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RESEARCH ARTICLE

A COMBINATION OF *Nilavembu Kudineer* AND *Adathodai Manapagu* IN THE MANAGEMENT OF DENGUE FEVER

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ABSTRACT

In the present scenario Siddha system of medicine plays a vital role to combat against viral infections such as Dengue fever. It is an acute febrile illness caused by arthropod borne virus, the global prevalence of which has grown dramatically in recent decades. A large proportion of population who need hospitalization for this febrile ailment are mostly in paediatric age groups. Hence there is a need to explore effective Siddha formulations for its management. This pilot study is a descriptive clinical documentation of a set of Siddha formulations *Nilvembu Kudineer* (NVK) and *Adathodai Manapagu* (ADM) administered in twenty cases for a scheduled period of seven days. This documentation reveals that the scheduled intervention has a notable role in achieving satisfactory symptomatic relief and significant improvement in laboratory results. Further it is assured for safety in usage and no adverse effects were noted.

INTRODUCTION

Background

Dengue virus is a human pathogen that has re-emerged as an increasingly important public health threat. In recent days wide range of studies is being focussed on dengue viral biology, vector biology including exploration of interactions between virus and human and the replication of dengue virus. Recent researches are emerging a question of genetic susceptibility as some individual develop severe symptoms where others have a decreased risk of infection. The ancient Siddha system of medicine considers the body as a conglomeration of three humours known as *Vatham* (*Wind*), *Pitham* (*Fire*) and *Kabam* (*Water*). Equilibrium between the three humours is necessary to maintain perfect health. Any derangement in the synergic action of these humours transforms the body as a fertile ground to pop-up any infection. *Nilavembu kudineer and Adathodai manapagu* are classical Siddha medicines being practiced since ages. They have literature evidence to combat against this morbid infection based on its symptomatic similarities and therapeutic value.

Dengue and its Epidemiology

Dengue fever is an acute febrile illness caused by several arthropod-borne viruses characterised by biphasic fever, myalgia, rash, leukopenia and lymphadenopathy. Four well defined types of dengue viruses have been identified called DENV-1, DENV-2, DENV-3 and DENV-4 which belong to the family flaviviridae. The virus strain risk is greatest for DENV-2 followed by DENV-3, DENV-4 and DENV-1. Nearly 2.5 billion people are at risk from dengue. WHO currently estimates there may be 50 million cases of dengue infection worldwide every year. An estimated 500,000 cases of DHF require hospitalization of which a very large proportion is children.

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At least 2.5% of cases die although the case fatality could be twice as high (Nelson, Kleigman *et al*., 2008; OP Ghai *et al*., 2009).

Pathophysiology

Primary infection with a particular serotype of dengue results in the production of cross reactive antibodies. When there is a re-infection of same serotype the residual antibodies produced during the first infection are able to neutralise the second viral infection however when no neutralizing antibodies are present (i.e.) infection due to another serotype of dengue virus the resulting infection and disease are severe. The antibodies bind to virions instead of neutralising them they increase the uptake by cells. The presentation of antibody binded virion to T cells causes production of cytokines which results in endothelial cell dysfunction causing capillary permeability, micro vascular leakage, hemo-concentration, circulatory insufficiency.

Viral Transmission

Dengue viruses are transmitted to humans through the bites of infective female Aedes egyptii mosquitoes. Mosquitoes generally acquire the virus while feeding on the blood of infected person. After virus incubation of 8 – 10 days, an infected mosquito is capable during probing and blood of infected person. After virus incubation of 8 – 10 days, an infected mosquito is capable during probing and blood feeding of transmitting the virus to susceptible individuals for the rest of its life. The virus circulates in the blood of infected humans for 2 – 7 days as approximately the same time as they have fever (Nelson, Kleigman *et al*., 2008; OP Ghai *et al*., 2009).

Dengue - A Siddha Review

Siddha system classifies fever into 64 types based on the cause, the affected biological humour, altered physical constituents and presenting clinical features. Hence each type of *suram* as mentioned in

Siddha literatures can be considered as single disease rather than a symptom itself. Therefore dengue fever can be correlated to *Pitha suram* which is mentioned in a text named *Agasthiyar sura nool 300* and another one text *Sura vagadamI* (Kuppusamy mudaliyar 2007). The symptoms mentioned in literature can be correlated with Dengue and Dengue haemorrhagic fever which is shown in Table 1.

Table 1. Comparision of *Pitha suram* with dengue

1	*Udal sigappu niram adaithal* (Red spots on the body)	Petechial haemorrhage
2	*Siruneer sigappu niram adaithal* (Red colour urine)	Hematuria
3	*Malam sigappu niram adaithal* (Blood in faeces)	Melaena
4	*Manakalakam, mayakam, Padukaiyel thangamai* (Anxiety, loss of consciousness and restlessness)	Dengue encephalitis symptoms of Restlessness and altered sensorium
5	*Okaalam* (Sensation of vomiting)	Nausea
6	*Neervetkai* (Thirst)	Dehydration
7	*Vairu kazlithal* (Loose stools)	Dysentry
8	*Edaividamal athiga suram kaithal* (High grade fever)	Hyperpyrexia

Table 2. Inpatients record

S.NO	IP.NO	AGE	SEX	SIGNS AND SYMPTOMS	ADMISSION		DISCHARGE	
					PLATELET	PCV (%)	PLATELET	PCV (%)
1	7821	11 yrs	FC	Afebrile, cough and cold.	41,000	45.5	1.3 lakhs	39.5
2	7113	4 ½ yrs	MC	Intermittent fever, Vomiting.	68,000	34.7	1.27 lakhs	34.1
3	7129	12 yrs	FC	Fever for 3 days with vomiting.	41,000	36.6	1 lakh	38.4
4	7884	3 yrs	FC	Fever, Melena one episode.	97,000	36.2	1.41 lakhs	37.4
5	7838	4 yrs	FC	Afebrile, abdominal pain.	74,000	34.0	1.33 lakhs	32.8
6	8075	10 yrs	FC	Fever, Vomiting, Loose stools	59,000	43.0	1.44 lakhs	35.9
7	7128	4 yrs	MC	Fever, Abdominal Pain.	20,000	43.4	1.63 lakhs	35.8
8	7834	5 yrs	MC	Fever, loose stools.	58,000	46.2	73,000	32.1
9	7837	7 yrs	FC	Afebrile, vomiting	13,000	41.5	1.41 lakhs	34.2
10	7542	5yrs	FC	Intermittent fever, vomiting, reduced urine output.	43,000	37.9	1.17 lakhs	38
11	8526	6yrs	MC	Fever, abdominal pain.	90,000	38.3	1.02 lakhs	35.7
12	8463	6yrs	FC	Afebrile, vomiting, loose stools.	32,000	50.5	90,000	31.6
13	8890	10yrs	FC	Fever, loose stools.	39,000	30.4	88,000	29.3
14	8141	3yrs	FC	Abdominal pain, vomiting.	35,000	35.8	1.33 lakhs	34.8
15	6574	6yrs	MC	Fever, headache, vomiting.	28,000	41.3	1.99 lakhs	36
16	8146	12yrs	FC	Fever, loose stools.	43,000	47.3	2.43 lakhs	39.2
17	8436	12yrs	FC	Afebrile, abdominal pain.	24,000	47.3	1.3 lakhs	37.2
18	7794	10yrs	FC	Vomiting ,abdominal pain, loose stools	37,000	43.5	1.49 lakhs	41.9
19	7685	6yrs	MC	High grade fever, vomiting.	48,000	48.2	1.06 lakhs	36.7
20	7627	7yrs	MC	Intermittent fever, vomiting.	18,000	48.1	1.64 lakhs	33.4

Noi Guna Iyal (Pathology) of *Pitha suram*

Siddha physiology deals with the subtle mechanism of interactions between the three humours *Vatham, Pitham and Kabam* in a normal body, *Anila pitham* which resides between stomach and intestine helps digestion and in drying up moist substances. This regulates the other types of *Pitham* and counter balances *Vatham* and *Kabam.* Due to both external (environmental) and internal (diet and life style) etiological factors *Manthagni* (decrease in *Pitham*) which is a pathologic state is produced resulting in indigestion, decreased metabolic function and deposition of *Amam (Kilathagam)* a type of *Kabam.* This paves way for the entry of micro organisms which actively settles at gastro intestinal tract and may enter into circulation or tissues due to the deposition. According to literature, to compensate the vitiated *Kabam* there is an exploding increase in *Pitham* followed by *Vatham.* Since *Pitham* resides in *Senneer* (blood) one of the eight constituents which frame the body, the vitiated *Pitham* dries up the *Saaram* (plasma) due to its characteristic unique nature of fire. This can be correlated with fever, increased Packed Cell Volume (PCV), decreased platelets and bleeding tendencies in dengue fever. Alteration in *Vatham* results in pain, vomiting, nausea and loose stools which are relatively correlated with myalgia, arthalgia, nausea, vomiting and diarrhoea which are the clinical manifestations of dengue fever (Shanmugavelu 2003).

Selection of Drugs

The combination of *Nilavembu Kudineer* and *Adathodai Manapagu* will work in synergy in equalising vitiated *Pitham. Nilavembu Kudineer* consists of nine ingredients of medicinal plants origin which are *Andrographis paniculata (Nilavempu), Vetiveria zizanioides (Vettiver), Cymbopogan jwarancusa (Vilamichu ver), Santalum album (Chandanam), Trichosanthes cucumerina (Peipudal), Cyrerus rotundus (Koraikilangu), Zingiber officinale (Cukku), Piper nigrum (Milaku), Mollugo cervicana (Parppadakam).* It is prepared by taking all the ingredients in equal proportion and made in to coarse particles added with eight times of water which is boiled and reduced to one fourth of the initial volume and filtered for use. It is given in dosage of 20ml bid for 3-5 years age group and 30ml bid for 5-12 years vice versa[7]. *Adathodai Manapagu* consists of *Adhatoda vasica (Adathodai)* and palm jaggery (*panai vellam*). It is prepared by cleansing the leaves, cutting them to fine bits and boiling with eight times quantity of water and reduced to one fourth of the initial volume to which purified palm jaggery is added and boiled until the watery content gets evaporated and prepared into a manner of finished product (*Kambi patham*)is obtained. It is given in a dosage of 10ml bid for 3-5 years age group and 20ml bid for 5-12 years vice versa [7].

MATERIALS AND METHODS

This observational documentation is prepared by noting down the variables of the case series admitted in the In Patient Department. The dengue cases admitted in the Paediatric Department were given the scheduled drugs as stated in the dosage levels with a period of seven days. The symptoms were recorded as per the predesigned protocol. The investigations of all routine tests were advised. To assessing the normal state of the cases the PCV and Platelet count are taken into account (Table 2). The variables and the before and after treatment investigations were statistically analysed by using SPSS (version 17) software. Since there is no arm to compare, the data obtained were analysed only for making hypothesis which can be extended for further study in future.

Inclusion and Exclusion Criteria

The cases that were included in this study consisted of Age group of 3 to 12 years with clinical symptoms of dengue and thrombocytopenia

with increased PCV. The patients who went through IV infusion of platelets were excluded.

Selection of Cases and Observation of Datas

Among the 40 patients who were administered with *Nilavembu Kudineer and Adathodai Manapagu*, 20 patients were dropped due to discontinuity of the treatment. The remaining twenty cases were taken and administered with the same medicine and the results were observed periodically for seven days. The laboratory parameters PCV & platelets count for each case is documented.

Table 3. Summary Statistics

Variable	Minimum	Maximum	Mean	Standard deviation
Age	3	12	7.175	3.1258
PCV beforeTreatment	30.4	50.5	41.485	5.7041
PCV after Treatment	29.3	41.9	35.700	3.0265
Platelets Before Treatment	13000	97000	45400	22926
Platelets afterTreatment	73000	243000	133650	39321

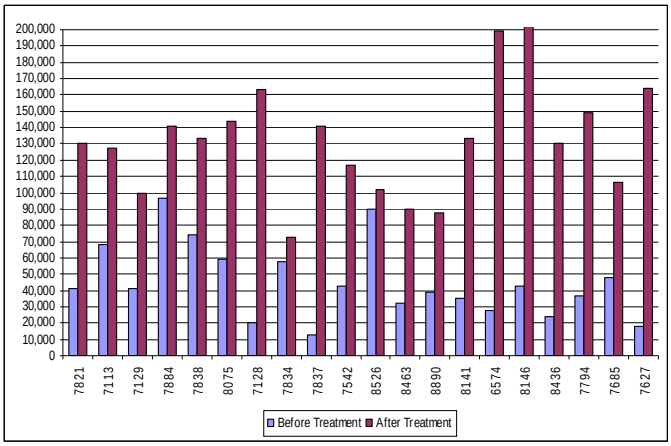

Fig.4. Shows platelet count before and after treatment

Table 4. Paired t-Test: Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	P1 - P2	.88250	.50006	.11182	1.11654	.64846	7.892	19	.000
Pair 2	PCV 1 - PCV 2	5.7850	5.8320	1.3041	3.0556	8.5144	4.436	19	.000

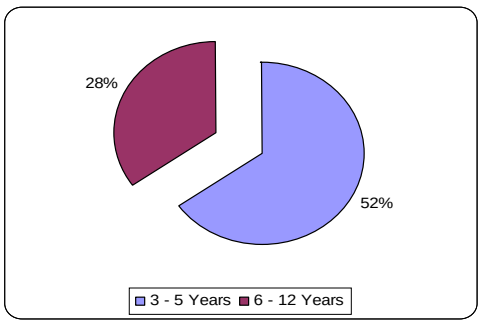

Fig.1 shows the distribution of age

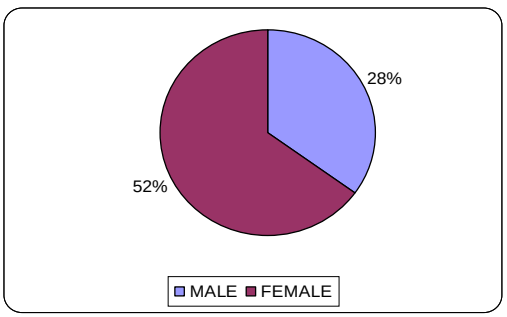

Fig.2 shows the distribution of sex

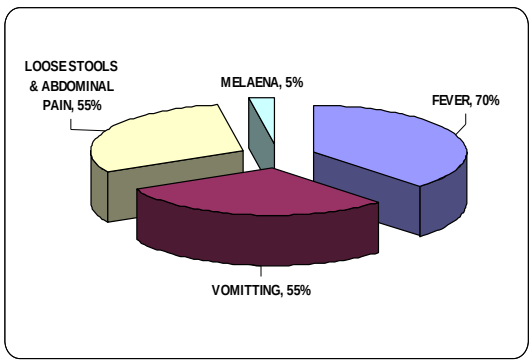

Fig.3 shows clinical symptoms

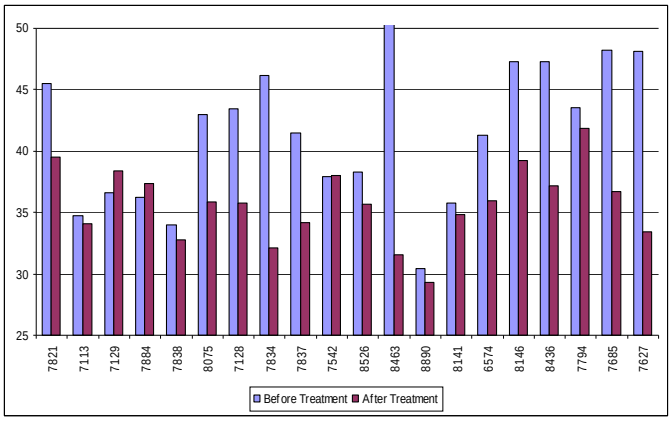

Fig.5. shows packed cell volume (%) before and after treatment

The changes in the symptoms and the clinical outcome were documented. Statistical analysis denotes that the female were more in number according to gender distribution. The Mean age was 7.175 with the S.D 3.1258. There is a mean increase in platelet count after the treatment. Packed cell volume showed a mean decrease after the treatment. Paired t-test resulted that there is a statistically significant difference in PCV and platelet counts after the treatment. (Table 3 and 4).

DISCUSSION

Among the twenty cases who were observed out of them thirteen had fever and vomiting at the admission, ten cases were reported to have abdominal pain, six patients had loose stools and one patient had melena. All patients were weak and lethargic. Dehydration was managed with oral fluids such as porridge (*Kanjee*), orange juices, coconut water and water in all the patients. On observation of the results there was a drastic increase in platelet count each day and steady decrease in PCV. Only 2 cases showed an increase in PCV. The cases were discharged on improvement in clinical symptoms and with platelet count above one lakh.

Conclusion

The case study of twenty patients indicates that the combination of *Nilavembu Kudineer* and *Adathodai Manapagu* has showed good

response in thrombocytopenia in dengue fever. This combination is safe in paediatric age group without any adverse effect and efficient when taken with conventional symptomatic institutional treatment, for the prevention of any further complications. Hence the administration of the selected medicine reduces the hospitalization time thus saving the cost of human productivity. This is only a preliminary study, further studies regarding the antiviral action clinical trial of this combination is required.

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