

ASSESSMENT OF EFFECT OF KUTAJA (*HOLARRHENA ANTIDYSENTERICA*, WALL) IN DIFFERENT *DOSHICA ATISARA* IN INFANTS: A CLINICAL STUDY

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Abstract: **Introduction:** The incidence and risk of diarrheal diseases is highest among the children particularly in infants younger than one year. Although, *Atisara* (~diarrhea) and number of drugs for its treatment have been described in *Ayurveda*, but it is difficult to select one drug which is more efficacious in particular *Dosha* specific type of diarrhea. **Objectives:** This observational study was designed to compare the efficacy of syrup *Kutaja* (*Holarrhena antidysenterica*, Wall) in the treatment of various *Doshajanya atisara* in infants. **Materials and Methods:** Thirty infants, suffering from acute diarrhea were included in the study after obtaining written informed consent from parents. Two infants were lost to follow up. So that, data on 28 infants was analyzed for the *Doshika atisara*. The trial drug *Kutaja* was given to infants in dose of 15 mg/kg/dose, 8 hourly for two days, and were evaluated at 24 and 48 hours follow up. The primary outcome variable includes frequency and consistency of stools while the secondary outcome includes abdominal distension, pain in abdomen, appetite, fever, perianal rashes and vomiting. **Observations and Result:** *Kutaja* significantly reduced the frequency, foul smell and mucus in stool. The secondary outcome in infants was seen similar in all types of *Atisara* except better improvement in appetite of infants suffering with *Kaphaja* as well as *Pittaja* type of *Atisara*, and perianal rashes in *Pittaja atisara* cases. No effect was seen in *Sannipataja atisara*. **Conclusion:** The *Ayurvedic* pediatrician should use *Kutaja* preparation in children suffering with diarrhea, more rationally, caused by *Kaphaja* and *Pittaja atisara*.

Keywords : *Doshika atisara*, *Kutaja*, *Holarrhena antidysenterica* Diarrhea, Infantile diarrhea

INTRODUCTION

Diarrheal disorder is the second most common cause of child deaths worldwide, accounting for a large proportion (9%) of childhood deaths, with an estimated 0.71 million deaths per year globally [14]. Both, the incidence and the risk of mortality from diarrheal diseases are greatest among children younger than 1 year of age [19]. Diarrhea causes undernutrition, further worsens milder forms of malnutrition [23], leading to diminished growth and impaired cognitive development in children in resource limited countries [36].

In *Ayurveda*, *Atisara* (~diarrhea) has been categorized into six types [4,25,30] i.e. *Vataja*, *Pittaja*, *Kaphaja*, *Sannipataja*, *Bhayaja* and *Shokaja* [4,25,30] (*Acamaja*) [25] according to the involvement of *Doshas*.

However, *Atisara* has also been described as one of the major symptoms of certain specific disorders viz. *Ksheeralasaka* [37], *Vyadhija Phakka roga*, *Graha roga* [28,31,32,39] etc. and in infants caused by *Pittajanya Stanya Dushti* (Breast milk vitiated by *Pitta Dosha*) [3,37]. However, a number of drugs / formulations have been described in *Ayurvedic* texts for the treatment of diarrhea, but it is very difficult to decide which one drug or recipe is more effective on particular *Dosha* specific diarrhea.

The ingredient of trial drug, bark of *Kutaja* (*H. antidysenterica*, Wall), has *Kapha-Pitta-Rakta Samgrahika* and *Upashoshana* property [1]. It is bitter and astringent in taste, have *Laghu* (~lightness) and *Ruksha* (dryness) property; subsides diarrhea, *Ama*, aggravated *Pitta*, *Rakta* and *Kapha* [7]. The crude aqueous

and alcoholic extracts of stem bark of *H. antidysenterica* exhibits also anti-bacterial activity against the known enteric pathogens [6,29].

Therefore, in view of above facts and to endorse the effect of *Kutaja* bark, the present study was carried out to assess the effect of syrup *Kutaja*, in different types of *Doshaja atisara* in infants (infantile diarrhea).

MATERIAL AND METHODS

Selection of Patients

Total thirty infants, attending OPD/IPD of KBBR of SSH, BHU, Varanasi, having symptoms of *Atisara* (diarrhea) were included in the study, irrespective of socioeconomic status and religion. As two patients were lost to follow up, 28 infants were analysed. Written informed consent was obtained from parents and following inclusion and exclusion criteria were considered.

(A) Inclusion Criteria

Patients of age up to one year, who were suffering from acute *Doshaja atisara* and having mild to moderate dehydration were included in the study.

(B) Exclusion Criteria

Patients who were suffering from severe dehydration/persistent vomiting, shock, high grade fever, septicemia, meningitis, any associated organic disease or bleeding disorder or signs of any severe illness were excluded from the study.

Ethical Clearance

The Ethical Committee Clearance number (ECC No.) is 2014-15/EC/1338.

INVESTIGATIONS

Hemogram and stool examination (routine and microscopy as well as culture and sensitivity for enteropathogen) of the selected infants were carried out at the time of their registration. Viral culture on stool was not considered in this study.

The signs and symptoms of *Doshika atisara* (diarrhea) described in various *Ayurvedic* texts [2,16,26,34] was used for the purpose of diagnosis, and to assess the response of the drug *Kutaja*.

The primary outcome variables were frequency and consistency of stools, while the secondary outcomes includes abdominal distension, pain in abdomen, appetite, fever,

perianal rashes and vomiting. The score for each sign and symptom ranges from 0 to 4. The mean of the score of each feature was done at registration and on subsequent follow ups.

The change in the mean score was used for the assessment of effect of the trial drug.

Kutaja

The drug syrup *Kutaja* (150 mg/5ml) was prepared from the *Kwatha* (decoction) of stem bark of *Kutaja* (*H. antidysenterica*, Wall) after identification of the crude drug in *Dravyaguna* Department, BHU. The decoction of *Kutaja* was prepared in accordance to *Kwatha kalpana* [22]. The trial drug *Kutaja* was given as 15 mg/kg/dose, thrice in a day along with WHO recommended ORS to avoid dehydration. Drug dose was determined according to *Yogarajnakar* [38] by considering the yield of the *Kutaja*. Dose of *Churna* (powder) for one year old infant is 12 *Ratti* i.e.1500 mg (1 *Ratti* ~125 mg). The average weight of one-year infant is 10 kg, and then dose for one-year-old infant is 1500 mg or 150 mg/kg/day. In preparation of syrup, dried water extract was used. A prepared dried water extract of said drugs yielded 10 % of total raw drugs taken as *Churna* (powder). The dose of *Churna* for one-year-old infant is 1500 mg, while on the basis of 10 % yield, it is 150 mg. Then per kg dose or dried water extract will be $150/10 = 15\text{mg}$, thus dose of syrup *Kutaja* was taken 15mg/kg/dose and given thrice in a day.

Diet: No diet restriction was done during the study. The patient who developed fever was advised for tepid water sponging.

Follow up

Follow up visits were done at 24 hours and 48 hours. If infant has not shown response in accordance to the study criteria then such case was shifted on contemporary antidiarrheal medicine as per the clinical symptoms and not included further in the clinical study and considered as non-responder to the drug.

Assessment of response of the the drug was done by applying scoring system as tabulated in Table 1 and 2.

OBSERVATIONS AND RESULTS

The mean age and mean weight of diarrheal infants were 5 months and 6.19 kg respectively. 28.57% of total infants were found undernourished with male predominance (64.28%).

In this observational study, out of 28 cases of *Atisara*, maximum cases (53.60%) belonged to *Pittaja atisara* while minimum cases (10.70%) were of *Vataja atisara* (Table-3).

Stool of 64.2% infants was found sterile on stool culture, while 8 cases (28.50%) have growth of *E.coli*. Incidence of *Entamoeba histolytica* and *Ascaris lumbricoides* was observed in 3.57% cases (Table-4).

In *Vataja atisara*, higher mean score (>2.00) was observed in frequency of stool, color, consistency, abdominal distension and pain in abdomen at registration. After administration of *Kutaja* syrup in recommended doses, these signs and symptoms were reduced on subsequent follow ups. The maximum reduction is seen in frequency of stool (1.75) followed by color (1.33) & consistency of stool (0.50).

In *Pittaja atisara*, higher mean score (>2.50) was observed in frequency of stool, color, smell, consistency, and perianal rashes at registration. When syrup *Kutaja* was administered, these signs and symptoms were reduced on subsequent follow ups. The maximum reduction is seen in frequency of stool (2.40) followed by color (1.73) and consistency (1.74) of stool (Table-5).

In *Kaphaja atisara*, higher mean score (>2.50) was observed in frequency of stool, color, mucus, smell, consistency, and appetite at registration. When syrup *Kutaja* was administered, the maximum reduction is seen in frequency of stool and appetite (2.00) followed by color, mucus and consistency (Table-5).

In *Sannipataja atisara*, higher mean score (>2.50) was observed in frequency of stool, color, mucus, smell, consistency, pain in abdomen, appetite and perianal rashes at registration. However, when syrup *Kutaja* was administered, change in mean score of frequency, consistency & mucus of stool etc. was observed less than one (Table-5)

DISCUSSION

28 infants of both sex, who had developed the sign and symptoms of different types of *Doshika atisara*, were treated by syrup *Kutaja* irrespective to type of *Atisara* in spite of diagnosis as *Vataja*, *Pittaja*, *Kaphaja* and *Tridoshaja atisara*.

Kutaja (*H. antidysenterica*-Wall) is known for its antidiarrheal and anti-dysenteric activity[33], due to having pharmacodynamic properties viz. *Kapha-Pittahara*, *Deepana*, *Amahara*[7], *Samgrahi* [1,7] as well as antiamebic [13]and antihelminthic [9] properties.

The present preliminary observational study suggests that *Kutaja* has better effect on stool frequency, consistency, foul smelling, color, mucus, and pain in abdomen as well as reduced appetite in infants who were suffering with *Kaphaja atisara* followed by *Pittaja atisara*.

This effect of *Kutaja* syrup on stool frequency and consistency may be attributed by astringent and *Samgrahi* properties respectively. Astringent property of *H. antidysenterica* is attributed to the presence of alkaloids as connesine [8] and tannin [21] which may produce antisecretory activity by precipitating superficial proteins, forms a protective layer over the mucous membrane.

Appetite and vomiting had been improved in almost all the cases, but better improvement was seen in *Kaphaja atisara*. *Agnimandya* (reduced digestive power) and product of improper digestion 'Ama' has direct role in pathogenesis of *Atisara*. The *Deepana*, *Katu-Kashaya rasa*, *Amahara*, *Ruksha* [7] and *Kapha-Pittahara* properties of *Kutaja* [1,7] are responsible for improvement in appetite along with normalising stool colour, foul smell, mucus etc. Elimination of mucus and subsidence of abdominal pain may also be ascribed to anti-inflammatory and analgesic properties of *Kutaja* (*H. antidysenterica*) [10,24].

E. coli is an important cause of acute diarrhea in children less than 1 year [5,15,18,20]. In the present study, 53.70% cases of infantile diarrhea were found sterile while 46.30% cases were infective on stool culture. Among the infective cases (n=22), *E. coli* was the most common (75.00%)

enteropathogen. This finding is in conformity with earlier studies.

Higher incidence of *E. coli* is seen also in *Pittaja atisara* followed by *Kaphaja* and *Sannipataja atisara* (table no.2). The incidence of *E. coli* in different types of *Doshika atisara* may be attributed to different strains.

Anti-adherence effect against the pathogenesis of EPEC in host epithelial cells [12], anti-bacterial activity against the known enteric pathogens [18,19], activation of histamine receptors and relaxation of gastrointestinal tract by Ca^{++} channel blockade provides the basic ground for its usefulness in gut motility problems like colic pain and diarrhea [11].

CONCLUSION

Therefore, it may be concluded that *Kutaja* (*Holarrhena antidysenterica*, Wall) has a significant role in reducing signs and symptoms of *Pittaja atisara*, and also in infants suffering with *Kaphaja atisara* up to some extent. So, the *Kutaja* preparation can be used more rationally in children suffering with *Pittaja* and *Kaphaja* types of *atisara*. Further, to affirm these findings a longitudinal study on large sample size is required.

Limitation of the study: The results obtained from this study cannot be generalised but provides a lead for further planned randomised controlled trial on adequate sample size.

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Tables: 1-5 see next page

Table-1: Scoring Criteria for Stool Characteristics [17]

Stool characteristics	Score				
	0	1	2	3	4
Frequency	-	5-10/d, having normal color, consistency, smell	<5/d; having abnormal color, consistency or smell	6-10/d; having abnormal color, consistency or smell	>10/d; having abnormal color, consistency or smell
Color	-	Yellowish (normal)	Relatively reduced Yellowish, Whitish, Reddish, Greenish, and blackish	Yellowish White Red Green "Black	-
Mucus	Absent	Not visible	Occasionally	Frequent	-
Foul smell	-	Normal	Mild foul smell	Excessive foul smell	-
Consistency	-	Soft and Formed	Semisolid	Watery	-
Frothy	Absent	Not visible	Present	-	-

Table-2: Scoring Criteria for the Sign and Symptoms [17]

Sign and symptom	0	1	2	3	4
Cough & cold	Absent	Subside	Present	-	-
Fever	A febrile (Absent)	Subside	Mild	Mod	High
Distension of Abdomen	Absent	Subside	Mild [Occasional]	Moderate [most of the time associated with the stool passage]	Severe [Always associated with passage of stool]
Pain in Abdomen	Absent	Subside	Mild [Occasional cry before or during defecation]	Moderate [most of the time baby has cry before or during defecation]	Severe [excessive cry before, during or between two defecation]
Appetite	Normal	Subside	Reduced	Significantly reduced	-
Vomiting	Absent	Subside	1-2/d	3-4/d	>5/d
Perianal rashes/proctitis	Absent	Subside	Minimal rashes	Rashes over perianal area	Rashes over perianal area & proctitis

Table-3: Incidence of different type of *Atisara* as per sex and nutritional status of infants

Atisara type (n=28)	Sex		Nutritional status	
	Male n(%)	Female n(%)	Under nutrition n(%)	Healthy n(%)
<i>Vataja</i> (n=3)	1 (33.3)	2(66.7)	2 (66.7)	1 (33.3)
<i>Pittaja</i> (n=15)	10 (66.7)	5(33.3)	5 (33.3)	10 (66.7)
<i>Kaphaja</i> (n=6)	5 (83.3)	1(16.7)	1(16.7)	5 (83.3)
<i>Sannipataja</i> (n=4)	2 (50.0)	2(50.0)	0(0.0)	4 (100.0)

Table-4: Incidence of type of enteropathogens on stool examination (R/M & culture) in different type of *Doshika atisara*-

Stool R/M & Culture (n=28)		<i>Vataja</i> <i>Atisara</i> n(%)	<i>Pittaja</i> <i>Atisara</i> n(%)	<i>Kaphaja</i> <i>Atisara</i> n(%)	<i>Sannipataja</i> <i>Atisara</i> n(%)	Total <i>Atisara</i> n(%)
Culture	Sterile	2 (7.1)	12 (42.8)	4 (14.3)	0 (0.0)	18 (64.2)
	<i>E. coli</i>	1 (3.6)	3 (10.7)	2 (7.1)	2 (7.1)	8 (28.5)
R/M	<i>Entamoeba histolytica</i>	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)	1 (3.6)
	<i>Ascaris lumbricoides</i>	0 (0.0)	0(0.0)	0 (0.0)	1 (3.6)	1 (3.6)

Table-5: Effect of syrup *Kutaja* on different signs/symptoms developed in infants suffering from *Vataja*, *Pittaja*, *Kaphaja* and *Sannipataja Atisara* at registration and on subsequent follow ups

Sr. No	Sign and Symptoms	<i>Vataja</i>			<i>Pittaja</i>			<i>Kaphaja</i>			<i>Sannipataja</i>		
		At Reg. (R)	F2	R-F2	At Reg. (R)	F2	R-F2	At Reg. (R)	F2	R-F2	At Reg. (R)	F2	R-F2
1.	Frequency	3.75	2.00	1.75	3.53	1.13	2.40	3.00	1.00	2.00	3.25	2.50	0.75
2.	Colour	2.66	1.33	1.33	2.73	1.00	1.73	2.66	1.00	1.66	2.50	2.00	0.50
3.	Mucus	0.75	0.25	0.50	1.26	0.33	0.93	2.83	1.00	1.83	2.75	2.00	0.75
4.	Foul smell	1.00	1.00	0.00	2.53	1.06	1.47	2.50	1.00	1.5	2.50	2.00	0.50
5.	Consistency	2.75	2.00	0.75	2.80	1.06	1.74	2.50	1.16	1.34	3.00	2.25	0.75
6.	Froth	2.00	1.66	0.34	0.66	0.26	0.40	0.33	0.16	0.17	1.50	1.50	0.00
7.	Abdominal distension	2.60	2.00	0.60	0.80	0.20	0.60	0.66	0.33	0.33	2.00	1.50	0.50
8.	Pain in abdomen	3.33	2.66	0.67	1.00	0.21	0.79	0.83	0.33	0.50	2.75	2.25	0.50
9.	Cough	0.60	0.60	0.00	0.53	0.53	0.00	1.33	1.00	0.33	2.00	1.50	0.50
10.	Fever	0.00	0.00	0.00	1.00	0.13	0.87	0.33	0.00	0.33	1.50	1.00	0.50
11.	Appetite	1.66	1.00	0.66	1.53	0.13	1.40	2.66	0.66	2.00	2.75	2.20	0.55
12.	Vomiting	0.66	0.00	0.66	0.33	0.06	0.27	1.00	0.00	1.00	1.50	1.50	0.00
13.	Perianal rash	0.00	0.00	0.00	2.73	1.33	1.40	0.00	0.00	0.00	2.75	2.25	0.5
	Total mean score	1.67	1.11	0.55	1.64	0.57	1.07	1.58	0.58	0.99	2.36	1.88	0.48