



A CLINICAL STUDY TO EVALUATE THE EFFICACY OF DARVYADI LEHA IN GARBHINI KAMALA W.S.R. TO INTRAHEPATIC CHOLESTASIS IN PREGNANCY

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ABSTRACT

Ayurveda, the science of life has its origin in Vedic literature. Since the evolution of the life in the universe, women have been placed on extreme worship place due to her power of Janani. Garbhini Kamala has not been mentioned in Ayurvedic classics as an independent disease. Only the treatment of Garbhini Kamala has been quoted in the classics under Kashyapa Samhita Khill Sthana and Kashyapa Samhita Chikitsa Sthana. Darvyadi Leha has been explained in the context of Garbhini Kamala in Bhaisjya Ratnavali having the Triphala, Trikatu, Daruharidara, Vidanga along with Lauha Bhasma. After obtaining approval from Ethical Committee and informed consent, Open label randomized controlled type of study in 2 groups was conducted with pre and post investigation design to prove the efficacy of Darvyadi Leha in Garbhini Kamala. Outcome of the treatment after 30 days was statistically significant in the remission of the symptoms of Garbhini Kamala.

KEYWORDS : Darvyadi Leha, Garbhini Kamala, Intrahepatic cholestasis.

INTRODUCTION

Life is a liable entity in a world of flux and change, health and disease are linked aspects of that all-pervading instability. Child bearing and delivery are also physiological entities which are always ready to convert into pathological entities, if uncared.⁽¹⁾ So, here "Prakriti Sthapanam" is essential to prevent the pathology.

Garbhini Kamala is closely related to Intrahepatic Cholestasis in Pregnancy in terms of similarities in manifesting sites. It is a clinical manifestation of increased serum levels of bilirubin. It is clinically manifested as yellowish discoloration of sclera, mucus membranes and urine. Obstetric cholestasis is one of the most common causes of jaundice in pregnancy.

Samprapti⁽²⁾

यथा दुष्टेन दोशेण यथा चानुविसर्जिता ।
निवृत्तिरामयस्यसौ संप्राप्तिजातिरागतिः ।।

Samprapti Ghataka of Bahupitta Kamala⁽³⁾ are as follows:

Dosha - Pachaka Pitta, Ranjaka Pitta

Dushya - Rasa, Rakta, Mamsa

Udbhavasthana - Koshtha (Yakrut, Pleeha)

Adhishthana - Yakrita

Strotasadushti - Rasavaha, Raktavaha, Annavaha

Agni - Jatharagni, Rasadhatwagni, Raktadhatwagni

Sadhya Asadhyatwa - Kashtasadhya

Strotodushti Laxana - Atipravritti, Vimargamana

Marga - Bahya and Aabhyantara

Way Of Vitiated Pitta Dosha In Bahupittakamala

As Kamala is Pitta dominant disease, Pittaj nanatmaja vyadhi, shown in Fig.no.1.



Fig no.1: Showing vitiation of Dosha and Dushya in Bahupitta Kamala

1. Rudhapatha Kamala

Here the term Shakhshrita kamala refers to one of the trividha rogmarginas and that is the Bahyarogmarga.⁽⁴⁾ The modes of pitta vitiation is shown in Fig.no.2.

Lakshanas of Shakhshrit Kamala:

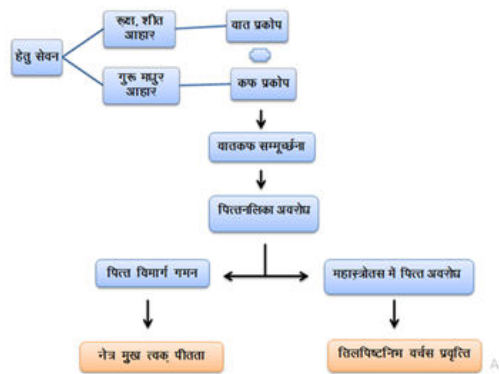


Fig.no. 2 : Way of Vitiated Pittadosha in Rudhapatha Kamala⁽⁵⁾

Yellowish discoloration of the skin, sclera, mucous membranes, and excretions due to hyper bilirubinemia and deposition of bile pigments are seen in Jaundice⁽⁶⁾. Pregnancy is a cholestatic condition. The stasis of bile in canaliculi with rise in canaliculi with rise in conjugated bilirubin is probably due to excess circulating estrogen.⁽⁷⁾ The incidence of IHCP varies from 0.02-2.4% of pregnancies about 70% of them present in last trimester and is associated with high maternal and perinatal morbidity and mortality rates.⁽⁸⁾

Table no.1 : Showing Liver Function Tests in Pregnancy^(9,10)

LFT	Non Pregnant	1 st Trimester	2 nd Trimester	3 rd Trimester
Bilirubin (micromole/L)	0-17	4-16	3-13	3-14
AST (IU/L)	7-40	10-28	11-29	11-30
ALT (IU/L)	0-40	6-32	6-32	6-32
GGT (IU/L)	7-41	5-37	4-43	3-41

ALP (IU/L)	20-125	6-375	Increases progressively to Term
Albumin (g/L)	35-55	Falls by 10g/L	Increases progressively to Term
Globulin (g/L)	30-50	Increases progressively to Term	
Fibrinogen (g/L)	2-4	Increases progressively to Term	

Intrahepatic Cholestasis Of Pregnancy^[11]:

- In most of the cases, it is seen in the second half of pregnancy.
- This is because of high estrogen levels in susceptible women.
- Incomplete clearing of bile acids in the liver which accumulate in plasma.

Pathogenesis

Cholestasis represents an exaggerated response of the liver to the normal increase in endogenous estrogen during pregnancy. Leslie and colleagues (2000) reported that plasma estrogen levels are decreased in affected women.^[12] Bile acids are incompletely cleared by the liver and accumulate in plasma.

There is a role for mutations in the genes that control hepatocellular transport systems.^[13] One of such genes is Multidrug resistance 3 (MDR 3) gene found with progressive familial intrahepatic cholestasis.^[14]

Hyperbilirubinemia is due to accumulation of conjugated pigment, but the total level never exceeds 4 to 5 mg%.^[15] The changes disappear after delivery.

MATERIALS AND METHODS

Study Design

A double arm randomized case control, open, comparative clinical study conducted at R.G.G.P.G. Ayurvedic College and Hospital, Paprola.

Study Participants

From March 2021 to May 2022, a total number of 30 cases from participating center suffering from Garbhini Kamala (Intrahepatic Cholestasis in Pregnancy) were enrolled as per the protocol specifically designed for this clinical trial and randomized in two groups. All the participants were recruited from the OPD level and were screened in accordance with the inclusion and exclusion criteria mentioned in the protocol. Before initiation of the recruitment of the participants, approvals of the Institutional Ethical Committees were obtained vide IEC No.Ayu/IEC/2019/1229. Written consent of the participants was obtained in the IEC-approved consent form. The study was registered in India's Clinical Trial Registry CTRI/2021/04/032854.

Inclusion Criteria

- Patients were willing for the trial.
- Female patient presented with features of Garbhini kamala.
- Pregnant females presented the picture of impaired liver functions.

Exclusion Criteria

- Patient who were not willing for trial.
- Patients had eclampsia, severe preeclampsia, HELLP syndrome.
- Patients had acute fatty liver (acute yellow atrophy of the liver).
- Patients with severe hyperemesis gravidarum.
- Patients with Viral hepatitis, chronic hepatitis.
- Patients had drug induced jaundice, surgery requiring obstructive jaundice, cirrhosis, tumors and other major systemic disorders.

Study Intervention

The enrolled patients of group one were administered with Standard group (Group I) drug Tab Ursodeoxycholic acid ~8mg/kg/day in two divided doses as study interventions for 30 days followed by 10 days of drug free period. Group II includes trial drug Darvyadi Leha. The drug was administered in the dose of 10gm BD for 30 days followed by 10 days of drug free period. After necessary quality checks, trial drug was procured and prepared by Institutional pharmacy, Charak Pharmacy.

Sample Size And Treatment Protocol

A total of 30 patients of Garbhini Kamala were enrolled. The recruited patients were randomly divided and 15 patients were allotted to Group I i.e. the control group and 15 patients were allotted to Group II i.e. the study group.

Assessment Criteria

Assessment was done based upon subjective as well as objective criteria by using MS Excel. Subjective criteria includes gradation on symptoms of the patients while objective criteria included lab investigations of the registered patients.

Statistical Methods

The scores of criteria of assessment was analyzed statistically in form of mean score B.T. (Before treatment), A.T. (After treatment), (B.T- A.T.) difference of mean, S.D. (Standard Deviation), S.E. (Standard Error).

Student paired 't' test was carried out at $p > 0.05$, $p < 0.05$ and $p < 0.001$ for intra-group comparisons of the scores while unpaired 't' test was used to analyze the intergroup comparison of the results. The results were considered significant or insignificant depending upon the value of 'p'.

- Highly significant - $p < 0.001$
- Significant - $p < 0.05$
- Non significant - $p > 0.05$

RESULTS

A total of 30 patients were enrolled in the study and all the patients completed the study without any dropout. On statistical analysis with an appropriate test on each criteria:

Intergroup comparison of Subjective Criteria shown in Table no.2 and Fig.no.3 & Objective criteria in Table no.3 & Fig.no.4

Overall comparative results of both group shown in Table no.4 & Fig.no.5.

Table no.2: Inter group comparison of effect of therapy over subjective criteria of assessment

Parameter	Percentage relief	Diff. in %age Group I Group II	S.D ±	S.E ±	Unpaired 't' test	P	Result
Icterus	87.5	90.625	-3.12	0.58	0.22	-0.29	>0.05 NS
Urine discoloration	81.25	80.95	0.3	0.76	0.29	2.03	0.05 NS
Stool discoloration	78.94	85.71	-6.77	0.70	0.27	0.73	>0.05 NS
Aruchi	63.15	66.66	-3.51	0.62	0.24	0.55	>0.05 NS
Hrullasa/ Chardi	53.33	90	-36.67	0.67	0.25	-0.25	>0.05 NS
Daha	61.11	88.88	-27.77	0.51	0.19	1.8	>0.05 NS
Avipaka	70.58	84.61	-14.03	0.67	0.25	0.25	>0.05 NS
Pruritis	83.33	86.66	-3.33	0.57	0.22	-0.30	>0.05 NS

Hatendariy α	83.33	83.33	0	0.51	0.19	0	>0.05	NS
Daurbalya	77.27	84.61	-7.34	0.58	0.22	1.76	>0.05	NS
Sadana	60	63.63	-3.63	0.54	0.20	-0.31	>0.05	NS
Karshana	80	83.33	-3.33	0.50	0.19	-0.34	>0.05	NS

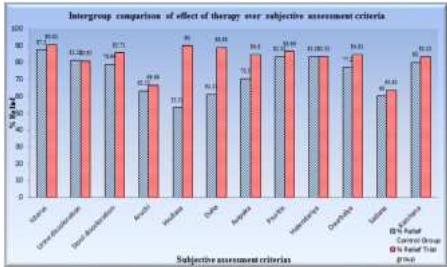


Fig. No.3 Showing Intergroup comparison of effect of therapy over subjective assessment criteria.

Table No.3: Inter Group Comparison Of Effect Of Therapy Over Objective Criteria Of Assessment

Parameter	Percentage relief	Diff. in %age Group I (Control Group)	%age Group II (Trial Group)	S.D ±	S.E ±	Unpaired t test	P	Result
Hb gm%	-10.89	-16.41	5.52	0.84	0.32	1.76	>0.05	NS
TSB	34.61	53.67	-19.06	0.27	0.10	-1.74	>0.05	NS
DSB	32.75	39.28	-6.52	0.12	0.04	-0.41	>0.05	NS
SGOT	83.75	70.43	13.31	52.2	20.11	4.24	<0.001	HS
SGPT	82.80	72.32	10.51	49.10	18.91	2.18	<0.05	S
ALP	51.99	36.84	15.14	58.63	22.58	1.68	>0.05	NS
S. Albumin	31.37	24.58	6.78	2.09	0.80	0.63	>0.05	NS
S. Bile acids	17.40	26.30	-8.9	1.3	0.5	-2.04	>0.05	NS
U. Bile salts & pigments	66.60	80.00	-13.3	0.48	0.18	0	>0.05	NS

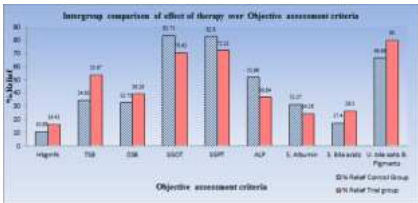


Fig No.4 Showing intergroup comparison of effect of therapy over objective assessment criteria.

Table No.4: Overall comparative effect in Both Groups of 30 patients

Assessment	Group I	Group II
Complete Improvement	6.6%	13.3%
Moderate Improvement	46.6%	73.3%
Mild Improvement	46.6%	13.3%
Unimproved	0%	0%

The table depicted that Group II showing more percentage in complete and moderate improvement in patients than Group I.

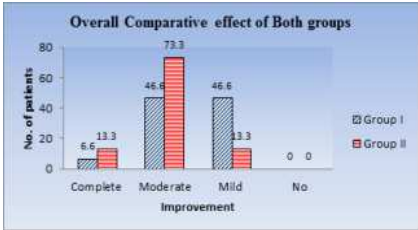


Fig. No. 5 Showing Overall comparative effect of both groups

Assessment Of Safety

None of the subjects during the course of study reported of any major adverse effect due to use of the intervention in either of the two groups.

DISCUSSION

Garbhini Kamala is Pitta Pradhana Tridoshaja Vyadhi^[16] along with Agni Dushti due to the formation of Ama as a result of Srotorodha by aggravated Kapha Dosha.

Out of 11 contents of Darvyadi Leha, 9 contents have Laghu Guna. Laghu guna is Lekhaniya^[17] that helps in removing the Srotorodha^[18] and alleviation of aggravated Kapha Dosha. 6 contents have Ruksha Guna. Ruksha Guna has properties opposite to Pitta Dosha that would help in Pittashamaka and Kaphashamaka.^[19] 3 drugs have Snigdha Guna. Snigdha Guna helps in Vatashamana.^[20] 3 drugs have Teekshana Guna. Teekshana Guna helps in Daha, Paka Sravana^[21] that helps in Pitta Sravana, also helps in Kaphashamana, acts on Srotorodha that would result in alleviation of the symptoms of the disease. 2 drugs have Guru Guna. Guru Guna is Balya^[22] that helps in provide strength to the body and helps in Vatashamana.^[23] 1 content have Sara Guna. Sara Guna is Anulomaka^[24] that helps in Anulomana of aggravated Doshas and thus, provide the normal coloration to the urine and stool by restoring the natural pathway of the Doshas. 1 drug have Sheeta Guna. Sheeta Guna helps in Pittashamana.^[25]

Out of 11 constituents of Darvyadi leha, 8 drugs have Madhura vipaka i.e. Vatapitta shamaka and 3 drugs have katu vipaka i.e. kaphashamaka.^[26] As a whole, Darvyadi leha works on tridosha, pacifies the vitiated doshas. 4 drugs have Sheeta Veerya that pacifies vitiated Pitta Dosha.^[27]

Katu Rasa, Laghu, Ruksha and Tikshna Guna have Deepana Pachana properties.^[28] Majority of drugs in Darvyadi Leha have Deepana -Pachana property.

Mandagni is one of the important causes of Kamala Roga and Darvyadi Leha contains Daruharidara and Trayushna which increases Agni^[29,30] and play vital in Samprapti Vighatana of Kamala Roga.

Darvyadi leha contains Daruharidara which have Yakrututtejaka and Pittasaraka property.^[31] It contains well known Rasayana drugs also like Triphala, Vidanga, Pippali and Lauha Bhasma. Dhatus get required nourishment with the help of Rasayana drugs and thereby, helpful in Dhatupushti.^[32]

Trikatu having Deepana- Pachana properties helpful in Ama Pachana. It also has Yakrututtejaka^[33] property that is helpful in proper physiological functioning of liver.

Lauha Bhasma due to its Sheeta Veerya^[34] is Pittashamaka as helpful in Bahupitta Kamala. It is also Balya, Vrishya, Tridoshahara and Rasayana.^[35]

Cumulative Effect Of Darvyadi Leha

Darvyadi Leha has shown improvement in the condition which can be attributed the various ingredients and their chemical constituents. Daruharidara contains various vitamins, tannins, alkaloids etc.^[36]

Lauha Bhasma is the source of iron in Darvyadi Leha and helps in increasing Hb in RBC.^[37] Triphala helps in blood purification as it has antioxidant properties which helps in scavenging free radicals which also decreases oxidative stress^[38,39] also has hepatoprotective properties.^[40]

Trikatu and Vidanga help in increasing bioavailability of

constituents of herbs administered concurrently^[41] as well as may be helping in absorption of the Vitamin B12 and Iron, which is thought to be the action of Piperine containing compounds present in Trikatu and Vidanga. This suggests the efficacy of Darvyadi Leha in Garbhini Kamala. Probable mode of action of Darvyadi Leha based on Rasa-Panchaka of majority of drugs is shown in Fig.no.6 along with Samprapti Vighatana of the disease in Fig. no.7.

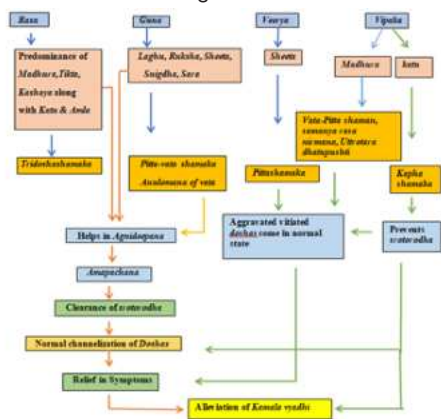


Fig. No.6: Showing probable mode of action of Darvyadi Leha

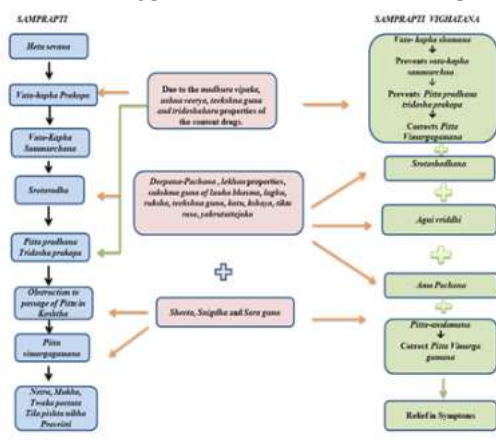


Fig No. 7: Showing Samprapti Vighatana of the disease.

CONCLUSION

The following conclusion can be drawn after scrutinizing the study regarding Garbhini Kamala.

- Garbhini kamala has close resemblance with Intrahepatic cholestasis in Pregnancy in terms of similarities in manifesting sites.
- The main principles of management of Garbhini kamala is Pitta Pradhana Tridosh Shamana, Vatanulomana, Srotoshodhana, Amapachana, Agnideepana.
- It was observed that patients could tolerate the treatment quite well and there were no adverse effects noted during the course of trial.

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