

Evaluation of the biochemical changes in bile under the influence of compound indigenous drug in biliary stone diseases

Abstract

Background

Biliary stone disease is an old aged anguish of mankind. Many chemical agents and traditional medicines have been tried to dissolve biliary stones but all have come with limited success. "Phaltrikadi" has also been used to treat jaundice since ages as an "Ayurvedic Polyherbal Formulation" with acceptable good results. Since "Phaltrikadi" is clinically very effective, the main objective of the study were –

- To know its effects on various inorganic and organic contents of bile especially when the bile is proven lithogenic i.e. in patients of Cholelithiasis and Choledocholithiasis.
- To evaluate the prophylactic effect of the compound drug on biliary stone diseases as well as changes in bile juice composition that is responsible for the recurrence of stones after successful cholecystectomy.

Methods

Total 64 patients of Cholelithiasis and Choledocholithiasis after cholecystectomy with choledochotomy and T-tube drainage were allocated in two groups for the study-

Group A (Treated Group) - 34 cases; drug was given in the form of freshly prepared decoction from 4th post operative day to 10th post operative day. Group B (Control Group) - 31 cases; no drug will be given to the patients of in this period. Screening of biochemical changes of Bile juice was done by various biochemical procedures in Intraoperative bile juice (Lithogenic bile), Third postoperative day (Pre-therapy sample) and Tenth postoperative day (Post therapy sample). All data was evaluated and presented accordingly with the help of Student "t" test and Paired "t" test.

Results

No adverse event was noted in any patient. All patients responded well with the decoction. Progressive decrease in sodium ion concentration in bile is highly significant in Group A as compared to Group B. Similar trends were also observed in biliary Potassium (K^+), Calcium (Ca^{++}), Magnesium (Mg^{++}) and Chloride (Cl^-) levels. All of these were significantly decreased in Group A than Group B. In the present study, total protein level was significantly decreased. Likewise, total cholesterol concentration showed progressive decline after initial rise on third day. Bile concentration of triglyceride and phospholipid showed progressive rise during therapy whereas no statistical significance was encountered in phospholipid concentration.

Bilirubin concentration was progressively decreased during treatment in Group A and this decline was also significant after therapy when compared to Group B.

Conclusions

It is concluded that the trial drug "PHALTRIKADI KWATH" has got potential in relieving the biliary stone disease by maintaining the bile chemistry in equilibrium as may be helpful in avoiding the recurrence of stones after successful cholecystectomy. The trial drug has significant effects on various inorganic and organic ingredients which are responsible for biliary stone formation. Thus it can be used in biliary sludge cases to avoid frank gallstones formation.

Keywords: gallstone, phaltrikadi kwath, decoction, cholecystectomy, cholelithiasis

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Pankaj Srivastava

Department of Surgery, Om Surgical Center & Maternity Home, India

Correspondence: Pankaj Srivastava, Laparoscopic, Thoracic, Thoracoscopic & VATS Surgeon, Om Surgical Center & Maternity Home, Sri Krishna Nagar, Paharia, Ghazipur Road, Varanasi, UP, India, Tel +91-542-2586191, Email drpankajbns@gmail.com

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Introduction

Biliary stone disease is multifactorial disease, mainly caused by metabolic derangement of bile juice composition. Cholesterol, lecithin and bile salts play major role in the pathogenesis of stones. No doubt, infection and cholecystitis are important factors but one cannot give

them preference over metabolic derangement, which is a proved and well-known fact. Despite of cholecystitis, the clinical settings in which primary stones of the biliary duct system occur include post-traumatic biliary stricture, narrowed biliary enteric anastomosis, and stenosis of sphincter of oddi, sclerosing cholangitis and Asian cholangiohepatitis. So in these settings one may be victimised with biliary stones after

cholecystectomy and if efficient medical management is available in time that will be definitely cost-effective. It can be concluded that for stone formation presence of gall bladder is not mandatory.

Surgical management has certain undesirable complications like hemorrhage, bile leakage, post cholecystectomy syndrome, and most important recurrence of stones in the biliary tract. So, to explore some preventive aspect of the disease, the present clinical trial was designed to evaluate the efficacy of the trial drug- "Phaltrikadi Kwath" on the bile. Phaltrikadi Kwath, a well-known formulation is widely used by Ayurvedic physicians for the treatment of jaundice and anaemia but its evaluation on scientific parameters has not been widely done yet.¹ On our literary survey, we found that the ingredients of the Phaltrikadi Kwath possess various biological activities like; hepatoprotective action, immuno-stimulation, anti-inflammatory- antispasmodic action, choleric and cholagogue properties etc that will be helpful in biliary stone diseases. As far as type of formulation is concerned, Kwath (Decoction) has been proved more effective than any other type of extract.²

Material & methods

It is evident from the preceding reviews of literatures that biochemical and physicochemical properties of the bile juice play major role in the pathogenesis of the biliary stones. Bile is an osmotic solution of bile acids, cholesterol, phospholipids, bile pigments, and inorganic electrolytes and all contribute in some or other way in the formation of biliary stones. Therefore, it is prudent to carry out this research work in the direction of these pathogenic factors.

The present study was planned to evaluate the effect of polyherbal formulation "Phaltrikadi Kwath" on the pathogenic factors in bile responsible for stone formation in patients with cholelithiasis and choledocholithiasis.

Selection of the cases

To evaluate the effect of Phaltrikadi Kwath on biochemical parameters in bile juice clinical study of randomly selected 64 patients was conducted. All the cases of cholelithiasis with choledocholithiasis were selected from patients attending Outpatient department/ Inpatient department of Department of Shalya Shalakya, S.S. Hospital, Institute of Medical Sciences, Banaras Hindu University Varanasi. All the patients were treated by cholecystectomy and choledochotomy with T-tube drainage.

Informed consent was taken from all patients in defined format regarding their participation.

All the 64 patients were analyzed for age, sex, occupation, dietary habit, bowel habit, and clinical features. These observations were recorded in a specially designed Performa. All the patients were subjected to routine hematologic, urine and stool investigations.

Criteria of inclusion

Patients of all age group, from both sexes, having cholecystitis / cholelithiasis with choledocholithiasis treated by cholecystectomy with choledochotomy (common bile duct exploration) with T-tube drainage. The patients were randomized sequentially they get operated.

Criteria of Exclusion

- Jaundice associated with malignancy
- Congenital biliary anomalies
- Common bile duct stricture

- Patients with HIV infection
- Patients with hepatitis B infection

Investigational drug

In the era of traditional medicines in India, Ayurveda has very rich legacy to treat different illnesses including jaundice since thousand years. Medicinal plants with the hepatobiliary mode of action remain essential therapeutic agents for the treatment of cholestasis. They are denoted as cholagogue (promoting the flow of bile from the liver and gallbladder into the intestines) and choleric (increasing bile production). "Phaltrikadi" has been mentioned in classics i.e "Bhaishajya Ratnavali (12/22)" and "Sharangdhara Samhita (2/75)" that "Phaltrikadi Kwath" is containing Haritaki (*Terminalia Chebula*), Vibhitaka (*Terminalia bellirica*), Amalaki (*Emblica officinalis*), Guduchi (*Tinospora cordifolia*), Vasa (*Adhoda vesica*), Kutki (*Picrorhiza kurroa*), Chirayita (*Swertia chirayita*) and Neem-bark (*Azadirachta indica*).

The composition of the decoction is as follows:

All the ingredients of the compound drug will be taken in equal proportions and in dried form as referred in Ayurvedic classic Sharangdhara Samhita (Dr. Srivastava Shailja, First edition, 1996, page 147). The drug was prepared and standardized as per the laid guidelines.³ The drug will be given 50 mL orally twice daily in the form of freshly prepared Decoction (Kwath); to the patients of Treated Group (Group A) from 4th post operative day to 10th post operative day, whereas nothing will be given to the patients of Control Group (Group B) in this period.

Methods for biochemical evaluation

Screening of biochemical changes in bile was carried out by various biochemical procedures with the help of following samples labeled as:

Sample I	-	Intraoperative bile
Sample II	-	Third postoperative day (Pre-therapy sample)
Sample III	-	Tenth postoperative day (Post-therapy sample)

In this study, all the relevant biochemical constituents of the bile, which are possible and feasible, were estimated quantitatively by enzyme kit methods. The parameters are inorganic (Na^+ , K^+ , Ca^{++} , Mg^{++} , Cl^-) as well as organic (Protein, Phospholipid, Cholesterol, Bilirubin Total, Triglycerides).

Observations & results

Statistical analysis was performed on a personal IBM compatible computer with M Stat Statistical Software. The data will be entered in dBase-III package. For comparison of mean difference between the groups, Student "t" test and Paired "t" test will be used.

Distribution of patients according to age

Total 64 patients were divided into 3 age groups. Out of these, the youngest patient was of 32 years while the eldest one was of 64 years. Average age of the patients in Group A (Mean \pm SD; 46.48 \pm 7.8) and Group B (Mean \pm SD; 46.84 \pm 6.38) is almost similar. Age has been positively correlated with cholesterol secretion rate and negatively correlated with bile acid synthesis, perhaps offering an explanation for age as a risk factor in cholesterol gallstone formation.^{4,5}

Distribution of patients according to sex

Observations of sex incidence in both the groups revealed that maximum number of patients were females i.e. 71% as compared to 29% of males. Epidemiological studies also show that gallstones are more common in women than in men, as endogenous estrogens at puberty or during pregnancy and exogenous estrogens given as contraceptives, postmenopausally, or pharmacologically all increase biliary cholesterol saturation and are associated with gallstone formation.⁶

Distribution of patients according to dietary habit

While observing the dietary habits of patients, it was found that 58% patients were non-vegetarians whereas 42% patients were vegetarians. Most cholesterol is endogenously synthesized, and dietary cholesterol has only limited impact on cholesterol saturation. Vegetable protein intake, however, seems to be negatively correlated with gallstone incidence.⁷

Distribution of patients according to addiction

In this present study, it was observed that maximum number of patients (33%) had a habit of tobacco chewing followed by smoking (23%) and alcohol (17%). However, 8 (27%) patients had no addiction.

Distribution of patients according to presenting features

All the patients were analyzed according to their presenting features and as per pre-designed proforma. It was also observed that no major difference was found between the both the groups regarding

their symptomatology. Majority of the patients complained of upper abdominal pain with nausea and fever. Jaundice was noticed in more than 90% patients of both the groups. It was most often associated with fever and chills. Some patients had history of rigor also. Vomiting was a presenting feature in 40% and 47% patients of Group A and B respectively.

Preoperative hematological parameters of patients

All the cases were subjected to surgical treatment therefore preoperative assessment of hematological parameters and other lab investigations were performed. Routine TLC, DLC, Hemogram, Fasting blood sugar level, Blood urea and Serum Creatinine etc. were estimated and found within normal range except hemoglobin levels which were at insignificant lower levels. Liver function test was also performed in all patients.

Assessment of inorganic parameters in bile

In the present study, the following inorganic ions were chosen and assayed by the different enzymatic kit methods – Ca⁺⁺, Mg⁺⁺, Cl⁻, whereas Na⁺, K⁺ were estimated by Flame Photometry. The predominant biliary cation is sodium, which is present in normal human bile in concentrations ranging from 141-165mmol/L. In our study, the sodium concentration is low as compared to standard and showing progressive decline during therapy. Progressive decrease in sodium ion concentration in bile is highly significant in Group A as compared to Group B (Table 1). Similar trends were also observed in biliary Potassium (K⁺) (Table 2), Calcium (Ca⁺⁺) (Table 3), Magnesium (Mg⁺⁺) (Table 4) and Chloride (Cl⁻) levels (Table 5). All of these were significantly decreased in Group A than Group B.

Table 1 Effect of polyherbal formulation on sodium level in bile

Effect of polyherbal formulation on sodium level in bile									
Groups	Bile Samples						Paired 't' Test/(p' value)		
	Sample I		Sample II		Sample III		I & II	II & III	I & III
Group A	107.33±18.57		92.12±17.41		80.30±13.99		4.848 p<0.001	7.714 p<0.001	8.442 p<0.001
Group B	131.64±17.77		122.90±15.80		112.70±15.85		6.078 p<0.001	9.079 p<0.001	10.518 p<0.001
Unpaired 't' Test	EVA	EVNA	EVA	EVNA	EVA	EVNA	Paired 't' Test at 'df' (Gr.A)= 32 Paired 't' Test at 'df' (Gr.B)= 30 Unpaired 't' Test at –		
t Value	-5.343	-5.350	-7.389	-7.412	-8.696	-8.662	Equal variances assumed 'df' = 62		
p Value	p<0.001	p<0.001	p<0.001	p<0.001	p<0.001	p<0.001	Equal variances not assumed 'df' = 60.7 [df = Degree of Freedom]		

Table 2 Effect of polyherbal formulation on potassium level in bile

Effect of polyherbal formulation on potassium level in bile									
Groups	Bile Samples						Paired 't' Test/(p' value)		
	Sample I		Sample II		Sample III		I & II	II & III	I & III
Group A	4.92±1.19		4.03±1.18		3.40±1.22		4.848 p<0.001	7.714 p<0.001	8.442 p<0.001
Group B	4.76±1.10		4.27±1.10		4.09±1.10		6.078 p<0.001	9.079 p<0.001	10.518 p<0.001
Unpaired 't' test	EVA	EVNA	EVA	EVNA	EVA	EVNA	Paired 't' Test at 'df' (Gr.A)= 32 Paired 't' Test at 'df' (Gr.B)= 30 Unpaired 't' Test at –		
t Value	0.551	0.553	-0.850	-0.852	-2.458	-2.473	Equal variances assumed 'df' = 62		
p Value	NS	NS	NS	NS	p<0.05	p<0.05	Equal variances not assumed 'df' = 60.7 [df = Degree of Freedom]		

Table 3 Effect of polyherbal formulation on calcium level in bile

Effect of polyherbal formulation on calcium level in bile									
Groups	Bile Samples						Paired 't' Test / ('p' value)		
	Sample I		Sample II		Sample III		I & II	II & III	I & III
Group A	3.145±0.626		2.677±0.574		2.343±0.513		8.048 p<0.001	5.498 p<0.001	8.453 p<0.001
Group B	2.966±0.614		2.733±0.617		2.480±0.540		5.888 p<0.001	6.283 p<0.001	8.766 p<0.001
Unpaired 't' test	EVA	EVNA	EVA	EVNA	EVA	EVNA	Paired 't' Test at 'df' (Gr.A)= 32 Paired 't' Test at 'df' (Gr.B)= 30 Unpaired 't' Test at –		
t Value	1.151	1.152	-0.378	-0.378	-1.039	-1.037	Equal variances assumed 'df' = 62		
p Value	NS	NS	NS	NS	NS	NS	Equal variances not assumed 'df' = 60.7 [df = Degree of Freedom]		

Table 4 Effect of polyherbal formulation on magnesium level in bile

Effect of polyherbal formulation on magnesium level in bile									
Groups	Bile Samples						Paired 't' Test / ('p' value)		
	Sample I		Sample II		Sample III		I & II	II & III	I & III
Group A	16.45±1.75		15.32±1.52		14.94±1.98		6.889 p<0.001	3.967 p<0.001	8.302 p<0.001
Group B	17.23±1.36		16.74±1.42		16.51±1.70		4.243 p<0.001	1.826 NS	4.243 p<0.001
Unpaired 'T' Test	EVA	EVNA	EVA	EVNA	EVA	EVNA	Paired 't' Test at 'df' (Gr.A)= 32 Paired 't' Test at 'df' (Gr.B)= 30 Unpaired 't' Test at –		
t Value	-1.993	-2.009	-3.305	-3.312	-3.393	-3.409	Equal variances assumed 'df' = 62		
p Value	NS	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05	Equal variances not assumed 'df' = 60.7 [df = Degree of Freedom]		

Table 5 Effect of polyherbal formulation on chloride level in bile

Effect of polyherbal formulation on chloride level in bile									
Groups	Bile Samples						Paired 't' Test / ('p' value)		
	Sample I		Sample II		Sample III		I & II	II & III	I & III
Group A	147.27±14.58		162.15±18.66		142.69±27.93		-6.619 p<.001	5.252 p<0.001	1.157 NS
Group B	174.41±22.87		169.51±19.58		157.74±18.06		2.217 p<0.05	4.792 p<0.001	5.031 p<0.001
Unpaired 'T' Test	EVA	EVNA	EVA	EVNA	EVA	EVNA	Paired 't' Test at 'df' (Gr.A)= 32 Paired 't' Test at 'df' (Gr.B)= 30 Unpaired 't' Test at –		
t Value	-5.698	-5.622	-1.541	-1.538	-2.540	2.574	Equal variances assumed 'df' = 62		
p Value	p<0.001	p<0.001	NS	NS	p<0.05	p<0.05	Equal variances not assumed 'df' = 60.7 [df = Degree of Freedom]		

Assessment of organic parameters in bile

In the present study, the following organic parameters were chosen and assayed by the different enzymatic kit methods.

In the present study, total protein level was significantly decreased within the groups during therapy and in Group A as compared to Group B (Table 6). In the present study, total cholesterol concentration showed progressive decline after initial rise on third day. After cholecystectomy rise in cholesterol concentration is a matter of speculation. Overall, cholesterol concentration was significantly

decreased in Group A than Group B (Table 7). Bile concentration of triglyceride (Table 8) and phospholipid (Table 9) showed progressive rise during therapy and triglyceride was significantly raised in Group A than Group B whereas no statistical significance was encountered in phospholipid concentration. Bilirubin concentration was progressively decreased during treatment in Group A and this decline was also significant after therapy when compared to Group B (Table 10). This may be due to free flow of bile after removal of obstruction and effect of the drug.

Table 6 Effect of polyherbal formulation on protein level in bile

Effect of polyherbal formulation on protein level in bile									
Groups	Bile Samples						Paired 't' Test / ('p' value)		
	Sample I		Sample II		Sample III		I & II	II & III	I & III
Group A	10.64±4.40		8.52±3.82		6.82±3.35		9.173 p<0.001	7.189 p< 0.001	9.236 p< 0.001
Group B	11.22±3.79		10.02±3.64		8.86±3.49		10.750 p<0.001	9.036 p<0.001	15.030 p<0.001
Unpaired 'T' Test	EVA	EVNA	EVA	EVNA	EVA	EVNA	Paired 't' Test at 'df' (Gr.A)= 32 Paired 't' Test at 'df' (Gr.B)= 30 Unpaired 't' Test at –		
t Value	-0.563	-0.566	-1.600	-1.603	-2.380	-2.377	Equal variances assumed 'df' = 62		
p Value	NS	NS	NS	NS	p<0.05	p<0.05	Equal variances not assumed 'df' = 60.7 [df = Degree of Freedom]		

Table 7 Effect of polyherbal formulation on cholesterol level in bile

Effect of polyherbal formulation on cholesterol level in bile									
Groups	Bile Samples						Paired 't' Test / ('p' value)		
	Sample I		Sample II		Sample III		I & II	II & III	I & III
Group A	515.57±64.95		540.72±67.76		483.71±72.01		-6.692 p<0.001	12.632 p<0.001	5.704 p<0.001
Group B	569.52±99.16		593.70±105.76		556.89±103.35		5.207 p<0.001	7.323 p<0.001	1.848 NS
Unpaired 'T' Test	EVA	EVNA	EVA	EVNA	EVA	EVNA	Paired 't' Test at 'df' (Gr.A)= 32 Paired 't' Test at 'df' (Gr.B)= 30 Unpaired 't' Test at –		
t Value	-2.590	-2.557	-2.401	-2.369	-3.303	-3.267	Equal variances assumed 'df' = 62		
p Value	p< 0.05	p<0.05	p< 0.05	p< 0.05	p< 0.05	p<0.05	Equal variances not assumed 'df' = 60.7 [df = Degree of Freedom]		

Table 8 Effect of polyherbal formulation on triglyceride level in bile

Effect of polyherbal formulation on triglyceride level in bile									
Groups	Bile Samples						Paired 't' Test/('p' value)		
	Sample I		Sample II		Sample III		I & II	II & III	I & III
Group A	198.17±70.42		231.72±75.59		251.97±76.26		-3.548 p<0.01	-4.373 p<0.001	-5.204 p<0.001
Group B	152.08±26.99		165.63±26.49		170.02±24.14		7.121 p<0.001	1.719 NS	-6.134 p<0.001
Unpaired 'T' Test	EVA	EVNA	EVA	EVNA	EVA	EVNA	Paired 't' Test at 'df' (Gr.A)= 32 Paired 't' Test at 'df' (Gr.B)= 30 Unpaired 't' Test at –		
t Value	3.415	3.497	4.607	4.723	5.718	5.869	Equal variances assumed 'df' = 62		
p Value	p<0.05	p< 0.05	p<0.001	p<0.001	p<0.001	p<0.001	Equal variances not assumed 'df' = 60.7 [df = Degree of Freedom]		

Table 9 Effect of polyherbal formulation on phospholipids level in bile

Effect of polyherbal formulation on phospholipids level in bile									
Groups	Bile Samples						Paired 't' Test/('p' value)		
	Sample I		Sample II		Sample III		I & II	II & III	I & III
Group A	20.54±4.31		21.27±4.47		20.63±4.97		-3.095 p<0.05	2.478 p<0.05	-0.304 NS
Group B	19.86±4.40		21.34±4.51		21.35±4.57		-7.211 p<0.001	-0.043 NS	-6.5075 p<0.001
Unpaired 'T' Test	EVA	EVNA	EVA	EVNA	EVA	EVNA	Paired 't' Test at 'df' (Gr.A)= 32 Paired 't' Test at 'df' (Gr.B)= 30 Unpaired 't' Test at –		
t Value	0.625	0.625	-0.064	-0.064	-0.608	-0.610	Equal variances assumed 'df' = 62		
p Value	NS	NS	NS	NS	NS	NS	Equal variances not assumed 'df' = 60.7 [df = Degree of Freedom]		

Table 10 Effect of polyherbal formulation on bilirubin level in bile

Effect of polyherbal formulation on bilirubin level in bile									
Groups	Bile Samples						Paired ' t ' Test/('p' value)		
	Sample I		Sample II		Sample III		I & II	II & III	I & III
Group A	6.67±2.11		5.47±2.12		4.01±2.21		8.691	9.746	11.944
							p<0.001	p<0.001	p<0.001
Group B	6.04±1.70		5.19±1.57		4.46±1.62		7.287	6.549	8.302
							p<0.001	p<0.001	p<0.001
Unpaired ' t ' test	EVA	EVNA	EVA	EVNA	EVA	EVNA	Paired ' t ' Test at 'df' (Gr.A)= 32		
							Paired ' t ' Test at 'df' (Gr.B)= 30		
							Unpaired ' t ' Test at –		
t Value	1.317	1.325	0.595	0.601	-0.925	-0.934	Equal variances assumed 'df' = 62		
p Value	NS	NS	NS	NS	NS	NS	Equal variances not assumed 'df' = 60.7		
							[df = Degree of Freedom]		

Discussion

Advancement of medical science towards the benefit of mankind resulted in discovery of different types of drugs for the management of different diseases. In spite of their advancement, there are some areas where appropriate drugs are yet to be discovered.

Biliary stone disease is such an area, which is still remaining dark according to modern medical science regarding the development of an appropriate drug. Research is going on in different countries for the development of anticholelithiatic drugs. So far whatever drugs are available have very few indications and therapeutic benefits and whatever studies have been carried out, were based on the dissolution of biliary stones.

The present study was designed to evaluate the biochemical parameters in bile in biliary stone diseases and effect of trial drug “PHALTRIKADI KWATH” on these deranged parameters. In fact, we have tried to evaluate whether this trial drug maintains the biochemical equilibrium of bile after cholecystectomy not the stone dissolving property of the drug. We have already reported the antioxidant property of Phaltrikadi Kwath, in which bile samples were analyzed at different intervals and the study points that the drug significantly lowers the oxidative stress in bile. As free radical injury is proved to be implicated in gall stone formation, reduction of free radical formation (oxidative stress) improves the biochemistry of bile and thus prevents the stone formation.³

Very recently we claimed that patients of asymptomatic and uncomplicated biliary sludge can have chance to recover from their ailment by offering them “Srivastava regimen for biliary sludge” which contained oral ampicillin, Ursodeoxycholic acid, and Phaltrikadi Kvatha (decoction) or Ghanbati (Tablet) for minimum of 45days, with dietary fat restriction, plenty of water intake and avoiding all the possible confounding factors of gallstone diseases. In most of the patients, biliary sludge vanished and gallbladder appeared completely normal in ultrasonography.⁸ The gallstones are frequently encountered in females and our study also favors this finding. In our study, the sex ratio is almost equal in both the groups with female preponderance (45 Females/19 Males). The mean age of patients in Group A is also almost equal to Group B (46.48±7.86 vs 46.84±6.38). The youngest patient was of 32years while the eldest one was of 64years.

Although a large literature exists on the relation of diet to gallstone risk, little consensus has emerged on the role of specific constituents in gallstone induction. In our study, vegetarians (42%) were affected less than the non-vegetarians (58%) and it is proved that vegetable protein intake seems to be negatively correlated with gallstone

incidence. The type of occupation between case and controls did not differ in our study for women but they did differ in men. As most of the victims were females in our study, the percentage of housewives was highest followed by laborers in both the groups. Tobacco chewing had emerged as a most common addiction in our study (33%) followed by smoking and alcohol. As such, tobacco chewing has not been looked into by other workers, even though these are common social habits in the Indian community. How nicotine could influence risk of Gallstone disease is not clear.

Alcohol did not influence the occurrence of gallstone disease. Almost a 20% cases were alcoholics in our study. The proportion of teetotalers or the current alcoholics did not differ in the 2 groups. This is similar to the reports by Schwesinger et al where alcohol was not associated with greater risk to gallstone disease.⁹ Several other workers however found that use of alcohol in small to moderate amounts may be protective against gallstone formation. The exact mechanism is not clear but probably it lowers the biliary cholesterol saturation index. The presenting features of both the groups were almost similar. Majority of the patients complained of upper abdominal pain with nausea and fever. Jaundice was noticed in more than 90% of patients. Vomiting and fever with chills were also present in one third of the patients.

All the patients were assessed preoperatively on hematological parameters and no significant differences have been observed in both the groups. Liver function test was also performed and it was observed that serum bilirubin and alkaline phosphatase were high in both the groups.

Estimation of inorganic parameters in bile

The inorganic electrolytes are largely responsible for the osmotic activity of bile, because osmotic activity of most of the organic solutes, such as bile acids, is lost by aggregation into mixed micelles. Sodium and Potassium are particularly important for bile formation and secretion as bile acid independent flow largely depends on these electrolytes. However, inorganic electrolytes may not provide a sufficient driving force for Bile-Acid Independent Bile Flow because their biliary secretion depends primarily on passive diffusion and solvent drag.

The concentration of calcium in bile, especially gallbladder bile, may even be higher, in comparison with its plasma concentration, than is the case with sodium and potassium. This may be due to micelle formation. In addition, the electronegativity of the gallbladder lumen may predispose to higher concentrations of divalent than of monovalent cations.

The trial drug has shown electrolyte lowering effect which is suitable in case of calcium as it is implicated in further stone formation and recurrence. Thus it has got litholytic property against gallstones particularly as a preventive measure.

Estimation of organic parameters in bile

Under organic parameters, biliary protein, total cholesterol, phospholipids, triglycerides, and total bilirubin were assessed. In humans, biliary protein concentrations between 0.02 and 5.3 g/L have been reported in hepatic bile and up to 5.5g/L have been found in gallbladder bile, accounting for less than 5% of total biliary solids.

Plasma proteins (primarily albumin), hepatocellular enzymes derived from the outer leaflet of the canalicular membrane and lysosomes, and several proteins peculiar to bile have been identified in bile.

A significant portion of albumin is derived from a newly synthesized pool and is directly secreted into bile. The functional significance of biliary proteins remains largely a matter for speculation. Biliary proteins have generated most attention in pathogenesis of gallstones, as total biliary protein content is increased in bile with cholesterol crystals compared with samples without crystals. Proteins identified as pronucleators include aminopeptidase N, immunoglobulins G and M, haptoglobin, fibronectin, and α_1 -antichymotrypsin.

Overall, assessment of the study reflects some important facts regarding the biliary physiology after cholecystectomy and the efficacy of trial drug on bile composition as well. Inorganic and organic parameters were assessed and overview suggests that the trial drug has got some promising role in the biliary stone disease as there were significant differences in above mentioned parameters in Group A as compared to Group B. Symptomatic relief was also observed in patients but could not be documented due to some limitations.

At last, we can lay down an impression that the trial drug "PHALTRIKADI KWATH" has got some potential in relieving the biliary stone disease by maintaining the bile chemistry in equilibrium as may be helpful in avoiding the recurrence of stones after successful cholecystectomy.

Conclusion

Biliary tract is most commonly affected by stone formation. In many countries gallbladder surgery has become the most common operative procedure due to gallstone disease. Surgery and recently developed modalities are only helpful for removal of formed stones but these have no role regarding the eradication of metabolic error or prevention of recurrence. Hence a drug is essentially required which has property like both the correction of deranged bile chemistry and prevention of recurrence. Many modern drugs and chemicals have been tried with the concept of dissolution of stones but got limited success. In Ayurveda Phaltrikadi Kwath is described for the management of obstructive jaundice, widely used for the same in all over the country and abroad as well. Therefore it was selected for the present study.

Drug is proved as a potent cholagogue that increases the bile flow. The inorganic parameters were assessed and it is concluded that the drug decrease electrolyte concentrations in bile especially

calcium level which is well known lithogenic factor and implicated in gallstone formation. Drug also decreases the biliary protein level, bilirubin level and cholesterol as well. These are the important metabolic factors responsible for the causation of the gallstones. By lowering the concentrations of the above-mentioned organic solutes it decreases the possibility of the recurrence and also causes rapid postoperative recovery of the patients.

As there are very few studies and research work available on bile chemistry further studies are required. Likewise in the present study the drug is proved to be effective and promising in the management of biliary stone diseases further more elaborative studies are needed to find out the effect of the drug on nucleation time, which can give a better idea regarding the anticrystallization property of the drug.

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Conflicts of interest

No conflict of interest declared by the author.

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