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SHORT COMMUNICATION

Clinical Efficacy of an Ayurvedic Formulation in the Management of Dengue: A Short Report

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ABSTRACT

Introduction: Dengue is potentially a fatal illness prevalent in the tropical regions of the world, and an outbreak of this lead to serious complications like dengue shock syndrome and dengue hemorrhagic syndrome. Development of a precise solution/ formulation for dengue is highly essential and is the need of the hour. In this endeavor, a polyherbal ayurvedic formulation was identified and used as an adjuvant to the existing treatment protocol by World Health Organization (WHO) (standard care) for dengue. The objective of this study was to observe the platelet trends and prevention of complications in dengue patients and also to evaluate the improvement in clinical signs and symptoms with minimum recovery days.

Materials and Methods: An observational retrospective cohort design was adopted. Thirty-five patients of either sex, of age between 16 and 60 years, were selected from Shri BMK Ayurveda Mahavidyalaya, JN Medical College and Dr. Prabhakar Kore Hospital and Medical Research Centre of KLE Higher Education and Research Centre, Belagavi. The case records belonging to dengue patients who were confirmed by positive NS-1 antigen or IgM test with thrombocytopenia, and classical features of dengue who were treated with standard care suggested by WHO along with Polyherbal Ayurvedic formulation decoction in the dose of 40 ml twice a day for ten days and were followed up further for atleast four days.

Results: Platelet count has increased in all patients. Significant progressive increase in platelet count was observed from 1st to 5th day which was statistically significant when value of 3rd day was compared to that of 5th day. Early improvement in clinical features of dengue was observed, and no case of complications was noticed.

Conclusion: The polyherbal Ayurvedic formulation decoction and WHO prescribed standard care is seen as a good adjuvant for dengue which showed a potential increase in platelet count and speedy recovery of patients.

Keywords: Ayurveda, Dengue, Thrombocytopenia.

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INTRODUCTION

Dengue is a mosquito-borne acute systemic viral infection caused by the dengue virus (DEN). The virus DEN is a positive single-stranded RNA virus consisting of four distinct serotypes, DEN-1 to DEN-4. The latest studies have found an additional distinct virus namely, DENV-5.[1,2] Dengue occurs in tropical countries, where over 3.6 billion people are at risk of dengue[3] with over 50 million infections occurring across 100 countries globally.[4] In India, large numbers of cases are reported in metropolitan cities. Rural India is also affected by a large extent. The fatality caused by dengue is very high amongst the children. Notably, India reported an annual average of 20,474 dengue cases and 132 deaths by the disease in 2006-2012. According to National Vector Borne Disease Control Programme (NVBDCP) the worst affected areas in India in 2014 (till November) were Maharashtra, Kerala, and Punjab with a range of 33320 cases and 86 deaths.[5] Dengue is endemic, fastest spreading disease which is of a serious concern worldwide at the present scenario. Dengue may become fatal due to plasma leakage, fluid accumulation, respiratory distress, severe bleeding, or organ impairment. Thrombocytopenia is a hallmark of acute dengue infection which normalizes with recovery, and it has always been one of the criteria used by WHO as a potential indicator of clinical severity.[6,7] As per WHO guidelines in 2009 the definition of severe dengue generally describes the rapid decline in platelet count.[8] Although, there is no specific treatment for dengue, In the absence of proper care, the case fatality rate can be high at 20% in patients with severe dengue.

The clinical picture of dengue may be compared to a type of *Sannipataj jwara*[8] – a variety of pyrexia mentioned

in Ayurveda, presenting with cardinal features viz. *jwara* (pyexia), *shira shula* (headache), *nirbhugne lochana* (retro-orbital pain), *asthi-sandhi shula* (arthralgia), *chhardi* (vomiting), *kotha/rakta mandalotapatti* (rashes). Hence, the drugs mentioned for the management of *sannipataj jwara* are planned to provide in dengue fever.

Thrombocytopenia is a constant manifestation of dengue fever, which often leads to life-threatening severe dengue manifested as dengue hemorrhagic fever (DHF) and the dengue shock syndrome (DSS). Both hemorrhagic diathesis and circulatory collapse are the fatal complications of the dengue infection.[9]

The ingredients of this formulation and traditional combination are frequently used by Ayurveda physicians in such conditions; hence the study was designed to document the efficacy of the Ayurvedic formulation in the management of dengue.

MATERIALS AND METHODS

An observational retrospective cohort design was adopted. Thirty-five patients of either sex, of age between 16 and 60 years, were selected from Shri BMK Ayurveda Mahavidyalaya, JN Medical College and Dr. Prabhakar Kore Hospital and Medical Research Centre of KLE Higher Education and Research Centre, Belagavi. As the study was done by data mining of old case records and identity or personal details of any patient were not revealed in the study. Hence, the ethical committee of our institute granted consent waiver. The case records belonging to dengue patients who were confirmed by positive NS-1 antigen or IgM test with thrombocytopenia, and classical features of dengue who were treated with standard care suggested by WHO[10] along with polyherbal Ayurvedic formulation decoction in the dose of 40 ml twice a day for ten days. Many patients have been successfully treated with the study drug during this period but only the patients who have shown 100% drug compliance with proper documentation of clinical criteria under study during treatment and were followed up further for at least four days, were considered for the study.

The objective of the study was to observe the changes in platelet count, improvement in clinical signs and symptoms and development of complications if any. Ethical clearance with consent waiver is taken from the Ethics Committee for Research on Human Subjects, KLE University Belagavi before the retrospective study.

Preparation of Ayurvedic Formulation for Oral Administration[11]

Ayurvedic formulation given to the patient was prepared by adding 40 grams of the powder to 640 ml of water (1 part of drug: 16 parts of water) and made into a decoction. This mixture was boiled on a low flame until the volume reduced to one eighth (80 ml) of total volume. This was filtered and collected in a sterile container. Eighty milliliters of the filtrate was given orally twice a day (40 ml at morning time and 40 ml at night time) after food.

RESULTS

Of the total 35 patients under observation different symptoms were found in all to be clinically categorized as fengue. *Jwara* (pyrexia) was found in 20 patients only, though clinically it should have been in all. The observation was hindered as few patients had taken antipyretic as a self-precaution. However, all were tested positive for NS-1 antigen or IgM.

It was observed that most of the clinical features subsided in the initial five days after intervention. Out of 20 patients, *jwara* (fever) subsided in 14 patients on the 2nd day itself and gradually fever subsided in three, two and one patient on 3rd, 4th and 6th day respectively. There were 14 patients exhibiting *Asthi–sandhi shula* (*arthralgia*) and in six, two, five and one patient, it subsided on 2nd day, 3rd day, 4th and 6th day respectively. Twenty-three patients showed symptoms of *Shirasula* (headache) and relief in symptoms were observed in twelve, four, six and one patient on the 2nd, 3rd, 4th and 6th day respectively. The symptoms of *angasthaliyata* (body ache) were observed in 20 patients and it subsided in five, four, three, six and one patients on 2nd to 6th and 14th day respectively. It was also observed that *Swasa kasa* (respiratory symptoms) was exhibited in nine patients, which subsided in three, three, one, one and one patients on 2nd, 3rd, 4th, 5th and 6th day respectively. Of the seven patients exhibiting *Raktamandalotpatti* (urticarial rashes), the symptoms subsided in one, three, one, one, and one patients on 2nd to 7th day respectively. *Nirbhugne lochne* (retro-orbital pain) was exhibited by 11 patients in total, which subsided in nine and two patients on 3rd and 4th day respectively. The overall result showed early improvement in clinical findings (Fig. 1).

In the present study, 2.8% patients were having platelet count less than 5000/microliter, 28% patients were having between 5000-20000/microliter, 34.2% patients were having between 20000 to 50000/microliter and

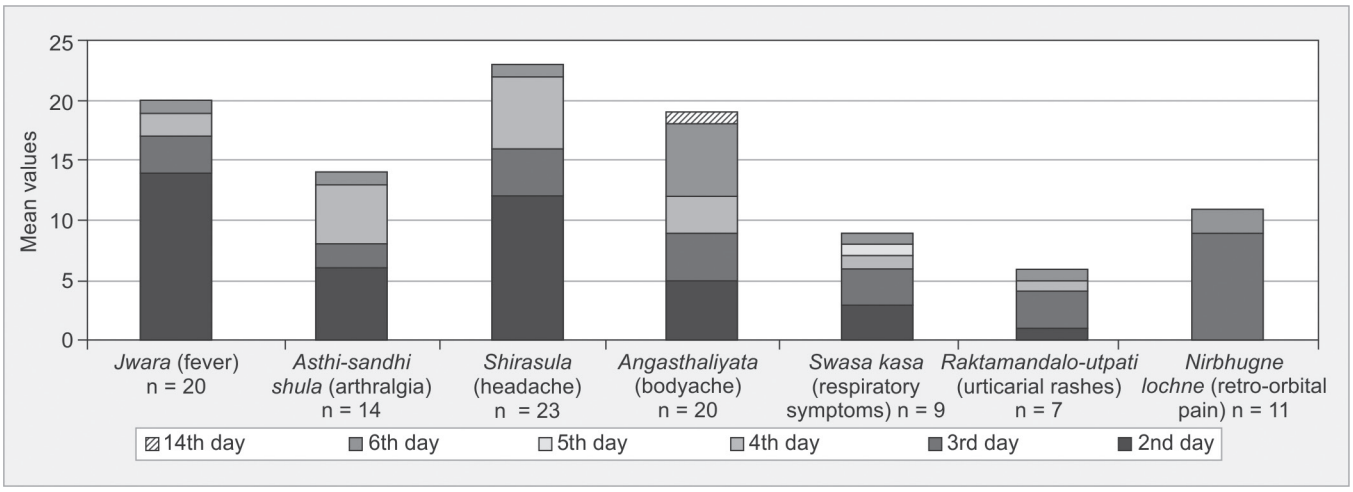

Fig. 1: Relief pattern of various clinical features observed day wise

rest 34% patients were having between 50000–1,50000/ microliter of blood.

In 27 patients there has been a substantial increase in blood platelet count. Average platelet count on the baseline of these 27 patients was 48.62 thousand per microliter which rose to 80.81 thousand per micro liter on the 3 rd day and further increased to 145.70 thousand per microliter on 5th day. From 1st to 3rd day the mean increase was 66.21% which increased by 80.30% from 3rd day to 5 th day (Fig. 2). There were also few cases whose response to medicine was not as anticipated up to 5th day, 8.5% of cases under observation showed sign of downfall in blood platelet count when observed on day 3 and day 5 respectively. Subsequently, the cases showed improvement from day 6 onwards. There were 14.2% cases which showed minimal change in platelet count up to 5th day; however, all the patients on subsequent days showed a positive increase in platelet count.

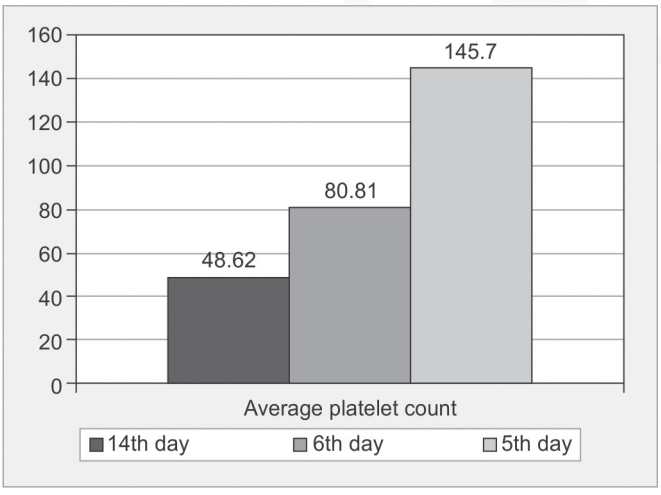

Fig.2: Increase in average platelet count during the treatment

On comparison of platelet count, on 1st to 5th day and 3rd to 5th day, the result was statistically significant $p < 0.05$ (Table 1). The significant result implies that the patients administered with Ayurveda formulation decoction along with standard care helped in increasing platelet count drastically without any adverse reaction.

Table 1: p-value for the comparison by one way ANOVA test

Days	*Results*	*p-value*
1st day and 3rd day	0.2633	$p > 0.05$
1st day and 5th day	0.0010	$p < 0.05$
3rd day and 5th day	0.0010	$p < 0.05$

DISCUSSION

The early improvement observed in clinical features might be due to a decoction of the Ayurveda formulation. The ingredients of the formulation are *Tikta drvaya*[12] (drugs bitter in taste), which has pharmacological activities as antipyretic, antiviral, analgesic and immune-modulatory action. Drugs also have a hepato-protective action that averted multi-organ failure.

Significant improvement was noted in platelet count, and this may be attributed to immuno-modulatory and anti-viral effects of drugs present. In dengue, a patient immuno-modulation plays an important role for the production and the destruction of platelets because, in the presence of virus-specific antibody, the virus binds to the platelets and causes the immune mediated destruction of the platelet. On treatment with the standard care and the Ayurvedic formulation, all the symptoms subsided within seven days. On overall observation of the study, no patients reported serious complications like dengue hemorrhagic syndrome (DHS), dengue shock syndrome (DSS), as the Ayurvedic formulation also contains herbs

which are effective in *raktapitta*[13] (bleeding disorder) which might have helped to check capillary plasma leakage by having hemostatic action.

CONCLUSION

The polyherbal Ayurvedic formulation is found to be a good adjuvant and induces a rapid increase in platelet count and speedy improvement in clinical features. No fatality was observed. The drug did not produce any adverse drug reaction (ADR) and medicine was well tolerated. However, few patients noticed difficulty in palatability of decoction. Taking leads on benefits of this intervention obtained from the clinical observations, CCRAS has developed a coded formulation for the clinical management of dengue through systematic drug development process viz. standardization, quality assurance, preclinical safety studies. The preclinical safety studies have revealed the safety of the formulation while a double-blind randomized control trial as add on therapy to standard conventional management of dengue is under progress.

CONTRIBUTORY ROLE

Professor Vaidya K.S. Dhiman and Dr Manoj Nesari conceptualized and designed the intervention. Dr N. Srikanth coordinated and supervised the study. Professor B.S. Prasad, Dr V.A. Kothiwale, Dr Rekha Patil, Sukumar Nandigoudar, and Dr S.L. Hoti were involved in retrospective cohort analysis and study. Dr Shruti Khanduri and Dr. B.S. Sharma were involved in the preparation of the formulating.

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