Cochrane Central Register of Controlled Trials

Treatment of Renal Stones With Frankincense (Luban)

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Abstract

Investigator Brochure of Olibanum (Boswellic Acid):

A. Clinical Research

Olibanum has been utilized as an important fixative in perfumes, soaps, creams, lotions, and detergents in the leading products of the perfume and cosmetic industry, as it has an oriental note in its scent. The interest of pharmaceutical companies created a third market for olibanum. Since ancient times, it has been used in folk medicine for its antiseptic, antiarthritic, and anti- inflammatory effects. For this reason, olibanum has gained increasing attention from scientists in the last 20 years to better define its medical effects and identify the constituents that are responsible for these effects.4 Animal studies and pilot clinical trials support the potential of B. serrata gum resin extract (BSE) for the treatment of a variety of inflammatory diseases like inflammatory bowel disease, rheumatoid arthritis, osteoarthritis and asthma.5 Moreover, in 2002 the European Medicines Agency classified BSE as an 'orphan drug' for the treatment of peritumoral brain oedema.6 The pharmacological effects of BSE have been mainly attributed to boswellic acids, especially 11-keto-b-boswellic acid (KBA) and acetyl-11-keto-b-boswellic acid (AKBA), which were proposed as selective 5-lipoxygenase (5-LO) inhibitors.7 Thus, instead of 5-LO inhibition by AKBA, inhibition of cathepsin G (catG) and acid might represent the principal mode of action of BSE.8 The gum resin is

obtained by incision of the stem or branches of B. serrata. Following air-drying, the gum resin exudate consists of translucent, roundish or irregularly shaped, variable size pieces of up to 3 cm. The main components are volatile oils (5-15%), pure resin (55-66%) and mucus (12-23%). The gum resin typically contains 30% boswellic acids.9 The β-boswellic acid, is considered to be one of the main active components of frankincense. These are some of the chemical compounds present in frankincense: acid resin (56 per cent), soluble in alcohol and having the formula C20H32O4; gum (similar to gum Arabic) 30-36%; 3-acetyl-beta-boswellic acid (Boswellia sacra); alpha-boswellic acid (Boswellia sacra); 4-O-methyl-glucuronic acid (Boswellia sacra); incensole acetate phellandrene .The work of Ibn Sina (Avicenna) of the 11th century refers to the use of frankincense in inflammation and infection of the urinary tract.10 In Kenya it is used for dressing wounds and, when mixed with sesame oil, is taken to reduce the loss of blood in the urine from schistosomiasis infestation. The Antimicrobial activity of Boswellia resin have been suggested by studies.11 The biological activities of essential oils including: Antioxidant activity; Acetylcholinesterase inhibition; Antimicrobial activity and Antifungal activity.11 The antibacterial activity of oleo-gum resins of B. sacra, known as Hoojri, Najdi, Shathari, and Shaabi has been reported.3 All the four oils were effective against both Gram-positive and Gram-negative bacteria. The clinical isolates of Bacillus subtilis, Micrococcus luteus, Staphylococcus aureus, Klebsiella pneumoniae, and Enterobacter aerogenes were sensitive to all the oils, while those of Pseudomonas aeruginosa, Escherichia coli, and Proteus vulgaris were resistant to the Shathari, Najdi, and Hoojri oils, respectively.3 Anticancer activity: multiple pathways that could be activated by frankincense oil to induce bladder cancer cell death.12 The anti-inflammatory and analgesic activities of Boswellia serrata, and B. sacra have been reported.13 Recently It has been shown that the aqueous stem bark extract of Boswellia papyrifera oral administration has a Nephro-curative effects on acetaminophen-induced kidney damage in rats and that effect was found to be dose- and time- dependent.14 In addition, Oleo-gum-resin of Boswellia serrata Roxb induced Reno-protective action against Gentamicin induced nephrotoxicity in Albino rats.15 Also Zingiber officinale Roscoe (Ginger), Arabic gum (AG), and Boswellia have been found to be beneficial adjuvant therapy in participants with acute renal failure and CRF to prevent disease progression and delay the need for renal replacement therapy.16

B. Basic Research

Morphological studies of frankincense on kidney stones done at a preclinical setup, results attached in Appendix I.

Research Methodology Problem: Renal stones are common and people prefer non-surgical treatment approaches

Aim of study (Question): Can we treat renal stones with a harmless easily available natural product like Luban (Boswellia) given as capsules of active oils? And can Luban protect the kidneys from the sequel of inflammation and kidney damage induced by nephrolithiasis.

Study design

A. Study Groups (Arms) and interventions:

This is a clinical Phase I & II (Safety, Efficacy) double-blind simple-randomized controlled treatment trial

involving 100 participants in 4 groups (25 participants each group)

Group 1: 25 participants with radiopaque stones (Calcium Oxalate) treated with Luban

Group 2: 25 participants with radiopaque stones (Calcium Oxalate) treated with Uralyt-U

Group 3: 25 participants with radiolucent stones (Uric acid) treated with Luban

Group 4: 25 participants with radiolucent stones (Uric acid) treated with Uralyt-U

B. Inclusion criteria:

• Participants with renal stones equal or less than 10mm in size

C. Exclusion criteria:

- Participants with renal pathology (Renal anomalies, multiple renal cysts, renal tumors)

- Participants with comorbidities (DM, CKD)

D. Withdrawal criteria

- Participants under treatment protocol who pass a stone and documented to be the stone under evaluation

- Participants who have uncontrolled pain with the need for surgical intervention to remove the stone

E. Outcome measures

- Primary Endpoints: The primary end point (effect) is reduction of stone size by 50% or complete disappearance after 1 years of treatment.

- Secondary Endpoints: The secondary end point (toxicity) is the participants intolerance of the treatment or development of side effects.

F. Measurements:

Participants factor: Age (18-70 years), Sex, comorbidities, first time or recurrent former of stone, presentation

Stone factor: size in mm, location, composition (stone analysis if possible), Side of kidney.

G. Data handling and record keeping:

Source data (participants data collected) will be recorded in the case report form, CRF (data collection sheet) specified for each participant. The CRF will be kept in a key-protected file cabinet and a scanned electronic copy in a password-protected computer until analysis is carried out. Source data verification will be carried out from the source data if any inconsistencies arise by the means of regular research team meeting and review of the collected data. Correct and consistent completion of participant initials and study ID number will be regularly checked by the designated research nurse.

H. Safety assessment:

The principal investigator along with the sponsor will ensure the right and safety of the participants are

protected and the study data are accurate and complete and the study is being conducted in compliance with the protocol and Good Clinical Practice (GCP), and regulatory requirements. The study will have a very strict adverse reaction reporting system to identify any risks or side effects that may occur and not recognized before. This will be done by a continuous record of a table of anticipated and unanticipated serious adverse events grouped by organ system, with number and frequency of such event in each arm of the clinical trial. The principal investigator will be regularly updated to take decisions about the actions to be taken in case of a serious risk to patients occurred. All adverse events (AEs) and adverse reactions (AR), wither serious or not and wither suspected or unexpected, that may have been caused by the study conduct or the investigational medicinal product will be filled in the specified forms and reported to the sponsor immediately.

I. Procedures for reporting deviations from the original plan:

Deviations from the protocol and GCP will be monitored and corrected if become apparent. Every effort will be done to ensure compliance with the protocol and preparation for the unexpected will be anticipated by a systematic approach of dealing and documenting the devotions in the participants study file.

J. Quality control and quality assurance:

Serious breaches that have the potential to affect the safety of participants or integrity of the study will be monitor closely and if occur will be investigated, reported to the sponsor and acted upon immediately. The principal investigator will be leading the role in the resolution of a serious breach and actions will be recorded in the participants study file.

Statistical analysis:

For each type of stones (radiopaque, radiolucent), the two independent treatment arms (Luban and conventional) will be compared for the two categorical outcomes of no effect or good effect, with good effect defined as reduction of stone size by 50% or complete disappearance after 1 year of treatment. The Chi-squared test will be used to calculate wither the two treatment groups are the same or different and 95% confidence interval will be calculated. The significance level will be at $p < 0.05$. The analysis will be based on intention-to-treat basis (participants will be analyzed in their original group even if they deviate from the protocol). An interim analysis of the results will be done at 6 months of follow up to look for any serious adverse effects.

Methods and Randomization:

Participants who satisfy the study criteria will be recruited over a period of one year (September 2019 to September 2020). They will be randomly distributed to either the Luban treatment (AKBA-Incense 2 capsules daily, 30% 3-acetyl-11-keto-ß-boswellic acid, from ZeinPharma) or the conventional treatment Uralyt-U (Potassium Sodium Hydrogen Citrate, 10g orally in 3 divided doses with pH target 6.2-6.8 for Calcium Oxalate stones and 7.0-7.2 for Uric Acid stones) as a positive control, using a computer-generated list of random numbers with even number for Luban treatment. Before inclusion: blood (Creatinine, Urea, K, Na, Ca, P) and urine (urine analysis, urine culture) tests, Radiological (x-ray KUB, US abdomen, CT abdomen) will be carried out. Participants will be followed up every 3 months for 1 year. Each visit the following will be

done: clinical and physical assessment, blood tests, urine tests and CT abdomen.

Information

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