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Evaluation of anti lithiatic effect of Maavilinga Kudineer Chooranam (MKC) on 1% ethylene glycol induced lithiasis in albino rats

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Abstract

Urinary stone disease has afflicted humankind since antiquity and can persist, with serious medical consequences, throughout a patient's lifetime. In our Siddha system Urolithiasis may be compared to Kalladaippu. Kalladaippu is the most common diseases of present society due to modern life style and abnormal diet habits. Currently, open renal surgery for urolithiasis is unusual and used only rarely since the introduction of extracorporeal shockwave lithotripsy (ESWL), which has revolutionized urological practice and almost become the standard procedure for eliminating kidney stones. However, in addition to the traumatic effects of shock waves, persistent residual stone fragments and the possibility of infection, suggest that ESWL may cause acute renal injury, a decrease in renal function and an increase in stone recurrence. In the indigenous system of medicine, the Maavilinga Kudineer Chooranam (MKC) is reported to be useful in the treatment of urinary stones. In the present study, an effort has been made to establish the scientific validity for the antilithiatic property of MKC using ethylene glycol induced lithiasis model in albino rats.

Keywords: maavilingam, mkc, urinary stones, antilithiatic, eswl

Introduction

Siddha system is one of the oldest systems of medicine in India. Siddha system is based on truth and philosophy. This Medicine system has unique features like removal the root cause of the disease and perfect remedy for body, mind and soul. The incidence of Urolithiasis is very common in the world. In our Siddha system Urolithiasis may be compared to Kalladaippu. Kalladaippu is the most common diseases of present society due to modern life style and abnormal diet habits. The efficacy of invasive therapies such as extra corporeal shock wave lithotripsy and ureteroscopy has been proven by several studies. However these techniques are not risk free and they are problematic and quite expensive and complication. In the Siddha text, MAAVILINGA KUDINEER CHOORANAM is indicated for Kalladaippu. It is less expensive and it has no complications. In this study, Antilithiatic property of MKC is analysed.

Materials and Methods

" Maavilinga Kudineer Chooranam" is a poly herbal formulation which indicated as a drug in Siddha sastric text for treatment of urinary stone, burning micturition, dysuria etc. The ingredients of Maavilinga kudineer chooranam are Crateva magna, Pavonia odorata, Tribulus terrestris, Aerva lanata. The drug was prepared as per the text.

Ethylene glycol induced hyperoxaluria model (5) was used to assess the antilithiatic activity in albino rats. Animals were divided into six groups containing six animals in each.

Treatment protocol:

The grouped animal's received the treatment as follows

Group I Received normal diet and served as controls.
Group II Lithiatic control: The animals were given normal diet and 1% Ethylene glycol in drinking water for 28 days.

Prophylactic Study:

Group III Received 1% ethylene glycol in drinking water and then treated with Maavilinga kudineer chooranam at a dose of 100 mg/kg orally for 28 days
Group IV Received 1% Ethylene glycol in drinking water and then treated with Maavilinga kudineer chooranam at a dose of 200mg/kg orally for 28 days.
Group V Received 1% Ethylene glycol in drinking water and treated with Maavilinga kudineer chooranam at a dose of 300mg/kg orally for 28 days.
Group VI Received 1% Ethylene glycol in drinking water and treated with cystone at a dose of 500mg/kg orally for 28 days.

Collection and analysis of urine:

All animals were kept in individual metabolic cages and 24 h urine samples were collected on 28th day of calculi induction treatment. Urine was analyzed for oxalate , magnesium, phosphate, uric acid, creatinine and total protein.

Results

Table 1 Effect on urinary biochemical parameters on the day 28

GP	Protein (mg/dl)	Magnesium (mg/dl)	Calcium (mg/dl)	Uric acid (mg/dl)	Creatinine (mg/dl)	Oxalate (mg/dl)	Phosphate (mg/dl)
GP_1	71.92± 2.95	4.30± 0.52	5.68± 0.50	8.14± 0.68	0.82± 0.10	17.86± 1.45	35.94± 2.85
GP_2	152.32 ± 5.30$^{**(a)}$	1.15 ± 0.20$^{**(a)}$	25.20± 1.90$^{**(a)}$	16.60 ± 1.60$^{**(a)}$	1.61 ± 0.14$^{**(a)}$	30.72 ± 3.20$^{**(a)}$	76.64 ± 4.30$^{**(a)}$
GP_3	88.35 ± 3.92 $^{**(b)}$	2.60 ± 0.30$^{**(b)}$	19.30 ± 2.15$^{**(b)}$	10.60 ± 0.95$^{**(b)}$	0.99 ± 0.09$^{**(b)}$	24.30 ± 2.45$^{**(b)}$	45.60 ± 3.75$^{**(b)}$
GP_4	84.52 ± 3.55$^{**(b)}$	2.82 ± 0.40$^{**(b)}$	13.45 ± 0.80$^{**(b)}$	12.35 ± 0.84$^{**(b)}$	0.92 ± 0.11$^{**(b)}$	22.14 ± 2.32$^{**(b)}$	40.82 ± 3.22$^{**(b)}$
GP_5	85.15± 3.70$^{**(b)}$	2.66 ± 0.44$^{**(b)}$	15.70 ± 0.60$^{**(b)}$	9.95 ± 0.85$^{**(b)}$	0.89 ± 0.09$^{**(b)}$	23.22 ± 1.92$^{**(b)}$	36.25 ± 2.30$^{**(b)}$
GP_6	81.30± 2.85$^{**(b)}$	3.33 ± 0.58$^{**(b)}$	17.68 ± 0.42$^{**(b)}$	8.92 ± 0.76$^{**(b)}$	0.84 ± 0.10$^{**(b)}$	20.22 ± 1.88$^{**(b)}$	35.25 ± 2.30$^{**(b)}$

GP_1- Normal; **GP_2**- Lithiatic Control; **GP_3**- MKC (100mg/kg);
GP_4- MKC (200mg/kg); **GP_5**- MKC (300mg/kg); **GP_6** - Cystone herbal tablets (500mg/kg)

- Values are expressed as mean ± SEM
- Values were found out by using ONE WAY ANOVA Followed by Newman keul's multiple range tests.
- **(a) Values were significantly different from normal control (GP_1) at P< 0.01
- **(b) Values were significantly different from Lithiatic control (GP_2) at P<0.01

As traditional medicines are usually taken by the oral route, same route of administration was used for evaluation of antilithiatic effect of the MKC at a dose of 100, 200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg against ethylene glycol induced urolithiasis in rats.

In the present study, male rats were selected to induce urolithiasis because the urinary system of male rats resembles that of humans [13] and also earlier studies have shown that the amount of stone deposition in female rats was significantly less.

Urinary supersaturation with respect to stone-forming constituents is generally considered to be one of the causative factors in calculogenesis. Evidence in previous studies indicated that in response to 28 day period of ethylene glycol (1% v/v) administration, young male albino rats form renal calculi composed mainly of calcium oxalate. The biochemical mechanisms for this process are related to an increase in the urinary concentration of oxalate. Stone formation in ethylene glycol fed animals is caused by hyperoxaluria, which causes increased renal retention and excretion of oxalate. Similar results have been obtained when rats were treated with ethylene glycol and ammonium oxalate. Therefore, this model was used to evaluate the antilithiatic effect of MKC at a dose of 100, 200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg against urolithiasis.

Effect of maavilinga kudineer chooranam on urinary parameters on day 28

The oxalate excretion was 24hr on day 28th respectively for GP_1. It increased significantly ($P < 0.001$) on day 28th day in GP_2 following ethylene glycol treatment. Treatment at a dose of Maavilinga kudineer chooranam (MKC) 100mg/kg, 200mg/kg and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg (GP_3 to GP_6) reduced the oxalate excretion significantly to ($P<0.01$) on 28th day treatment.

The urinary calcium excretion was increased significantly on day 28th day in GP_2 following ethylene glycol treatment. The calcium excretion was significantly reduced to treatment with MKC at a dose of 100, 200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg (GP_3 to GP_6) reduce the calcium excretion significantly to on 28th day treatment .

Likewise phosphate and creatinine excretion values gradually increased in GP_2 on the 28th day. However in (GP_3 to GP_6) grouped treated animals these elevated values were significantly reduced on 28th day respectively. However, regarding creatinine in (GP_3 to GP_6) these elevated values were significantly reduced on 28th day respectively.

Likewise urinary protein and uric acid concentration increased following ethylene glycol treatment in GP_2 and it reached maximum respectively on the 28th day. On treatment with MKC at a dose of 100, 200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg (GP_3 to GP_6) the protein and uric acid excretion was restored to near normal limits in (GP_3 to GP_6).

In GP_2 lithiatic control rats, the magnesium level in urine gradually decreased following ethylene glycol treatment on the 28th day . Subsequent administration of the MKC and cystone herbal tablets enhanced the magnesium excretion significantly on 28th day.

Discussion

In the present study oxalate and calcium excretion progressively increased in calculi- induced animals (GP_2), since it is accepted that hyperoxaluria, is a far more risk factor in the pathogenesis of renal stones than hypercalciuria, and the changes in urinary oxalate levels are relatively much more important than those of calcium. Increased urinary calcium is a factor favouring the nucleation and precipitation of calcium oxalate (or) apatite (calcium phosphate) from urine and subsequent crystal growth. However MKC at a dose of 100, 200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg lowered the levels of oxalate as well as calcium excretion.

An increase in urinary phosphate is observed in calculi induced rats (GP_2). Increased urinary phosphate excretion along with oxalate stress seems to provide an environment appropriate for stone formation by forming calcium phosphate crystals, which is epitaxially induces calcium oxalate deposition.Treatment with MKC at a dose of 100, 200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg restored phosphate level, thus reducing the risk of stone formation.

The increases in urinary uric acid excretion were observed in urolithiatic rats. Increased excretion of uric acid has been reported in stone formers and hyperoxaluric rats. Uric acid interferes with calcium oxalate solubility and it binds and reduces the inhibitory activity of glycosaminoglycans. The predominance of uric acid crystals in calcium oxalate stones and the observation that uric acid binding proteins are capable of binding to calcium oxalate and modulate its crystallization also suggests its primary role in stone formation. Treatment with MKC at a dose of 100,200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg lowered the excretion of uric acid and reduces the risk of stone formation.

Supersaturation, a step in the pathogenesis of nephrolithiasis, occurs when substances that make up the stone are found in the high concentration in urine, when urine volume decreases, and when urinary concentration of chemicals that inhibit stone formation decreases. Inhibitors of crystallization include citrate, magnesium, phosphate; nephrocalcin etc. Low urinary magnesium content is a common feature in stone formers . A similar condition was observed in the (GP_2) rats. Treatment with MKC at a dose of 100,200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg elevated the urinary magnesium level, and

thus, reduced the propensity to crystallize, thereby creating an ambience unfavourable for precipitation.

Increased excretion of proteins has been noted in hyperoxaluric rats and stone formers .A high urinary colloidal concentration favours crystal growth. Such a condition was observed with ethylene glycol treated rats, in this study. Administration of MKC at a dose of 100,200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg reduced the urinary protein excretion in the treated group rats, and hence minimizes the conditions favourable for crystal growth.

In calculi- induced rats (GP_2), marked renal damage was seen as indicated by the elevated serum levels of creatinine and uric acid. However, the prophylactic treatment MKC at a dose of 100, 200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg causes diuresis and hastens the process of dissolving the preformed stones and prevention of new stone formation in the urinary system.

Conclusion

Result shows the urinary calcium, oxalate, phosphate, uric acid, creatinine, protein excretion are increased significantly on day 28^{th} day in GP_2 following ethylene glycol treatment. The calcium, oxalate, phosphate, uric acid, creatinine, protein excretion are significantly reduced to treatment with MKC at a dose of 100, 200 and 300mg/kg and cystone herbal tablet at a dose of 500mg/kg (GP_3 to GP_6) reduce the calcium excretion significantly to on 28^{th} day treatment .

The test drug Maavilinga kudineer chooranam prevent calculi formation of kidney. so the test drug are responsible for anti lithiatic activity.

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