Role of Corticosteroids In Dengue Fever in Pakistan

Article *in* Pakistan Journal of Medical & Health Sciences · November 2021

DOI: 10.53350/pjmhs2115113014

6 authors, including:

Hina Aslam
Bahria University
17 PUBLICATIONS **41** CITATIONS
SEE PROFILE

Aamna Khokhar
Islamabad Medical & Dental College
47 PUBLICATIONS **57** CITATIONS
SEE PROFILE

Zunera Hakim
Rawalpindi Medical University, Rawalpindi, Pakistan
19 PUBLICATIONS **15** CITATIONS
SEE PROFILE

DOI: https://doi.org/10.53350/pjmhs2115113014

ORIGINAL ARTICLE

Role of Corticosteroids in Dengue Fever in Pakistan

HINA ASLAM[1], SYED FURQAN ALI SHAH[2], AAMNA KHOKHAR[3], AMOORA ARSLAAN[4], SARAH ZAHID[5], ZUNERA HAKIM[6]
[1]*Assistant Professor, Islamabad Medical and DentalCollege, Islamabad.*
[2]*Assistant Professor, Pak International Medical College, Peshawar*
[3]*Assistant Professor, Islamabad medical and dental college, Islamabad*
[4]*Senior lecturer , Islamabad medical and dental college, Islamabad*
[5]*Senior lecturer, Islamabad Medical and Dental College, Islamabad*
[6]*Assistant Professor, Rawalpindi Medical University, Rawalpindi*
Correspondence to Dr. Hina Aslam, Email: doc.hina.aslam1@gmail.com Cell: 0333-4386674

ABSTRACT

Aim: To compare and evaluate clinical efficacy of corticosteroids in thrombocytopenia in patients suffering from moderate to severe Dengue.
Methods: This randomized single blinded study was conducted at Furqan Clinic Gulbahar Peshawar from August 2021 to October 2021. 100 individuals of ages between 20 to 60 years irrespective of gender, with positive NS1 antigen test and no co-morbidities were included in study by convenient sampling technique. Patients with dengue and Covid-19 were excluded from the study. Randomization was done in four treatment groups. Consent was taken from all patients prior treatment with Cefixime, artemether/lumefantrine, IV Dexamethasone in adjunct to oral papaya leaf extracts. Duration of study was 3 months. Statistical analysis done using SPSS software version 24.
Results: Group C and D showed the significant increase in platelet count as compared to group A and B. Pronounced effect was observed in group D.
Conclusion: Intravenous Dexamethasone produced more beneficial effects in adjunct to oral carica papaya leaf extracts on thrombocytopenia with reduced risk of bleeding.
Keywords: Artemether, carica papaya leaf , Dexamethasone, Lumefantrine, platelet count

INTRODUCTION

Dengue is an acute febrile viral disease transmitted to humans via the bite of daytime active female mosquito genus *Aedes aegypt*[1]. As per WHO, approximately 400 million cases arise globally per year and among them, 40,000 die from the severe form of dengue[2]. In Pakistan, first outbreak was in 1994 but since 2010, we are facing its annual outbreaks thus WHO declared it as an endemic in our country[3]. Its incubation period is 4 to 7 days on an average[1]. Suspected patient presents with fever >2 days but < 10 days along with two symptoms out of headache, pain behind eye balls, body aches, rash or bleeding gums nose etc[4]. The disease is mostly asymptomatic but may become mild to moderately symptomatic in some and 1% may progress to complex forms like Dengue hemorrhagic fever (DHF) and possibly fatal Dengue shock syndrome (DSS)[5]. They includes coagulopathy, vascular damage, plasma leakage, hypovolemic shock and multi organ failure[6]. But an early identification and reasonable clinical management can reduce the fatality rate to <1%. There is no specific treatment for it and medical intervention remains supportive instead of curative[7]. Though Papaya leaves extract has been widely proved useful in alleviating thrombocytopenia[8]. The role of corticosteroids have remained partially conclusive around the world[7,9]. Due to inadequate evidences, WHO has also not yet approved its use in dengue[10]. But as corticosteroids are known to have a great anti-inflammatory property and have the ability to reduce the destruction of platelets[11]. So, its role in managing moderate to severe cases of dengue fever was taken into consideration in our study to further validate its vitality.

METHODS

The study was conducted at Furqan Clinic Gulbahar Peshawar from August 2021 to October 2021. Hundred individuals of ages between 20 to 60 years irrespective of the gender, with positive NS1 antigen test and no co-morbidities were included in study. Patients with dengue along with Covid-19 were excluded too from the study. Consent was taken from all patients**.** Randomization was done in four treatment groups. Patients in group A were treated **w**ith Oral Fluids, Oral Cefixime and Oral artemether/lumefantrine. Patients in group B received Intravenous (I/V) Fluids, Oral Cefixime, Oral antimalarials artemether/lumefantrine. Patients in group C received same treatments as the patients of group B with added oral Papaya extract. Patients in group D were treated with I/V Fluids, I/V Cefixime, Oral antimalarials, Oral Papaya extract and intravenous Dexamethasone. Tab Cefiget (cefixime), tab Gen M (artemether/ lumefantrine), injection Decadron were purchased from local hospital pharmacy of Pfizer company.

Frequency distribution & percentage for the variables is gender, treatment for dengue patients & Platelet's condition was calculated using SPSS version 24. Spearman's correlation between treatment and Platelet's condition was also found. Comparison of mean, median and standard deviation of platelet count in different treatment groups was also done

Received on 13-05-2021
Accepted on 23-10-2021

RESULTS

Table 1 showed the frequency distribution & percentage for the variables is gender, treatment for dengue patients & Platelet's condition. There are 42.9% patients whose platelets drops as they were getting oral treatment, 2.4% patients whose bleeding started as their platelets count are very low, 52.4% patients whose Platelets rise after getting proper treatment & 2.4% patients whose platelets count are still very low but has no bleeding.

Table 1: Frequencies & percentages

Parameter	Variables	Frequency	Percentage
Gender	Male	52	61.9
	Female	32	38.1
	Total	84	100
Treatment for Dengue patients	Group A	19	22.6
	Group B	21	25
	Group C	22	26. 2
	Group D	22	26. 2
	Total	84	100
Platelet's condition	Platelets drop	36	42.9
	Bleeding started	2	2.4
	Platelets rise	44	52.4
	No bleeding	2	2.4
	Total	84	100

Table 2 shows there is association between treatment with platelets condition as p-value is significant i.e., < 0.0001. Also,

Spearman's Correlation value with 0.809 represents that there is strong positive relation showing that when the oral treatment was given to dengue patients platelets were dropped & bleeding starts. But when there was increment in treatments like parenteral fluids along with oral antibacterial and antimalarial, thrombocytopenia was observed though there was no bleeding. Moreover, when Papaya extract & steroids added to treatment for dengue patients their platelets count starts rising & there was no bleeding case as well. The treatment group C who took Papaya extract along with previous treatment i.e., I/V fluids, oral antibacterial and antimalarial agents, p-value <0.000 (Table-3) shows significant difference for this treatment. Similarly, in treatment group D, where IV dexamethasone was started early alone with parenteral antibacterial and other treatment, the p-value <0.000 (Table-3) shows more significant difference for this treatment. Hence the treatments given to groups C and D increases overall platelets count condition.

Table: 2 Cross-tabulation & Association of Treatment with Platelets conditions

Treatment Groups	Platelets drop	Bleeding start	Platelets rise	No Bleeding	Total	P-value	Spearman Correlation
Group A	17	2	0	0	19	0.0001	0.809
Group B	19	0	0	2	21		
Group C	0	0	22	0	22		
Group D	0	0	22	0	22		
Total	36	2	44	2	84		

Table 3: Comparison of Mean, Median & Standard deviation of platelet count in different treatment groups

Treatment Groups	Mean	N	Std. Deviation	Median	P-value
Group A	70.68	19	17.033	77.00	0.260
Group B	59.86	21	17.687	66.00	0.260
Group C	142.59	22	22.585	145.00	0.000
Group D	213.95	22	49.036	229.50	0.000

DISCUSSION

A total of 100 patients diagnosed with dengue fever of moderate severity were treated with different group of drugs out of which 69.1% were male and 38.9 females. Probably, greater number of infected males might be due to prolong outdoor residing and negligence in prophylaxis[12]. However, non-significant results were found between gender in the present study. Group A was given oral fluids and medication which included Artemether/ Lumefantrine and oral Cefixime. Whereas, group B,C and D were administered with IV fluids in adjunct to oral anti-malarial , cephalosporin and papaya extracts with the exception of group D allocated with intravenous dexamethasone.

In the present study, there is strong positive relation statistically showing platelet drop and bleeding when oral treatment was given. This finding was in harmony to a study by Yunjia and colleagues[13] but contradictory to Qazi and colleagues[14]. On the other hand, the present study revealed statistically significant increase in the platelet count owing to intravenous fluid resuscitation in adjunct to oral Papaya leaf extracts and steroids with no bleeding disorder. This is in harmony to a study[14] which recommended intravascular volume deficits replaced by intravenous hydration with close monitoring of hematocrit and platelet count. However, is it contradictory to Nasir and colleagues who observed effectiveness of oral hydration in Dengue fever[15].

The treatment groups with oral as well as intravenous fluids but oral Artemether/ Lumefantrine and Cefixime showed non-significant difference (p=0.260) in the treatment of Dengue. However, the addition of oral papaya leaf extract to the previous regime showed beneficial effects in raising platelet levels with reduction in bleeding. Group C who took Papaya extract along with previous treatment , that is, I/V fluids, but oral Artemether/ Lumefantrine and Cefixime shows highly significant difference in increasing platelet count and no bleeding. Our study is coherent with the observations of Sathyapalan and colleagues who demonstrated the safety efficacy and immunomodulatory activity of Carica Papaya leaf extracts in Dengue[16]. Whereas, contradicts a study by Shoaib et al who showed non-significant difference in the doubling of platelet count and no additive effect[17].

Moreover, Group D who took oral Papaya extract & I/V steroid along with previous regime, that is, I/V fluids, I/V Cefixime & oral Artemether/ Lumefantrine showed highly significant difference (p-value <0.001) in improving overall platelets count condition along with reduced risk of bleeding. Our findings are supported by the study of Bendara and colleagues who emphasized on the role of corticosteroids in reducing complications with no serious adverse effects if administered intravenously in beneficial therapeutic doses[18]. However, the present study contradicts the observations by Rajapakse and colleagues who showed no effect of steroids in reducing IL-8 levels in Dengue[19].

CONCLUSION

Oral carica papaya leaf extract and intravenous dexamethasone has produced more beneficial effects in raising platelet count and reducing bleeding complication. Moreover, administration of steroids in treating dengue has not reported any adverse effect. Hematocrit shall be employed as additional parameter for prospective studies. Multicentric studies with large sample size may be conducted to authenticate the results of present study.

Conflict of interest: None to declare

REFERENCES

1. Kazaura M. Knowledge, attitude and practices about dengue fever among adults living in Pwani Region, Tanzania in 2019. Afr Health Sci. 2020;20(4):1601.
2. Bere AW, Mulati O, Kimotho J, Ng'ong'a F. Carica papaya leaf extract silver synthesized nanoparticles inhibit Dengue type 2 viral replication in vitro. Pharmaceuticals. 2021;14(8):718.
3. Irfan M, Aslam N, Masood A, Nadeem MA, Mohsin A. Liver and Gastrointestinal aspects of Dengue infected Patients, in Lahore, Pakistan.
4. Chen D, Zhang Y, Wu X, Wu J, Gong F, Qiao L, et al. A survey of clinical and laboratory characteristics of dengue fever epidemic from 2014 to 2018 in Guangzhou, China. Ann Palliat Med. 2020;9(1):70–81.
5. Ranawaka R, Jayamanne C, Dayasiri K, Samaranayake D, Sandakelum U, Hathagoda W, et al. Effect of Prior Symptomatic Dengue Infection on Dengue Haemorrhagic Fever (DHF) in Children. J Trop Med. 2021;2021.
6. Pang X, Zhang R, Cheng G. Progress towards understanding the pathogenesis of dengue hemorrhagic fever. Virol Sin. 2017;32(1):16–22.
7. Pawar V, Shinde DL. A comparative study of guduchi kwath and cap. platboost to increase the platelet count in dengue fever. Int J Sci Res. 2021;10(1).
8. Yap JY, Hii CL, Ong SP, Lim KH, Abas F, Pin KY. Quantification of Carpaine and antioxidant properties of extracts from Carica Papaya plant leaves and stalks. J Bioresour Bioprod. 2021;
9. Organization WH, Research SP for, Diseases T in T, Diseases WHOD of C of NT, Epidemic WHO, Alert P. Dengue: guidelines for diagnosis, treatment, prevention and control. World Health Organization; 2009.
10. Islam MD, Akter K, Chowdhury R Sen, Sarkar MAS, Rahman A. Persistent thrombocytopenia in Dengue Fever is rare but not uncommon-can be treated with steroid successfully. Bangladesh J Med. 2021;32(1):62–4.
11. Ingawale DK, Mandlik SK. New insights into the novel anti-

inflammatory mode of action of glucocorticoids. Immunopharmacol Immunotoxicol. 2020;42(2):59–73.
12. Ahmad N, Khan T, Jamal SM. A Comprehensive Study of Dengue Epidemics and Persistence of Anti-Dengue Virus Antibodies in District Swat, Pakistan. Intervirology. 2020;63(1–6):46–56.
13. Hu Y, Liu M, Qin H, Lin H, An X, Shi Z, et al. Artemether, artesunate, arteannuin B, echinatin, licochalcone B and andrographolide effectively inhibit SARS-CoV-2 and related viruses in vitro. Front Cell Infect Microbiol. 2021;526.
14. Arsalan Q, Qadar LT, Ochani RK, Tahir F, Majid Z. Collateral presentation of Malaria and Dengue viral Hemorrhagic fever: a rare case. Cureus. 2019;11(2).
15. Nasir NH, Mohamad M, Lum LCS, Ng CJ. Effectiveness of a fluid chart in outpatient management of suspected dengue fever: A pilot study. PLoS One. 2017;12(10):e0183544.
16. Sathyapalan DT, Padmanabhan A, Moni M, P-Prabhu B, Prasanna P, Balachandran S, et al. Efficacy & safety of Carica papaya leaf extract (CPLE) in severe thrombocytopenia (≤ 30,000/μl) in adult dengue–Results of a pilot study. PLoS One. 2020;15(2):e0228699.
17. Asghar MS, Hassan M, Rasheed U, Jawed R, Khan NA, Kazmi SJH, et al. A study on investigating the role of Papaya extracts in the management of acute thrombocytopenia in Dengue fever, is there any clinical significance? 2020;
18. Bandara SMR, Herath H. Effectiveness of corticosteroid in the treatment of dengue–a systemic review. Heliyon. 2018;4(9):e00816.
19. Rajapakse S, Rodrigo C, Maduranga S, Rajapakse AC. Corticosteroids in the treatment of dengue shock syndrome. Infect Drug Resist. 2014;7:137.