



Clinical Study

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Efficacy of Haritakyadi eye drops in Kukkunaka W.S.R to ophthalmia neonatorum – An open label clinical trial

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ABSTRACT

An open label clinical trial was conducted to evaluate the efficacy of Haritakyadi eye drops on Kukkunaka W.S.R to Ophthalmia Neonatorum in newborns at Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Kuthpady, Udupi. This trial was conducted on 30 newborns. The drops were instilled 8th hourly in a 3 divided doses per day for 3 days. The response was assessed by using various subjective and objective parameters and analysed statistically using Wilcoxon Signed Rank Test. Statistically significant results were obtained in subjective parameter and conjunctival swab culture. Study showed Haritakyadi eye drops is effective in relieving the clinical symptoms as well as controlling the growth of gram positive and negative organisms.

Keywords: Ophthalmia Neonatorum, Kukkunaka, Haritakyadi eye drops, Antimicrobial activity.

INTRODUCTION

The sensibility of Newborn period truly constitutes the foundation of human life as it is the most vulnerable phase of life. Newborn have unique health issues due to structural and functional immaturity of various body organs depending upon their gestational age and birth weight ^[1].

Acharyas have given prime importance to Nayanendriya ^[2] (Eyes) among Panchendriyas. Since eyes are the most precious and beautiful gift of the nature which plays a vital role in every individual, social development and progress. Eyes are very delicate and should be protected from the diseases for better perception of Indriyarthas. Kukkunaka is a disease which affects the eyes in newborn period. It is explained as Netra Vartmagatavikara which is Kaphapradhana Tridoshajavyadhi particularly seen in the Ksheerapa period. The clinical features explained in Ayurvedic classics like Abhikshamasrasravam (excessive lacrimation), Shotha (eyelid swelling), Paichilya (stickiness), Netramatikandu (itching in eye) is suggestive of inflammatory or infectious disease of eye. In contemporary science the same features are explained under the heading of Ophthalmia Neonatorum.

The term Ophthalmia Neonatorum is used in a broad sense to include all types of conjunctivitis of the newborn ^[3]. It may be caused by bacterial, viral or chlamydial infection or by toxic response to topically applied chemicals ^[4]. Ophthalmia Neonatorum produces various complications for the neonate in the infancy period or further life stages. Some of the common complications of the Ophthalmia Neonatorum include pseudo follicular formation in tarsal conjunctiva, nasolacrimal obstruction and blindness ^[5].

Acharyas have mentioned different types of treatment modalities like Aschotana, Parisheka, Anjana, application of Choorna, Pralepa etc. Aschotana means instillation of eye drops and in contemporary science this can be compared to Ophthalmic drops. Acharya Kashyapa has mentioned many formulations for the treatment of Kukkunaka and Haritakyadiyoga is one among them. By looking into the properties of drugs in Haritakyadiyoga almost all ingredients have Shotha hara, Ropana, Chakshushya property along with antibacterial and antimicrobial property which may help to overcome the symptoms of Kukkunaka. Hence Haritakyadiyoga in the form of eye drops was taken as trial drug for the study.

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MATERIALS AND METHODS

Table 1: Showing ingredients of Haritakyadi Eye Drops

S. No	Ingredients	Botanical name	Parts used	Quantity
1.	Haritaki	Terminalia chebula Retz.	Fruit rind	1 part
2.	Amalaki	Emblica officinalis Linn.	Fruit	1 part
3.	Daruharidra	Berberis aristata Dc.	Stem	1 part
4.	Yastimadhu	Glycyrrhiza glabra Linn.	Root	1 part
5.	Water			10 parts

Collection and authentication of raw drugs

The above mentioned drugs were collected from Sri Dharmasthala Manjunatheshwara Pharmacy, Udupi, Karnataka, India. The drug analysis and standardization was done at SDM centre for Research in Ayurveda and Allied Sciences, Udupi, Karnataka state, India and GC-MS analysis [6] of the drops were done at Department of Pharmacognosy, Siddha Central Research Institute, Arumbakkam, Chennai, India.

Method of preparation

Haritakyadi eye drops were prepared by using Haritaki (fruit kernel), Amalaki (fruit), Daruharidra (stem), Yastimadhu (root) in equal quantity. The above mentioned plant materials were taken and made into coarse powder and soaked overnight in 10 parts of water. Next morning, the soaked drugs were subjected for the distillation process. The vapours are condensed and collected in a receiver. In the beginning, the vapours consist of only steam and may not contain the essential principles of the drugs. It was therefore discarded. The last portion also may not contain therapeutically essential substance and was also discarded. The final product was in the form of drops. This method of preparation [7] of Arka is followed according to The Ayurvedic Formulary of India.

Aims and objectives

To evaluate and assess the antimicrobial activity of Haritakyadi Eye Drops in Kukkunaka W.S.R to Ophthalmia Neonatorum.

Source of data

Inborn neonates with signs and symptoms of Kukkunaka were selected from OPD and IPD of SDM Ayurveda Hospital, Udupi.

Study design

It is an open label clinical trial with pre and post-test design.

Method of collection of data

Selected Newborn was assigned in single group and detailed proforma was prepared with all points of history taking, physical signs and investigations.

Study sample

30 Newborns were selected based on inclusion and exclusion criteria.

Diagnostic criteria

Diagnosis was made on the lakshanas like Abhikshamasrusravam (excessive lacrimation), Shotha (eyelid swelling), Raktavarna (redness) and conjunctival swab culture.

Inclusion criteria

New born of either sex presented with two or more symptoms of Kukkunaka as per diagnostic criteria was included for the study.

Exclusion criteria

- Newborns having medical and surgical emergencies.
- Newborns with severe birth asphyxia with Apgar score < 5 at 10 min.
- Newborns with signs of sepsis.
- Preterm, LBW, IUGR neonates were excluded.

Assessment criteria

Subjective criteria

➤ Redness

- 0 - No redness
- 1 - Redness in any one eyelid
- 2 - Redness in both the eyelids
- 3 - Marked redness in both the eyelids

➤ Edema of eye lid

- 0 - No edema
- 1 - Slight swelling of upper/lower lids with no change in the inter palpebral fissure
- 2 - Swelling of upper and/or lower lid with decrease of inter palpebral fissure
- 3 - Swelling of both eye lids causes near or total closure of interpalpebral fissure

➤ Discharge

- 0 - No discharge
- 1 - Mild watery discharge confined to the lower fornix
- 2 - Sticky discharge
- 3 - Marked abundant discharge which can cause the eyelid to stick together

Objective criteria: Conjunctival Swab culture for the assessment of bacterial growth before and after the treatment.

Plan of intervention

Dose form: Drops

Dose: 1 drop in each eye

Time of administration: 8th hourly

Duration of treatment: 3 days

Lab investigation: Conjunctival swab culture

out. Non-parametric data and subjective parameters within the group are computed by Wilcoxon signed rank test.

STATISTICAL EVALUATION

The statistical analysis was carried out using the software SPSS 20.0. The frequency calculations along with non-parametric test have been carried

Ethical clearance: This trial has been cleared by Institutional Ethical Committees, Reference Number. SDMCAU/ACA-49/ECH80/16-17

OBSERVATIONS & RESULTS

Table 2: Showing an observation of 30 patients related to Demographic data and Disease

Observations	Maximum incidence	Percentage
Age	On day 2	33.3%
Sex	Male	73.3%
Religion	Hindu	66.7%
Socio-economic status	Middle class	53.3%
Symptom	Eye discharge	100%
Gravida	Multigravida	66.7%
Mode of delivery	Normal vaginal delivery	63.3%
Duration of labour	3-6 / 6-9 hrs	40%
Birth weight	2.5-3 kg	53.3%
Gestational age	Term	90%
Bacteria in culture media	Gram positive	89.9%
Bacteria identified	Staphylococcus	65.4%

RESULTS

EYE DISCHARGE

Table 3.1: Showing effect on eye discharge in the group

Parameter	Negative Ranks			Positive Ranks			Ties	Total	Z value	P value	Inference
	N	MR	SR	N	MR	SR					
D1-D2	27	14	378	0	0	0	3	30	-5.112	0.00	HS
D1-D3	30	15.5	465	0	0	0	0	30	-5.064	0.00	HS

1. On parameter of eye discharge, results compared on Day 1 to Day 2, 27 neonates showed negative results which is statistically highly significant with $Z = -5.112$, $p = 0.00$.
2. On parameter of eye discharge, results compared on Day 1 to Day 3, 30 neonates showed negative results which is statistically highly significant with $Z = -5.064$, $p = 0.00$.

REDNESS

Table 3.2: Showing effect on redness in the group

Parameter	Negative Ranks			Positive Ranks			Ties	Total	Z value	P value	Inference
	N	MR	SR	N	MR	SR					
D1-D2	22	11.5	253	0	0	0	8	30	-4.69	0.00	HS
D1-D3	26	13.5	351	0	0	0	4	30	-4.939	0.00	HS

1. On parameter of redness, results compared on Day 1 to Day 2, 22 neonates showed negative results which is statistically highly significant with $Z = -4.69$, $p = 0.00$.
2. On parameter of redness, results compared on Day 1 to Day 3, 26 neonates showed negative results which is statistically highly significant with $Z = -4.939$, $p = 0.00$.

EYE LID EDEMA

Table 3.3: Showing effect on eye lid edema in the group

Parameter	Negative Ranks			Positive Ranks			Ties	Total	Z value	P value	Inference
	N	MR	SR	N	MR	SR					
D1-D2	8	4.5	36	0	0	0	22	30	-2.828	0.005	S
D1-D3	10	5.5	55	0	0	0	20	30	-3.051	0.002	S

1. On parameter of eye lid edema, results compared on Day 1 to Day 2, 8 neonates showed negative results which is statistically significant with $Z = -2.828$, $p = 0.005$.
2. On parameter of eye lid edema, results compared on Day 1 to Day 3, 10 neonates showed negative results which is statistically significant with $Z = -3.051$, $p = 0.002$.

HAEMOLYTIC STAPHYLOCOCCUS

Table 3.4: Showing effect on haemolytic staphylococcus

Parameter	Negative Ranks			Positive Ranks			Ties	Total	Z value	P value	Inference
	N	MR	SR	N	MR	SR					
BT-AT	6	3.5	21	0	0	0	1	7	-2.449	0.014	S

On parameter of haemolytic staphylococcus, results compared on BT-AT, 6 neonates showed negative results which is statistically significant with $Z=-2.449$, $p=0.014$.

KLEBSIELLA

Table 3.5: Showing effect on Klebsiella

Parameter	Negative Ranks			Positive Ranks			Ties	Total	Z value	P value	Inference
	N	MR	SR	N	MR	SR					
BT-AT	1	1.5	1.5	1	1.5	1.5	0	2	0	1	NS

On parameter of Klebsiella, results compared on BT-AT, one neonate showed negative result and 1 neonate showed positive result which is statistically not significant with $Z=0$, $p=1$.

CITROBACTER

Table No.3.6. Showing effect on Citrobacter

Parameter	Negative Ranks			Positive Ranks			Ties	Total	Z value	P value	Inference
	N	MR	SR	N	MR	SR					
BT-AT	1	1	1	0	0	0	0	1	-	-	-

On parameter of Citrobacter, statistical test cannot be computed as there was one subject. However Clinically significant result seen in that subject.

STAPHYLOCOCCUS

Table No.3.7. Showing effect on staphylococcus

Parameter	Negative Ranks			Positive Ranks			Ties	Total	Z value	P value	Inference
	N	MR	SR	N	MR	SR					
BT-AT	11	6	66	0	0	0	6	17	-3.317	0.001	HS

On parameter of staphylococcus results compared on BT-AT, 11 neonates showed negative result. Which is statistically highly significant with $Z=-3.317$, $p=0.001$.

STREPTOCOCCUS

Table No.3.8. Showing effect on streptococcus

Parameter	Negative Ranks			Positive Ranks			Ties	Total	Z value	P value	Inference
	N	MR	SR	N	MR	SR					
BT-AT	2	1.5	3	0	0	0	0	2	-1.414	0.157	NS

On parameter of streptococcus, results compared on BT-AT, 2 neonates showed negative result. Which is statistically not significant with $Z=-1.414$, $p=0.157$.

DISCUSSION

Effect of treatment on subjective parameters

Eye discharge

The vitiated Doshas like Kapha and Pitta are lodges in the Ashruvahisirawhich afterwards flow out from the eyes as eye discharge. Statistically highly significant results were showed for this parameter as the trial drugs were having the properties like Shothahara [8], Rakta Prasadana, Lekhana, Vranaropna [9] might have given good response in relieving the eye discharge.

Redness

Redness is considered as Raga, Lohita, Netrata, Tamra, Akshi which is due to vitiation of Pitta and Rakta. The reduction in redness of eyes might be due to formulation contains the drugs which are Sheetavirya, Rakta Prasadana, Vrana ropaka [9] which is statistically highly significant.

Eyelid edema

Eyelid swelling is the sign of inflammation and can be considered as Shophya / Shwayatu as per Ayurveda. Due to obstruction of the Doshas there will be Sangha (obstruction) for the normal flow of Doshas, so

there will be manifestation of swelling over one or both the eyelids. The significant results were observed is due to the Shothahara [8], Vranaropana [9], Lekhana [10] properties of the trial drugs might have helped to reduce the eye lid edema.

Effect of treatment on objective parameters

In the present clinical trial, Haemolytic staphylococcus, klebsiella, Citrobacter, staphylococcus and streptococcus micro organisms were identified through conjunctival swab smear. The anti-microbial activity of Haritaki, Amalaki, Daruharidra and Yastimadhu showed significant results on Haemolytic staphylococcus, Citrobacter, staphylococcus. Recent research conducted proved that extract of Amalaki significantly reduced mean colony count on Escherichia coli, Staphylococcus, Klebsiella, Pneumoniae and Pastuerellamultocida by tube dilution [11].

CONCLUSION

Kukunaka is a common disease in neonates due to the vitiation of Tridoshas. By analysing the history and symptoms, it might be caused due to the Kapha Pradana Dushta Stanya Pana. The Lakshanas which were explained in classics for Kukunaka were also seen in Ophthalmia Neonatorum. Due to Laghu, RookshaGuna, SheetaVeerya and Lekhana, Chakshushya, Kandugna properties of Haritakyadi yoga helps to pacify the vitiated KaphaPradanaTridosha. The symptoms of Kukunakamight have reduced due to the Vedanastapana, Shotahara, VranaShodana and Ropana properties of drugs in Haritakyadi yoga. The main pathogenic organism responsible for the incidence of Ophthalmia Neonatorum is staphylococcus. In the present clinical trial, we have isolated maximum of this organism in the culture. Considering the improvement in both subjective and objective parameters, the drug Haritakyadi eye drops is found to be effective in relieving the clinical symptoms as well as controlling the growth of gram positive and negative organisms. Early diagnosis and adequate treatment definitely relieve the symptoms without leading to complications. Henceforth it is concluded from the clinical trial that Haritakyadi eye drops is effective in treating the disease Kukunakaw.s.r to Ophthalmia Neonatorum without any adverse effect.

ABBREVIATION

BT- Before Treatment
AT- After Treatment
HS- Highly significant
NS- Non significant
S - Significant
M.R- Mean Rank
S.R- Sum Rank
D- Day

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