV was given to patients for 4 days every 6-hourly and group P patients were not treated with dexamethasone with standard regimens. The patients were followed up during the hospital stay due to mortality. Data were categorized according to age, sex, disease duration, TLC at admission to cope with impact modifier. Chi-square test was performed after stratification. A <0.05 P value was taken significant.

RESULTS:

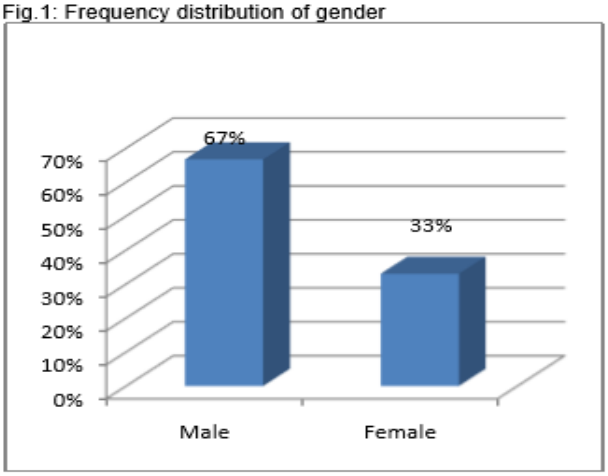
In this study, a total of 480 cases were recorded. The 40.98 ± 14.28 years was the patients mean age and the minimum age was 20 and 69 years (Table 1).

Table 1: Descriptive statistics of age (years)

n	480
Mean	40.98
SD	14.28
Minimum	20.00
Maximum	69.00

In our study, 66.67% of the patients were male and 33.33% were female. The M/F ratio of the patients was 2: 1 (Figure 1), with the results of the study showing that 55 of the 13 cases died in 55 of the dexamethasone group and 42 of the placebo group.

Fig.1: Frequency distribution of gender



A significant statistically variation was found between the placebo and study group and patients' mortality. p = 0.000 (Table 3).

Table 2: Frequency distribution of Mortality

Mortality	Frequency	%age
Yes	55	11.5
No	425	88.5
Total	480	100.0

Table 3: Comparison of mortality in both study groups

Mortality	Study group		Total
	Dexamethasone	Placebo	
Yes	13	42	55
No	227	198	425
Total	240	240	480

Chi value= 17.27
p-value=0.000 (Significant)

In our study, mortality occurred in 25 subjects in the dexamethasone group and in the placebo group it was 25 patients. Similarly, death was seen in patients over 35 years of age, 8 of them in the dexamethasone study group and 22 of them from placebo group. Statistically, there was a noteworthy variation in mortality and mortality between study groups and placebo groups in patients younger than 35 years. The P value was 0.002 and 0.005, respectively (Table 4).

Table 4: Comparison of mortality in both study groups stratified by age

Age group	Study group		Total
	Dexamethasone	Placebo	
≤35 years (P value 0.002)			
Yes	5	20	25
No	100	89	189
>35 years (p value 0.005)			
Yes	8	22	30
No	127	109	236

In this study, mortality in male patients occurred in 45 cases, of which 12 were from the group given dexamethasone and 33 were from the group as placebo. Similarly, mortality in female patients occurred in 10 cases, 1 from the dexamethasone study group and 9 from the group of placebo.

Table 5: Comparison of mortality in both study groups stratified by gender

Gender	Study group		Total
	Dexamethasone	Placebo	
Male (P value 0.002)			
Yes	12	33	45
No	144	131	275
Female (p value 0.010)			
Yes	1	9	10
No	83	67	150

There was a statistically important variation in mortality between male and female study groups (P value 0.002 and 0.1, respectively) (Table 5).

DISCUSSION:

This randomized control trial was performed at the DHQ Hospital Rawalpindi Medical Department to determine the efficacy of Placebo vs dexamethasone in reducing in hospital mortality in addition to usual antibiotics, as well as antibiotics used to treat patients for bacterial meningitis. In 1977, Centres for Disease Control and Prevention (CDC) conducted a nationwide scrutiny system to collect prospective data of epidemiology in previous reports supporting community and retrospective studies of bacterial meningitis cases[8-9]. The 1st study published has analysed 13,980 cases of BM reported to CDC from the USA 27 states from 1979 to 1982 Since 2012, three major trials have been conducted to assess the role of adjuvant dexamethasone treatment in adults Community-acquired bacterial meningitis[10]. In our study, there were no mortality in 55 patients, of which 42 were in the group given dexamethasone and 42 in the group of placeboes. There was a strong alteration in mortality between the study and placebo groups. P value = 0.000. Some of the studies supporting the findings of our study are discussed here[11]. In the Netherlands a national cohort observational study, if dexamethasone use adjunctively it reduced pneumococcal meningitis death from 31% to 22%. An RCT including 302 subjects with BM in European countries have shown that dexamethasone corticosteroid has a positive effect on adverse outcome and mortality[12]. In this EU analysis, placebo or dexamethasone was given before or after the 1st antibiotic dose. In pneumococcal meningitis patients, dexamethasone has much positive effect on mortality. This evidence was supported by a study that reported a significant difference in mortality with dexamethasone, i.e. 5.8%, 11.7% with placebo (p value> 0.05). Although the mortality rate was lower with dexamethasone, the difference was insignificant, so the authors could not make a reliable decision. However, in one study, the mortality rate with dexamethasone was significantly lower, i.e. 7%, and 15% with placebo (p = 0.04). The authors determined that early management with dexamethasone advances results in adults with acute BM. One study included 229 of 247 evaluable participants who survived the first trial period[13]. After a median follow-up of 13 years, mortality in the dexamethasone group was 22% compared with 33% in the placebo group (P = 0.029). A meta-analysis included the last four studies in adults and concluded that dexamethasone reduced mortality in high-income countries. In a

study by Qazi et al held in Pakistan, the 25% was the dexamethasone group death rate compared to 12% in the placebo group. The presentation at the hospital after four days of symptoms and with a change in conscious state was an independent predictor of death[14]. A study by Girgis et al. Showed that dexamethasone treatment was associated with decreased overall mortality compared to placebo (9.5% vs. 9.5%, 19.2%, P <0.01). 17. Patients with suspected bacterial meningitis did not conduct trials in Vietnam and Malawi. However, the Vietnam trial showed a reduction in mortality in confirmed bacterial meningitis patients. Currently, adjuvant dexamethasone is recommended for patients with suspected bacterial meningitis in high-income countries[15]. One study showed that 46 (53%) were treated with dexamethasone and 41 (47%) of 87 out of 99 patients receiving placebo did not show a significant difference between the patients in the group of dexamethasone and placebo.

CONCLUSION:

Our study results concluded that dexamethasone was more effective in reducing hospital mortality in bacterial meningitis patients than in the placebo group.

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