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Unveiling Homoeopathy as Medical Expulsive Therapy in Management of Ureteric Calculi

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Abstract

Increase the pace of stone expulsion down the ureter to prevent ureteral obstruction and reducing ureteral colic to prevent the need for more invasive and surgical procedures. Ureteric calculi- stone in ureter which is very common problem in Endourology. Explanation of current existing conventional MET options like alpha adrenergic antagonists, calcium channel blockers, nonsteroidal anti-inflammatory drugs with their side effects and finding empirical proofs for efficacy of Homoeopathy in management of ureteric calculi were the main focus of this review. A review of various published articles of randomized clinical trials, observational study, experimental studies, systematic reviews from 2021-24 are included. Indications for conservative management in ureteric calculi is mentioned based on which Homoeopathy can be considered as a treatment modality according to patients need, rather than rushing into surgical options directly as evidence clearly shows that have ability in spontaneous stone expulsion of calculi, reduce the size of calculi, the tendency of developing calculi. Research data available till now points towards the scope of Homoeopathy for expulsion of ureteric calculi in uncomplicated cases where surgical intervention is not required. Focusing more on patients need might give opportunity for approach of complementary and alternative medicines such as Homoeopathy to effectively tackle cases without invasive procedures unless mandatory. Thus, this review outlines CAM like Homoeopathy shows the potential to be the future of effective medical expulsive therapy due to available pre-clinical studies but require more clinical trials to demonstrate their efficacy.

Keywords: CAM, Clinical trials, Homoeopathy, In vitro experiments, Medical expulsive therapy, Ureteric calculi

1 Background

Urolithiasis, also called as urinary stones, is commonest condition approximately in 1 out of 10 individuals with increasing incidence and prevalence worldwide. Theories to explain Ureteric calculus are incomplete and may requires supersaturated urine, pH of urine, ionic strength, solute concentrations, complexation [1]. It is regarded as the third most prevalent urological condition and a common cause of morbidity [2, 3].

A stone in ureter usually comes from kidney above and often causes intermittent attacks of ureteric colic – waves of agonizing pain are typically referred to the groin, external genitalia, hematuria is a typical presentation of ureteric obstruction, most commonly due to calculi [4]. The size, location, composition, and symptoms of the stone all influence the management and therapy options for urolithiasis. Patients who have blocked, infected kidneys need a nephrostomy or stent placed immediately, while people who are afebrile, have a normal contralateral kidney, and have normal renal function are typically treated conservatively [5].

Since the mechanism of stone formation is a complex process resulting from several physicochemical events, such as supersaturation, nucleation, growth, aggregation, and retention of urinary stone constituents within tubular cells, it is shown that the best clinical evidence for homeopathy available till date allow positive evidence for its use in day to day clinical practice. An imbalance between the variables that encourage or prevent urine crystallization affects these stages. The pathophysiology of urolithiasis encompasses both the internal and external constitution and is not limited to the urinary tract alone. Since urolithiasis has multiple causes, a comprehensive approach is necessary for the efficient management of ureteric calculi [6].

1.1 Anatomy and Physiology of Ureter

The adult human ureter is a muscular tube that is physically separated into three sections: the proximal, middle, and distal ureter. It is primarily made up of smooth muscle cells and is bordered by the urothelium, a multilayered transitional epithelium. Smooth muscle cells are divided into two layers: the outer circular layer coats the ureteral walls and contracts to provide intraluminal pressure, while the inner longitudinal layer is responsible for ureteral shortening and urine movement. Urine is moved from the kidneys to the bladder by waves of smooth muscle contraction and relaxation traveling down the muscular tube, which is the main purpose of this organ. The interstitial cells of Cajal (ICC)-like cells, which are located in the renal pelvis and proximal sections of the human ureter, are the renal pacemaker cells that control this process. The absence of Back 5 ICC-like cells in the ureter's distal areas indicates that ureteral peristalsis begins at the renal pelvis, with the ureter's proximal part thereafter myogenically conducting down the ureteral tube.

1.2 Current Conventional Medical Expulsive Therapy

1.2.1 Alpha adrenoceptor antagonists

Functional tests conducted on isolated ureters from pigs and humans in vitro indicate that contraction is the primary response to noradrenaline, suggesting that α-adrenoceptors function more prominently than β adrenoceptors [5, 6]. There are three primary subtypes of α-adrenoceptors: α1A,1B,1D. G-proteins belonging to the G family primarily couple the subtypes of α-adrenoceptors to trigger the phospholipase C mechanism, hence inducing contraction of smooth muscle [7].

1.2.2 Calcium Channel blockers

Calcium channel blockers are frequently used to decrease smooth muscle contractions in illnesses including hypertension, angina, and arrhythmias since smooth muscle contraction in most tissues traditionally occurs via an increase in intracellular calcium. Thus, in isolated ureteral tissues from humans and pigs, calcium channel blockers such as nifedipine, verapamil, and diltiazem suppress spontaneous rhythmic activity and inhibit ureteral contractile activity induced by electrical stimulation, potassium, and phenylephrine [8]. Although nifedipine is effective in raising expulsion rate, most studies that have examined the usefulness of nifedipine alone as a therapy have found that it is significantly less effective than tamsulosin [9, 10]. In addition, compared to participants receiving a placebo or tamsulosin, nifedipine was linked to a greater frequency of side effects, such as headaches, nausea, and drowsiness [9].

1.2.3 Non-Steroidal anti-inflammatory drugs

It is commonly known that cyclooxygenase (COX) enzymes are necessary for the formation of prostaglandins (PG) because they convert arachidonic acid to an intermediate PGH, which is subsequently metabolized to PGD, PGE, PGF, and PGI. The COX enzyme has two isoforms: COX-1, which is expressed constitutively in many tissues, and COX-2, which is inducible and can be triggered by a variety of stimuli, such as nerve stimulation, mucosal injuries, and inflammatory mediators [11].

Earlier clinical trials examining the effects of non-steroidal anti-inflammatory medicines (NSAIDs) showed that NSAIDs can relieve colic in patients with urolithiasis given prostaglandins' apparent function in raising pain sensitivity [12]. The two NSAIDs that are most frequently used for ureteral colic are celecoxib and diclofenac ,in order to minimize many of the side effects the majority of trials have only included short-term NSAID prescriptions usually in conjunction with either α-adrenoceptor antagonists or calcium channel blockers have known to be a useful treatment [13-15].

1.3 Indications of Conservative Treatment in Ureteric Calculi

European and US(EAU/AAU) guidelines recommend, MET as an option when following conditions are met, with close follow-up which is clinically effective, as 88% of the patients did not require surgery for their stone [16].

1. Newly diagnosed ureteric stone < 10mm in adults, young people [NICE 2019 Guidelines for renal and ureteric stones management]
2. Well controlled pain
3. Good renal function
4. Periodic imaging to monitor stone position and assess hydronephrosis
5. A prerequisite for MET is that the patient is reasonably comfortable [Copyright © 2007 American Urological Association Education and Research, Inc.® and European Association of Urology® 33] with that therapeutic approach.

2 Materials and Methods of Literature Review

2.1 Search Strategy

Relevant articles and literature were searched using electronic databases. Following terms like (medical expulsive therapy or ureteral/ureteric stone) are used in search process.

2.2 Study Selection

The article selection was conducted according to the search strategy. The search and selection criteria were limited to inclusion and exclusion criteria mentioned. Studies that did not satisfy the mentioned criteria will be excluded.

- **Inclusion Criteria**
  - Latest publications from 2021-24, All studies/clinical trials/Homoeopathy articles related to topic published in peer reviewed, UGC care journals only.
  - Population with pre/newly diagnosed cases of ureteric calculi, intervention, outcomes (disease management) research and study design (meta-analysis, systematic reviews, randomized clinical trials, trials of any kind).
  - Inclusion criteria have been identified to limit the risk of bias and ensure the relevance of selected articles to research questions
- **Exclusion Criteria**
  - Articles with no proper evidence in prevalence study, survey, reviews/expert opinion articles involving the paediatric population.
  - In order to include additional significant contributions, the references of the eligible articles were evaluated by conducting a retrospective process to retrieve and analyse these sources.
  - Duplicated articles, case reports, citations will be excluded.
- **Information Sources**

Cochrane library, Medline, Embase, Elsevier.

- **Selection Process**

A Preliminary selection of studies after database searching process was performed independently by two researches, through title and abstract analysis, in order to verify the adherence to reviews topic and research topics. Identifying the primary papers [n=2679], excluding the studies based on titles[n=1009], excluding the studies based on full texts [n=590], excluding based on eligibility criteria [n=53], excluding based on dates [n=8]

First search: At the beginning articles were obtained using the search engines from individual databases using the main terminology in broader aspects. Specific key words were further applied step wise to the obtained articles which brought down the number to 53 after which eligibility criteria narrowed it to 8.

Second search: from the references of primary papers, many were screened but got removed after eligibility criteria assessment. so, none was added. Extracting data from final set of 10 papers with data analysis was done which showed the following information.

3 Results

The results of literature search are tabulated as follows:

4 Future Directions for Homoeopathy as Medical Expulsive Therapy

Making patient centered care as central idea for medical management, CAM can be given a chance in this particular field of urology to minimize the chances of surgery and increase the chances of conservative management unless associated with complications. Many Research articles are found to focus on the central idea of integrative medicine, differentiated by its patient-centered, holistic approach and its seamless integration of conventional and complementary therapies. Homeopathy involves the administration of personalized remedies that are specifically suited to address particular symptoms [17].

- Role of Homoeopathy in Spontaneous Stone Expulsion of Ureteric calculi remains unexplored.
- This genuine research work may set the foundation block for further advanced homoeopathic researches in Endourology.
- Lack of evidence based researches, with proper documentation regarding stone expulsion with the use of Homoeopathy.
- Scope of individualized homoeopathic medicines in SSP of ureteric calculi apart from specifics/ organopathic prescriptions shall be known.

Sr. No	Article Names	Authors	Year of Publication	Name of Journal	Summary	Comments
1	Efficacy -homoeopathic medicines in cases of urolithiasis-organopathy	Dr. Virendra Chauhan, Dr. Abhishek Dalmia, Dr. Sanjay Verma, Dr. Kruiti Saraswat	2021	International Journal of Homoeopathic Sciences	The constitutional approach is most suitable way, but at times patients are in acute pain, hence snap short prescription is to give relief to the patient. Organopathy : homeopathic case-taking the locality of the symptoms expressed and their relation to a specific organ determine the remedy.	PROS: Evidence attached. CONS: Follow up duration is not specified with accuracy.
2	A multicentric observational study of ascertaining the role of homoeopathic therapy-Urolithiasis	A. Siddiqui, Hari Singh, Jaya Gupta, C. Nayak, Vikram Singh, M. N. Sinha, A. K. Gupta, Paul	Aug 19, 2021	Indian Journal of Homoeopathic Sciences on	It is an observational study based on these results CCRH intends to take up Randomized Controlled Trial, outcome assessment pre and post was done by urolithiasis symptom score (USS). Pain, Dysuria and Hematuria were graded from 0- 3 as per severity of complaints.	PROS: 1.Observational study conducted by CCRH. 2. Non parametric test of Wilcoxon sign rank test was used. CONS: 1. It is not an RCT. 2. The marked improvement of cases is only 48%.
3	Preliminary Investigations on Ultra High Diluted Berberis Vulgaris-Experimental Urolithiasis	Ganesan T, Alok Kumar, Anil K	2021	National Library of Medicine	Biomineral Levels were reduced by B. vulgaris treatment. The decreased levels of urolithiasis inhibitor magnesium in urine was prevented by treatment with B. vulgaris. Serum creatinine levels were reduced by B. vulgaris treatment.	PROS: Strong anti urolithiatic potential was proved even in diluted doses. CONS: 1. It's an in vivo experimental study. 2. Clinical trial must be done to assess the exact efficacy.
4	Practice of Berberis V and Lycopodium in urolithiasis: A systemic review	Laila Sumreen , Rida Tanveer and Tahira Shamim	June, 2021	International journal of homeopathic sciences	It was taken up to evaluate the efficacy of Berberis vulgaris and Lycopodium in the treatment of urolithiasis. Total 1471 articles were evaluated. Total 195 patients were treated in these 7 studies and 7 case reports, Stone as large as 23 mm was expelled .	PROS: Positive alternative for conventional MET Options. CONS: Only 7 articles are used for review.
5	In vitro anti urolithiatic activity of macerated extract of Terminalia C. by using titrimetric method	V. Anu, S. Akhila, Iswarya Ajaya Kumar and Sneha Antony	June, 2021	International journal of pharmacognosy	In-vitro study was conducted to study the anti-urolithiatic effect of fruits of a macerated aqueous extract with standard drug Cystone Aqueous extract of fruits of Terminalia chebula proved a significant effect compared with standard drug Cystone.	PROS: Potential anti-urolithiatic effect is known. CONS: It's a pre-clinical study.

Sr. No	Article Names	Authors	Year of Publication	Name of Journal	Summary	Comments
6	Homoeopathic Medicine Tribulus Terrestris Q,12C,30C,200C,1M : an inhibitor of calcium oxalate, phosphate crystallization -Invitro study	Dr. Sharada Shankar Gowda, Prof. Dr. Tanveer A.Khan,Dr. Ajay Namdeo,Dr.Chetan H. Shinde	September, 2021	International journal of Scientific research	Scavenging activity was performed for mother tincture and 12C of Tribulus terrestris to test the presence of anti-oxidative property. It plays a major role as a reactive oxygen species in reduction of oxidative stress which helps in inhibition of urolithiasis. Q and 12C showed presence of anti-oxidant property as 33.11% and 0.95%	PROS: Modern techniques used. CONS: It's a pre-clinical study.
7	An Invitro study of homoeopathic medicine sarsaparilla Q,6C,12C,30C,200C,1M : an inhibitor of calcium oxalate, phosphate crystallization	Dr. Mugdhakumari R. Patel, Prof. Dr. Tanveer A. Khan, Dr. Ajay Namdeo Dr. Chetan H. Shinde	September, 2021	International Journal of Scientific Research	Calcium Oxalate crystallisation assay was experimented by using JASCO-UV/VISIBLE-630 Spectrophotometer. Maximum inhibition of calcium oxalate crystallisation has been noticed in Sarsaparilla Q,1M, 30C.Q was able to decolorize during DPPH assay in which Inhibition % was decreased as potency increased (Q>30C>1M)	PROS: Evidence for homeopathic drug efficacy. CONS: It is a pre-clinical study
8	An InVitro study of Hydrangea A. - homoeopathic preparation : an inhibitor of calcium oxalate crystallization.	Dr. Rupali Telang	2021	Indian journal of research in Homoeopathy	Spectrophotometric crystallisation assay was done , the slopes of nucleation and aggregation phases were calculated using linear regression analysis of Q,30,200C Hydrangea	PROS: Modern techniques of analysis used. CONS: It's a pre-clinical study.

5 Discussion

The results of invitro studies mentioned so far clearly indicates a strong anti urolithiatic properties of various homoeopathic remedies but clinical trials in this particular field are less, even if then control group must be included which is not seen. Flaws in research methodology must be properly addressed for clinical trials. The main key findings of this conceptual literature review are that the proof for efficacy of Homoeopathy as MET for management of ureteric calculi is evidenced by literary as well as empirical research data regardless proper study design, steps to minimize bias, with objective evidence, more clinical trials should be done to add more strength to currently existing ones.

6 Conclusions and Recommendations

This literature review analysed evidence about efficacy of Homoeopathy as medical expulsive therapy (MET) in the management of ureteric calculi. Literature available and researches also support this statement as it can provide the cost effective as well as conservative management in uncomplicated cases of ureteric calculi.

Despite the methodological quality of the included studies, this review summarizes potentially useful information to provide to patients suffering from ureteric calculi with the aim of supporting them with further conduction of high-quality studies. Further homogeneous studies, in design method and outcomes measurement, and with high methodological quality, are needed to better clarify whether there is additional benefit from other treatment modalities like Homoeopathy. Meanwhile, following the guidelines of conservative management of ureteric calculi can yield good results thus providing recommendations and interesting suggestions for future research.

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