LIQUORICE MILK AS A POTENTIAL STANDALONE THERAPY FOR GERD: A CASE SERIES

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ABSTRACT

Gastroesophageal reflux disease (GERD) occurs when there is a repeated backwash or backflow of stomach acid into oesophagus. This back wash also known as acid reflux can irritate the lining of oesophagus. A continuous acid reflux can cause irritations to patients in the form of symptoms like sour belching, heart burn, epigastric tenderness etc. While analysing the features of *Amlapitta (Hyperacidity)*, it resembles features of Gastro Oesophageal Reflux disease in its clinical presentation. Clinically *Yashtimadhu Ksheerapaka* (*Liquorice milk)* has promising results in reducing the symptoms and discomforts due to GERD. 20 study participants showed significant relief from the symptoms. The parameters considered for assessment was statistically significant at $p < 0.05$ confirming the effectiveness of *Liquorice milk* in GERD. The present case series highlights the clinical effectiveness of *Liquorice milk*, as a standalone medicine in management of GERD in 20 patients. Here the patients are observed prospectively. The medicine preparation was done based on the classical reference from the *Ksheerapaka vidhi (Medicated milk)* mentioned in *Sharangadhara Samhita*. The effect was measured by clinically assessing the symptoms using Modified Demeester's scoring system.

KEYWORDS

Amlapitta; GERD; *Liquorice milk*; *Glycyrrhiza glabra.*

ABBREVIATIONS

GERD - Gastroesophageal reflux disease, OPD- Out Patient Department, BT – Before Treatment, AT – After Treatment, LES - lower oesophageal sphincter

1. INTRODUCTION

Gastroesophageal reflux disease (GERD) disease is one of the most frequent disease conditions encountered by primary healthcare providers around the world. GERD is a common condition in which there is a repeated backflow of stomach acids into the oesophagus. [1]Around 10% - 20% individuals in Western countries and nearly 5% of those in Asia experience GERD symptoms at least once in a week. The prevalence of GERD is observed to be increasing by 4%, as it is proportionate with the modern lifestyle of mankind such as sedentary work pattern, increased stress and improper diet like fast food. Reflux becomes a disease when it causes frequent or severe symptoms or injury to oesophageal mucosa. Reflux may damage the oesophagus, pharynx or respiratory tract. Typical symptoms that lead to the diagnosis of GERD are regurgitation and heartburn (dyspepsia), nausea, bloating, epigastric pain. A chronic and persistent GERD can lead to much more serious conditions like Peptic ulcers or even oesophageal adenocarcinoma[9].

The condition which has a close resemblance to GERD explained in Ayurvedic classics is a condition of indigestion with sour belching [2]- *Hyperacidity* (*Amlapitta*). [3] It presents as indigestion, exhaustion, nausea, sour belching, burning sensation of chest and loss of appetite. Further progression of this condition can lead to the development of epigastric pain or even peptic ulcer.

This article presents a qualitative evaluation of cases that were treated with *Yashtimadhu Ksheerapaka (Liquorice milk)*. As a stand-alone medication, Liquorice milk was used to treat more than 60 cases of GERD. Among them, the current study of 20 patients who belong to the same age group, who presented to our OPD with clinical symptoms of GERD are given individually as a case series. All of the cases with mild to severe clinical symptoms were effectively treated and managed as a result of the intervention, with no additional complications. The assessment of symptoms before and after treatment was done based on objective parameters (Table.1) as per Modified Demeester's scoring system[4].

Symptoms	Score	Description
Dysphagia	0	None
	1	Occasional transient episodes
	2	Require liquids to clear
	3	Impaction requiring medical attention
Heartburn	0	None
	1	Occasional brief episodes
	2	Frequent episodes requiring medical treatment
	3	Interference with daily activities
Regurgitation	0	None
	1	Occasional episodes
	2	Predictable by posture

Symptoms	Score	Description
	3	Interference with daily activities

Table.1: Modified Demeester's Score

2. MATERIALS AND METHODS

2.1.1. Study Design

This is a prospective case series study conducted in the Shalya Tantra OPD of Amrita School of Ayurveda, Amritapuri, Kollam, Kerala, between December 2021 to December 2023.

2.1.2. Recruitment

Patients who came to OPD for regular consultation were recruited for the study. Inclusion for enrolment in study are

1. Symptoms of GERD – heartburn, regurgitation, dysphagia.
2. Age group – 18 to 50 years
3. Gender – both male and female
4. Similar dietary habits

People having glucose intolerance, lactose intolerance or allergy to liquorice preparations, pregnancy, lactating mothers or use of a proton pump inhibitor or H2-receptor antagonist in the I week prior to consultation in OPD and those who are younger than 18 years and older than 50 years are excluded from the study.

2.2. Preparation Of Medicine and Mode of Administration to Patients

Liquorice milk was prepared as per the classical reference from *Sarangadhara Samhita Madhyama Khanta*. Here the patients were advised to prepare the medicine by taking raw materials in a proportion of 1:8:32 [*Liquorice* powder: Milk: Water][5]. 6gms of *Liquorice* powder should be added with 48ml of milk and 192 ml of water. For the convenience of the patients, they were advised to use 50ml of milk added with 200ml of water. The mixture was heated on mild flame of 90-95-degree C until it was reduced to the quantity of milk (50ml) and it has to be filtered and used.

2.3. Intervention

The patients were instructed to take the prepared *Liquorice milk* half the quantity twice per day before food for 21 days (3 weeks). Each patient was advised to prepare and use medicine from home. They were explained thoroughly prior to sending them home.

2.3.1. Timeline Of Intervention and Assessment

• Day1 - Assessment of inclusion criteria
• Day 1- 7 - Administration of medicine
• First review after 7days - Continue medication
• Second review after 14 day - Continue medication.

• Third review after 21 days - Medication is stopped.

Study participant's data based on assessment criteria were recorded before the commencement of the study and after the intervention. First review was taken after 1st week; second review was done after 14 days (2nd week) and third review after 21 days (3rd week).

2.3.2. Patient information

Dysphagia, heartburn and regurgitation were assessed for each patient before administration of medicine and during each follow up, analogously with the Modified Demeester's scoring system (Table.2).

SL.NO	CASE CODE	DYSPHAGIA					HEARTBURN					REGURGITATION					AGE
		BT	AT1	AT2	AT3	BT-AT3	BT	AT1	AT2	AT3	BT-AT3	BT	AT1	AT2	AT3	BT-AT3	
1	NEE001	2	2	1	0	2	2	2	1	0	2	2	2	1	0	2	21
2	OMA002	2	2	2	1	1	3	3	2	1	2	1	1	1	0	1	48
3	USH003	0	0	0	0	0	2	2	1	0	2	2	2	1	0	2	50
4	PRA004	1	1	0	0	1	1	1	0	0	1	1	1	1	0	1	46
5	LEE005	0	0	0	0	0	1	1	0	0	1	0	0	0	0	0	20
6	AKH006	0	0	0	0	0	2	2	2	1	1	2	2	1	0	2	33
7	REK007	1	1	0	0	1	1	1	1	1	0	1	1	1	1	0	47
8	SOJ008	1	1	1	0	1	1	1	1	1	0	1	1	1	1	0	26
9	SHA009	1	1	0	0	1	2	1	0	0	2	0	0	0	0	0	34
10	SAS010	0	0	0	0	0	2	1	1	0	2	1	1	0	0	1	38
11	SAK011	2	2	1	0	2	3	2	2	1	2	0	0	0	0	0	30
12	CHA012	0	0	0	0	0	1	1	0	0	1	0	0	0	0	0	48
13	GAN013	1	1	0	0	1	1	1	0	0	1	2	2	1	1	1	24
14	GOP014	0	0	0	0	0	1	1	0	0	1	2	2	1	0	2	28
15	REM015	1	1	1	0	1	2	2	1	0	2	0	0	0	0	0	30
16	NIY016	0	0	0	0	0	1	1	1	0	1	1	1	1	0	1	40
17	RAV017	0	0	0	0	0	2	2	1	0	2	1	1	1	0	1	42
18	RAM018	0	0	0	0	0	2	2	1	0	2	1	1	1	0	1	36
19	LEE019	1	1	1	0	1	1	1	0	0	1	2	2	1	1	1	45
20	JAY020	0	0	0	0	0	2	1	1	0	2	1	1	1	0	1	36

Table title: DEMEESTER SCORE CHART

Table.2: Patient information sheet of assessment of intervention and demographic data.

2.4. Statistical Analysis

The data obtained were tabulated using Microsoft Excel and analysed for significance by deploying Friedman test and Wilcoxon's signed rank test.
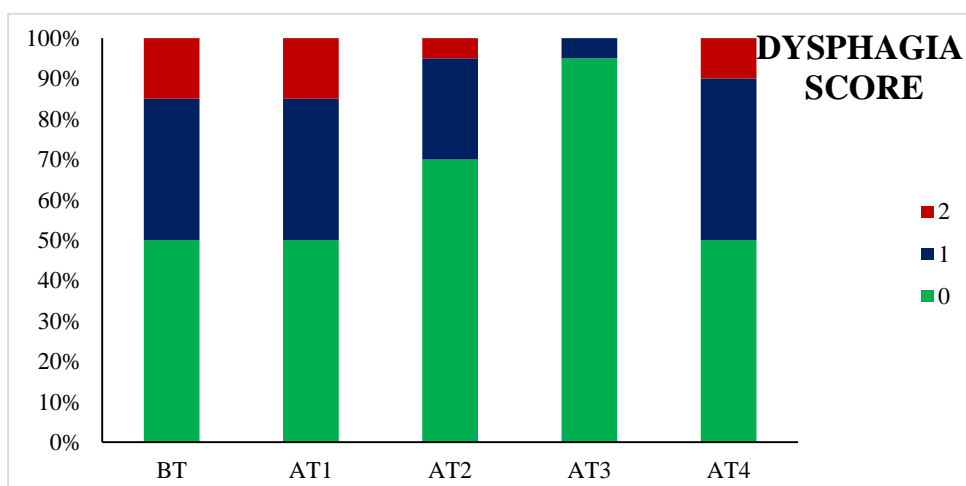
3. RESULTS AND OBSERVATIONS

3.1.1. Observations and statistical analysis of Dysphagia –

The presented data outlines dysphagia scores across different stages of assessment (BT, AT1, AT2 and AT3), accompanied by the results of a Friedman Test. BT – 3.43, AT1 – 3.43, AT2- 2.73 and AT3 – 2.13 respectively are the mean rank for each stage when Friedman Test was applied. The mean rank values reveal that AT3 exhibits the lowest dysphagia scores on average, third review has the lowest dysphagia score. The Friedman Test confirms statistically significant differences among different time points, with a p-value <0.05.

Paired comparison				Wilcoxon signed rank test			
		N	Mean Rank	Sum of Ranks	z	p	
BT vs AT1	Negative Ranks	0	0	0	0	1.000	
	Positive Ranks	0	0	0			
	Ties	20					
	Total	20					
BT vs AT2	Negative Ranks	6	3.5	21	2.449	0.014	
	Positive Ranks	0	0	0			
	Ties	14					
	Total	20					
BT vs AT3	Negative Ranks	10	5.5	55	2.972	0.003	
	Positive Ranks	0	0	0			
	Ties	10					
	Total	20					

Table.3: Wilcoxon signed-rank test for dysphagia.

Wilcoxon signed-rank test was carried out to comparing heartburn scores between different timepoints (BT, AT1, AT2 and AT3). For each pairwise comparison, the table presents the number of negative and positive ranks, the mean rank, the sum of ranks, the test statistic (z), and the corresponding p-value. The results indicate significant differences in heartburn scores between BT and each of the other conditions (AT2 and AT3) with their respective p-values (Table.3).
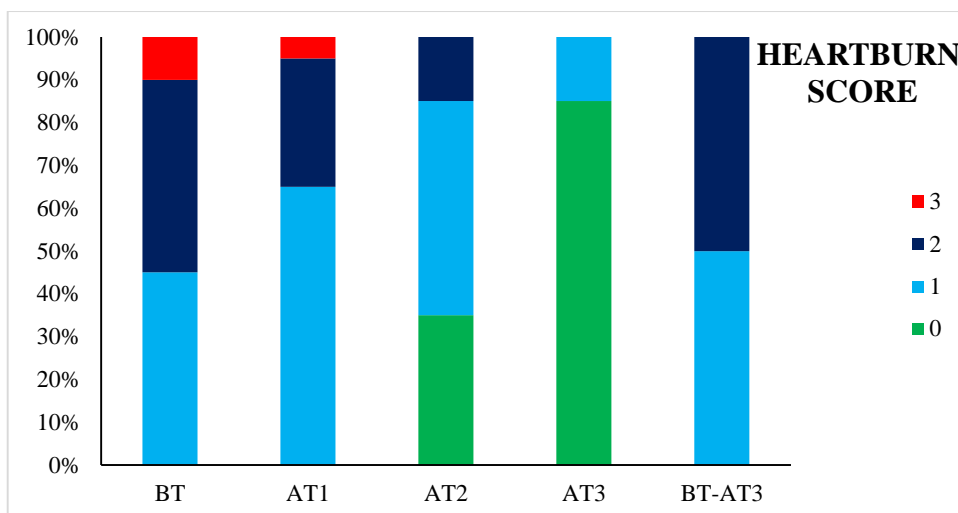

Graph.1. Dysphagia score

3.1.2. Observations and statistical analysis of Heartburn –

The presented data outlines heartburn scores across different stages of assessment (BT, AT1, AT2 and AT3), accompanied by the results of a Friedman Test. BT – 4.1, AT1 – 3.63, AT2- 2.3 and AT3 – 1.2 respectively are the mean rank for each stage when Friedman Test was applied. The mean rank values reveal that AT3 exhibits the lowest heartburn scores on average, third review has the lowest heartburn score. The Friedman Test confirms statistically significant differences among different time points, with a p-value <0.05.

Paired comparison			Wilcoxon signed rank test				
		N	Mean Rank	Sum of Ranks	z	p	
BT vs AT1	Negative Ranks	5	3	15	2.236	0.025	
	Positive Ranks	0	0	0			
	Ties	15					
	Total	20					
BT vs AT2	Negative Ranks	16	8.5	136	3.9	0.000	
	Positive Ranks	0	0	0			
	Ties	4					
	Total	20					
BT vs AT3	Negative Ranks	20	10.5	210	4.038	0.000	
	Positive Ranks	0	0	0			
	Ties	0					
	Total	20					
	Positive Ranks	0	0	0			

Table.4: Wilcoxon signed-rank test for heartburn.

Wilcoxon signed-rank test was carried out to comparing heartburn scores between different timepoints (BT, AT1, AT2 and AT3). For each pairwise comparison, the table presents the number of negative and positive ranks, the mean rank, the sum of ranks, the test statistic (z), and the corresponding p-value. The results indicate significant differences in heartburn scores between BT and each of the other conditions (AT2 and AT3) with their respective p-values (Table.4).

Graph.2. Heartburn score.

### 3.1.3. Observations and statistical analysis of Regurgitation

The presented data outlines regurgitation scores across different stages of assessment (BT, AT1, AT2 and AT3), accompanied by the results of a Friedman Test. BT – 3.6, AT1 – 3.6, AT2- 2.83 and AT3 – 1.63 respectively are the mean rank for each stage when Friedman Test was applied. The mean rank values reveal that AT3 exhibits the lowest regurgitation scores on average, third review has the lowest regurgitation score. The Friedman Test confirms statistically significant differences among different time points, with a p-value <0.05.

Wilcoxon signed-rank test was carried out to comparing regurgitation scores between different timepoints (BT, AT1, AT2 and AT3). For each pairwise comparison, the table presents the number of negative and positive ranks, the mean rank, the sum of ranks, the test statistic (z), and the corresponding p-value. The results indicate significant differences in regurgitation scores between BT and each of the other conditions (AT2 and AT3) with p-values of 0.008, 0.000 respectively (Table.5).

Paired comparison					Wilcoxon signed rank test		
		N	Mean Rank	Sum of Ranks	z	p	
BT vs AT1	Negative Ranks	0	0	0	0	1.000	
	Positive Ranks	0	0	0			
	Ties	20					
	Total	20					
BT vs AT2	Negative Ranks	7	4	28	2.646	0.008	
	Positive Ranks	0	0	0			
	Ties	13					
	Total	20					

Paired comparison			Wilcoxon signed rank test				
		N	Mean Rank	Sum of Ranks	z	p
BT vs AT3	Negative Ranks	15	8	120	3.578	0.000
	Positive Ranks	0	0	0		
	Ties	5				
	Total	20				

Table.5: Wilcoxon signed-rank test for regurgitation score.
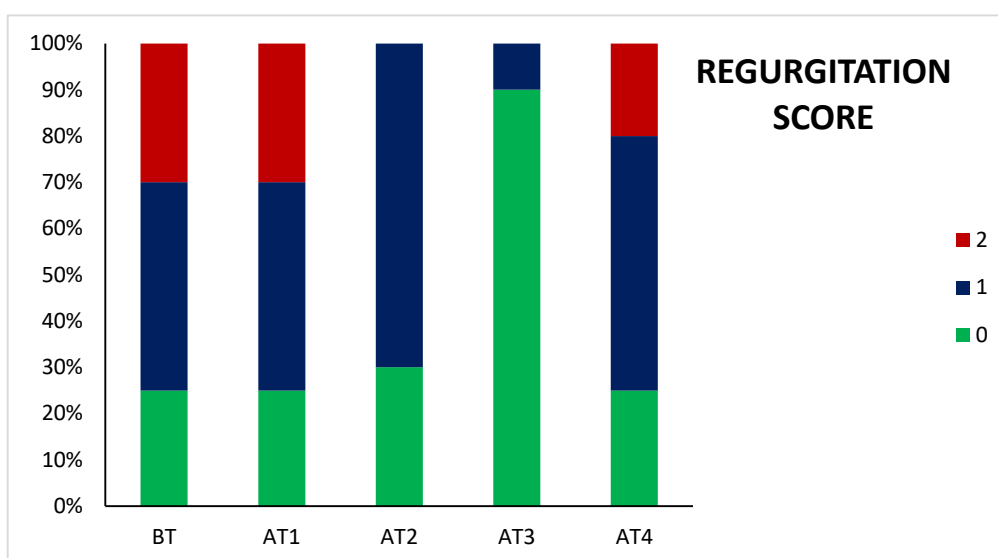
Graph.3. Regurgitation Score.

4. DISCUSSION

Liquorice is having the properties of wound healing, digestive, antispasmodic and anti-inflammatory effects which makes it an ideal drug of choice in GERD. The anti-inflammatory action is primarily mediated by glycyrrhizin, a phytochemical present in liquorice which invitro could inhibit factors responsible for inflammation as well as promote the healing of stomach ulcers[6,7]. To address the regurgitation without further vitiating the stomach ulcer condition, the medium or vehicle for administration of medicine chosen is milk[8]. Here, the form of administration preferred is *Medicated milk*. This particular preparation also helps neutralize the nauseating and the emetic nature of the medicine. As per the classical reference, this medicine is also having an analgesic property[5].

Strengths of this study is that, it is the first study to analyse the health outcomes of *Liquorice milk*, when administered as a stand-alone medicine in GERD, where a single medicine approach is rarely seen.

Limitations of the study was a smaller sample size, shorter duration and subjective assessment and lack of a control group. The study participants were not assessed for anatomical deformities like hiatus hernia, lax LES etc. in such conditions only symptomatic relief can be observed and recurrence of symptoms are also to be expected with any change in the diet or lifestyle of the patient. Diet modifications advised were also not recorded.

Maximum duration of medicine administered was three weeks. As per some studies and articles there are possible adverse drug reaction (ADR) from a chronic use of *Liquorice* leading to hypokalaemia and hypertension[9]. The dose of *Liquorice* powder used was 6gms for one day, which was given in a divided dose of 3gms twice a day. The maximum dose of powdered medicine as per classical reference is 12 gms[10]. But considering the emetic nature[11] of *Liquorice* and its possible ADR, we only advised half the quantity of maximum dosage, which is 6gms.

Even though the study was able to demonstrate the clinical effects of *Liquorice milk* through this study, it did not explain the mechanism of action of the medicine in this particular condition. Future studies can be done to strengthen the scientific basis of this medicine with a larger sample size and control group. An effective management of GERD can prevent the progression of this seemingly common lifestyle disease into fatal cancerous conditions like oesophageal adenocarcinoma.

5. CONCLUSION

Based on the demographic data, it was observed that GERD was more common in people between the ages of 18 and 50 and that majority of the people diagnosed with it were female. When they entered in the study, all of the participants followed a mixed diet consisting of both vegetables and non-vegetables. The majority of participants had steady socioeconomic level and were married.

The assessment was done based on the observations made in 20 study subjects. They were observed for the symptoms like 1. Dysphagia 2. Heartburn and 3. Regurgitation. The p value obtained for dysphagia on different stages of analysis was 1.000, 0.014 and 0.003 respectively. Here it is to be noted that the significant reduction in dysphagia was observed from second review onwards. The p values of heartburn at different stage of analysis were 0.025, 0.000 and 0.000. this shows significance from first week of administration itself. Finally, the significance of reduction in regurgitation is observed from the p values obtained at different stages of assessment were 1.000, 0.008 and 0.000. Here also, significant relief in regurgitation was seen from second week of administration of medicine. Statistically Significant reduction in symptoms; Dysphagia was recorded in the first review and a complete relief from symptoms was noted in almost all cases after second and third review, thus improving the quality of life of the study subjects. This study concluded that, *Liquorice milk* given as a stand-alone medicine for GERD is effective in reliving the symptoms within 1 week of administration and a complete cure was observed in 3weeks.

As a long-term administration of medicine was not advisable, the administration of medicine was terminated after 3weeks (21days), following the reduction in symptoms. But there are also

chances of recurrence of symptoms after 1month or so, which has to be monitored and recorded in further follow ups.

6. INFORMED CONSENT

All participants involved in this study were provided with informed consent after being fully informed about the study's purpose.

7. FUNDING STATEMENTS

8. AUTHOR CONTRIBUTION

1. Dr Aparna S – Visualization, methodology, writing original draft.
2. Dr Aswathy A – Visualization, supervision, selection and monitoring of assessment criteria.
3. Dr Rajeshwari PN – Conceptualization, supervision, writing - review and editing.

9. DECLARATION OF COMPETING INTEREST

Authors hereby declare that they have no conflicts of interest.

10. ACKNOWLEDGEMENT

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