

Evaluation of therapeutic effect of a Polyherbal formulation on Urinary Retention and Urinary Tract Infection in Experimental Animal Model

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ABSTRACT

Ethnopharmacological relevance

A variety of urological conditions, including urine retention, incontinence, urinary tract infections, and bladder stones, may arise in eunuchs after castration. Treatment for chronic conditions like urinary tract infections (UTI) with traditional Chinese medicine (TCM) offers a number of definite advantages. Benign Prostatic Hyperplasia (BPH) has been therapeutically treated in China for many years using the Qianliening capsule (QC), a formulation of traditional Chinese medicine. However, no research work has been done on the use of QC for the treatment of Urinary Retention and Urinary Tract Infection in Castrated Animal Model.

Aim and objectives of the study

Aim: To evaluate the therapeutic effect of a Polyherbal formulation on Urinary Retention and Urinary Tract Infection in a castrated Experimental Animal Model.

Objectives:

- To find out a new herbal drug treatment option for the Urinary Retention and Urinary Tract Infection in a castrated animal model.
- To understand the incidence of Urinary Retention and Urinary Tract Infection in castrated animal model.

Materials and methods

Castration and penectomy was performed on all rats. After 8-10 days of healing period, the body temperature, and 24 hour micturition frequency and total urine output (voiding behavior) was recorded for all rats. Increased micturition frequency and reduced urine output confirmed the presence of Urinary Retention in all rats. Biochemical indicators related to UTI and rise in body temperature confirmed the urinary tract infection induced by urinary retention. The treatment protocol lasted for 7 days for standard, control and QC (2.25gm/Kg, 4.5gm/Kg and 9gm/Kg) groups. The effects of QC over voiding behavior and urinary tract infection induced by urinary retention were evaluated.

Results

After treatment with different doses of QC (2.25gm/Kg, 4.5gm/Kg and 9gm/Kg), the biochemical indicators related to UTI like urine WBC count, pH and nitrite count were reduced. Body temperature was also improved upon treatment with QC. All QC groups showed dose-dependent improvement in the turbidity of urine. In case of voiding behavior study, 24 hour micturition frequency and total urine output was improved significantly only in the 9gm/Kg QC group.

Conclusion

QC has a remarkable therapeutic impact on UTI in castrated rats induced by urinary retention. The information offered in this study establishes the groundwork for future research into the treatment of UTI in the special population (Eunuchs) and offers a novel concept and approach.

Keyword: - Eunuchs; Urinary retention; Urinary stenosis; Urinary Tract Infection; Castration; Urological problems; Qianliening capsule

1. INTRODUCTION

Biological men who underwent voluntary castration for reasons other than male-to-female transsexualism are known as eunuchs. The term "eunuch wannabe" is used to describe those who want to or are intending to undergo elective castration. Many would-be eunuchs commonly utilize self-castration, have their testis surgically removed, or choose to castrate themselves through non-medical means. Some of them may also choose self-inflicted testicular damage via injections of toxic substances [1]. Eunuchs in India, are commonly known as 'Hijras' and are under-represented [2]. In India, the Eunuch Community has been around for many centuries. The majority of the male homosexual transvestites that make up the Hijra group of the Eunuch community in India are transvestites who dress and act like women and generally adopt female preferences and behaviors. All of them are males at birth, however they lose their external genitalia at or shortly following puberty. The other eunuch community subgroup is referred to as "Zanana," and members of this subgroup do not lose their male reproductive organs. According to reports, the Muslim rulers used "Khowajas," a different group of Eunuchs. For use in harems where the emperor's wives and concubines lived, the penis and scrotum of these were amputated before they reached puberty [3]. Penzer claims that there were three different kinds of eunuchs in the past, and they are as follows: 1) Castrati were those who had both their penis and testicles removed. 2) Spadones are people who have only had their testicles removed. 3) The term "thlibiae" refers to damaged or crushed testicles [4]. Since ancient times, the eunuchs or hijras have been a part of Indian society. Eunuchs were valued by monarchs and emperors as harem guards and companions. To classify them, the Sanskrit word "tritiya prakriti," or third nature, is utilised. The wide range of phrases used to translate the Hindi word "hijra" confuses the outsider. Other terms used to define the community include eunuchs, transvestites, homosexuals, bisexuals, hermaphrodites, androgynes, transsexuals, and gynomimetics. Intersexed, emasculated, impotent, transgendered castrated, effeminate, or sexually anomalous or dysfunctional are some other terms used for them. Some eunuchs are born with intersex sexual differentiation abnormalities and are given to community leaders by their patients [5]. There are two primary types of eunuchs in Mumbai: Aqua (who do not have a castration or penectomy), and Nirvan (who undergo penectomy and castration) [6]. In modern India, the castrated Hijra group is thought to number more than 2 million people. At least 40,000 men undergo chemical or surgical castration every year in North America to treat advanced prostate cancer. There are millions of genetic men alive today who no longer have functional testicles, taking into account both the Hijra and the several thousand of prostate cancer patients who are androgen-deficient. These people are eunuchs by nature [7].

In modern-day India, eunuchs frequently live in ghetto-like groups within their own communities. They make a living by dancing and celebrating births and marriages, but they frequently have to go to other means to make ends meet. Without the involvement and blessings of Eunuchs, no event is deemed complete. Yet, they continue to be a marginalized segment of our population [5]. Eunuchs are disdained by society and have been longing for identity and sense of belonging to a social group[3].

Castration is a procedure that results in loss of an individual's testes functionality. Surgical removal of the testes or in situ destruction of testicular function can be utilized to achieve castration. The production of spermatozoa as well as testicular hormones can be ceased due to castration [8].

According to Johnson TW et al, there are four things that might encourage thoughts of castration:

(i) childhood abuse, including parental threats of castration; (ii) homosexuality; (iii) exposure to animal castration as a young kid; and (iv) religious condemnation of sexuality [7].

The desire to undergo voluntary castration can be motivated by a number of things, including a desire to diminish libido, to rectify an impression of their dysmorphic (region of the body has a different form from normal) genitalia, or to indulge in a sexual fantasy[1].

Men used to be castrated, had their testicles removed, or had them destroyed in order to be rendered eunuchs and fit into specific social roles. Moreover, the penises of several of these eunuchs were removed. The major treatment for advanced prostate cancer (when the cancer has expanded beyond the prostate gland) is androgen deprivation therapy (ADT) [9].

Mukherjee reported a method of castration whereby adult Hijras performed demasculinization rites in which the victim's penis and scrotum were removed with a clean swipe of a knife [3]. The eunuchs in Mumbai (Nirvan group)

are castrated using traditional techniques. There are varying opinions regarding the precise castration procedure, and one would assume that there are a number of methods by which the Eunuchs (Hijras) are castrated. Two traditional methods of castration are described in the literature by Patwardhan et al. In the first approach, the boy was placed down on a solid surface on a day designated as auspicious by the Guru, and a string was tightly knotted around his testicles to stop the flow of blood. While being held down by many eunuchs, the penis and testicles were swiftly severed by a sharp knife. The second way was to wrap a thin but strong nylon thread around the penis and scrotum separately, after the person was under the influence of alcohol. For three days, he was kept under the influence of alcohol. The thread is tightened and held in place until the scrotum and penis slough off. On average, it takes two to three days. A local doctor sutures the area or allows it to heal on its own using turmeric powder and herbs [6]. Before consulting an endocrinologist, many Indian eunuchs have undergone crude surgery. This may comprise orchietomy as well as partial or total penectomy [5]. The genitalia (scrotum, penis, and testes) were removed with a single incision by a curved knife in case of Eunuchs of Chinese court [4]. Literature also mentioned that the process of making Skoptzys in men was extremely straightforward; the operator simply grabbed the portions that were to be removed with one hand and whacked them off with the other. Several websites on the internet provide detailed facts about the technique of castration in eunuchs that differ in different parts of the world and which are exhaustive. There may be other methods used elsewhere throughout India [6].

Urinary retention in Eunuchs is a castration-related adverse effect, according to Patwardhan et al. (2007). According to a case report by Patwardhan et al., four Eunuchs with chronic painful retention and long-standing obstructive urinary symptoms appeared at the outpatient department. In the squatting position, they required 20 to 40 minutes to strain and empty the bladder. According to reports, castration results in urethral stenosis, a physical narrowing of the urethral channel, which eventually causes a variety of urological issues in Eunuchs, including urine retention or dribbling, urinary incontinence, urinary tract infections, and bladder stones [6]. Medical studies on the Ottoman court eunuchs revealed that these eunuchs had experienced voiding difficulties [4]. The normally harmless bacteria get an opportunity to multiply and produce urinary tract infection due to incomplete outflow of urine (urinary retention) [10]. Castration resulted in urethral stenosis, which in turn caused a variety of urological issues in eunuchs, including urinary tract infections [4, 6]. In agreement with the aforementioned study, it is suggested that males may be more susceptible to urinary tract infections if they have structural defects such as urethral strictures or stenosis [11]. According to the literature data, urinary tract infection rate was appeared to be higher in patients with urethral stricture disease [12].

Traditional Chinese Medicine (TCM) often consists of a blend of herbal plants or extracts that contains hundreds of distinct ingredients with widely dissimilar physicochemical properties [13]. TCM is the term for a comprehensive method of diagnosis, pathophysiology, and therapy found in the Chinese materia medica and built on more than 2000 years of experience and knowledge [14]. TCM has been thoroughly researched and incorporated with western medicine since 1949 and gone through significant changes as a result of biomedical sciences. For instance, standardized herbal therapy formulations are now frequently utilized in tablets, capsules, and even ampoules in addition to the conventional decoctions of personalized prescriptions [15].

Recurrent Urinary Tract Infections can be prevented with antibiotics; however, usually reinfection occurs post treatment. Moreover, microbial resistance to antibiotics and potential long-term adverse effects of these drugs is a major issue. Alternative methods of treating these infections are therefore being considered, including Chinese herbal medicine [16].

Qianliening capsule (QC) is a traditional Chinese medicine formulation that consists of a combination of five natural products, including Dodder, Achyranthes, Astragalus, Leech and Rhubarb. Together, these products provide heat-clearing, detoxifying, blood-circulation-promoting, blood-stasis-removal, kidney tonification, and vitality-sustaining properties (replenishing the kidney qi in Chinese medicine) [17]. It has been reported that QC can improve a series of lower urinary tract symptoms (LUTS) (including frequency of urination, urinary urgency, thin urine flow and certain other voiding disorders) and boosts the urodynamic evaluation indexes in BPH patients [18]. The chemical constituents of Rhubarb, Astragalus [19], Achyranthes [20], and Dodder [21] are reported to have well established efficacy against microbes. Proven efficacy of QC against LUTS in BPH patients and antimicrobial properties shown by some of the components of it, may justify its use for the treatment of Urinary Retention and Urinary Tract Infection in castrated Experimental Animal Model. Therefore, QC was administered to the castrated rats, who developed UTI due to urinary retention caused by castration.

Table 1. Composition of Qianliening capsule (QC)[17].

Common name	Latin name	Part used	Daily adult dose (g)
Rhubarb	<i>Radix et Rhizoma Rhei</i>	Dried root	15
Leech	<i>Hirudo</i>	Dried body	3
Astragalus	<i>Radix astragali</i>	Dried root	12
Achyranthes	<i>Radix Achyranthis bidentatae</i>	Dried root	9
Dodder	<i>Semen cuscutae</i>	Dried seed	6

2. MATERIAL AND METHODS

2.1 Formulation Ingredients

Rhubarb (*Rheum emodi*) root powder was purchased from JK Botanicals Private Limited, Maharashtra, India. Astragalus (*Astragalus membranaceus*) root powder was purchased from One Herb, Kolkata, India. Dodder (*Cuscuta reflexa*) dried seeds were purchased from Land of Herbs, Uttar Pradesh, India and authenticated from Ms. N. Kakpure, Botanist Vidyabharati Mahavidyalaya, Amravati. Dried root of Achyranthus (*Achyranthus aspera*) was obtained from Aeshwarg Creations, Uttar Pradesh, India and authenticated from Ms. N. Kakpure, Botanist Vidyabharati Mahavidyalaya, Amravati. Dried Leech (*Hirudo medicinalis*) was obtained from Dr. Shah Panchkarma Ayurveda, Madhya Pradesh, India and authenticated from Dr. Sidhu Rathod, Zoologist Vidyabharati Mahavidyalaya, Amravati. Later, the Dodder seeds, Dried leech, and Achyranthus root were finely powdered. Table 1. represents the composition of Qianliening capsule with traditional chinese medicine. We have utilized Indian species of Rhubarb and Dodder in the composition of Qianliening capsule formulation due to similarity of chemical constituents and/or ease of accessibility/availability. Hereinafter, the formulation of Qianliening capsule (QC) with Indian species of Rhubarb and Dodder, will be referred to as Qianliening capsule (QC).

Table 2. Composition of Qianliening capsule (QC) with Indian species

Common name	Latin name	Part used	Daily adult dose (g)
Rhubarb	<i>Rheum emodi</i>	Dried root	15
Leech	<i>Hirudo medicinalis</i>	Dried body	3
Astragalus	<i>Astragalus membranous</i>	Dried root	12
Achyranthes	<i>Achyranthus aspera</i>	Dried root	9
Dodder	<i>Cuscuta reflexa</i>	Dried seed	6

At the time of treatment, all drug powders were mixed together and were dissolved in distilled water and stored at 4°C.

2.2 Establishment of UTI model in rats and Animal treatment

Male Wistar albino rats of 8-10 weeks age, kept in polyacrylic cages and maintained under standard housing conditions of temperature ($22 \pm 2^\circ\text{C}$) were used in this study. The relative humidity was maintained as 50- 60% and rats were fed standard rodent diet and water ad libitum. All the experiments were approved by the Institutional Animal Ethics Committee (IAEC) of Vidyabharti College of Pharmacy, Camp, Amravati -444602, Maharashtra (India).

Initially, the animals were divided into 5 groups containing 6 animals each. Each animal was placed in the metabolic cage and 24 hour micturition frequency and 24 hour total urine output was recorded. The 24 hour micturition frequency was recorded using a personal mobile camera recording. The 24 hour urine sample was collected and subjected to routine urine examination. The body temperature of all rats was measured by a thermometer under the rat arm for 3 minutes. Castration was performed according to the following procedure. Anaesthesia was induced by intraperitoneal injection of a cocktail of Ketamine hydrochloride (50 mg/kg) in combination with medetomidine hydrochloride (0.5 mg/kg) cocktail. Depth of anesthesia was checked by monitoring respiratory rate (anesthetized animals show reduced respiratory rate) or simply testing the animal response to gentle pressure on the hind paws. The skin on the ventral side of the scrotum was made visible by shaving the fur bilaterally using an electric clipper. The shaved skin was swabbed with 70% (v/v) ethanol followed by sterile Phosphate-buffered saline (PBS). All surgical instruments and hard surfaces were sterilized with 70% ethanol prior to use.

The anesthetized animal was placed on the operating table on its back with the tail towards the handler. Using a sterile scalpel, a single incision of 1.5 cm was made on the ventral side of the scrotum. With blunt forceps, the testicular fat pad on the left side was targeted and dragged through the incision. The muscles of the cremaster were severed. Using sterile, blunt forceps, the testicular fat pad was found and carefully drawn through the incision.

The testicular content was exposed by gently freeing the testicular fat pad with sterile, blunt forceps. The cauda epididymis, caput epididymis, vas deferens, and testicular blood vessels were exposed gently while holding the testicular sack with sterile tooth forceps. A single ligature was performed around the blood vessels to prevent bleeding following removal of testis. The cauda epididymis and caput epididymis were severed from the testis. The blood vessels were carefully cut to remove the testis. With blunt forceps, the remaining testicular sac contents were replaced. All these steps were repeated for the other testis. Penectomy was also performed with the help of scalpel. Betadine Powder, and turmeric powder was sprinkled over the wound periodically. Meloxicam Injectable solution was administered subcutaneously in the scruff (loose skin on dorsal neck) of castrated rats using a 1 cc syringe and a 27g needle.

Animals were housed individually and closely observed for approximately 2–4 hours until they fully recovered from anesthesia. Following the recovery period (approximately 24 h after surgery), the animals were grouped together as normal. Meloxicam Injectable solution was administered for a total of 3 days. After 8-10 days of healing period, the routine urine examination, body temperature, and 24 hour micturition frequency and total urine output was recorded for all rats. Increased micturition frequency and reduced urine output confirmed the presence of Urinary Retention in all rats. Urine analysis revealed the presence of WBC in urine which is one of the markers of UTI. Presence of ketone bodies and nitrites in urine of some of the castrated rats confirmed the urinary tract infection. The urine pH was also increased in all castrated rats suggesting UTI. In line with the infection, the body temperature of all castrated rats was increased. Upon confirmation of urinary tract infection induced by urinary retention with routine urine examination, the treatment protocol was initiated.

The compound to be tested was intragastrically administered consecutively for 7 days. The rats were divided into control group (Normal Saline), Standard group (0.05 gm/Kg levofloxacin tablets), QC 2.25 gm/Kg group, QC 4.5 gm/Kg group, and QC 9 gm/Kg group, each group contained 6 animals. After completion of treatment protocol, the routine urine examination, body temperature, and 24 hour micturition frequency and total urine output was recorded for all rats. The efficacy of the treatment (QC groups, standard group, control group) over all the above parameters was evaluated.

2.3 Statistical analysis

Data were analyzed using Graph Pad Prism 5 for Windows (version 6.01). The results are expressed as Mean \pm Standard error of mean (SEM). One-way Analysis of variance (ANOVA) followed by Dunnett's Multiple Comparison Test was used to test the significance of the difference between the variables in various groups. A p-value < 0.05 was considered statistically significant. Ordinal data was analyzed by comparing the number in each group among different treatment groups.

3. RESULTS

3.1 Effect of Qianliening capsule (QC) on voiding behavior in castrated rats with Urinary Tract Infection (UTI).

Micturition Frequency and total urine output

Only 9gm/Kg QC group showed significant difference between the micturition frequency when compared with control group (Normal Saline) (** $P < 0.01$) (Chart 1,a). Similarly, only 9gm/Kg QC group showed significant difference between the urine quantity when compared with control group (Normal Saline) (* $P < 0.05$) (Chart 1,b). To sum up, the 24 hour micturition frequency was decreased and total urine output was improved significantly only in the 9gm/Kg QC group.

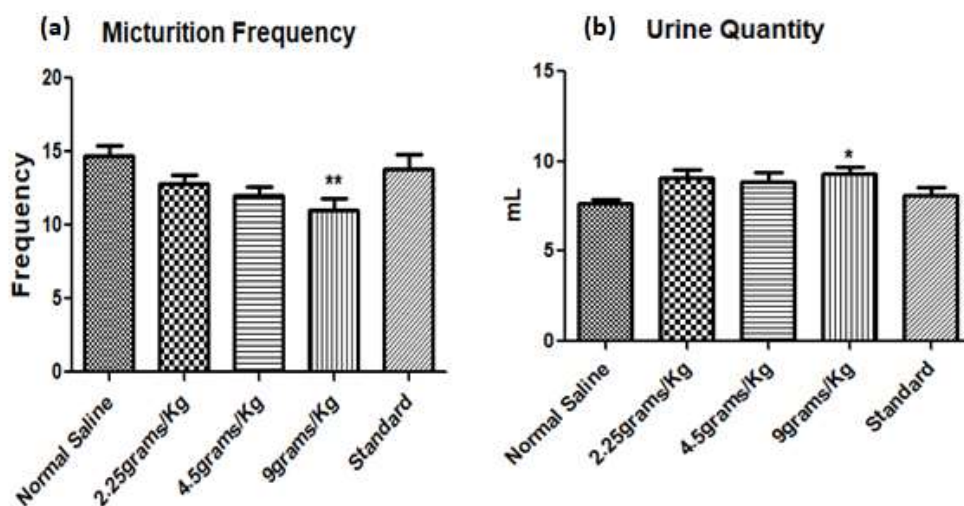


Chart -1: (a) The changes in Micturition Frequency in rats were measured in the control group (Normal Saline), Standard group (Levofloxacin), and QC groups. ** $P < 0.01$ 9gm/Kg QC group versus control group. (b) The changes in Urine Quantity in rats were measured in the control group (Normal Saline), Standard group (Levofloxacin), and QC groups. * $P < 0.05$ 9gm/Kg QC group versus control group.

3.2 Effect of Qianliening capsule (QC) on biochemical indicators in castrated rats with Urinary Tract Infection (UTI).

To evaluate the effect of QC on castrated rats with UTI, biochemical indicators were measured, and the results of these were presented below. There was a significant reduction in the urine WBC count in QC groups when compared to control group (** $P < 0.001$) (Chart 2,a). Additionally, almost similar improvement was noted in the urine WBC count of both the standard and 9gm/Kg QC group (Chart 2,b).

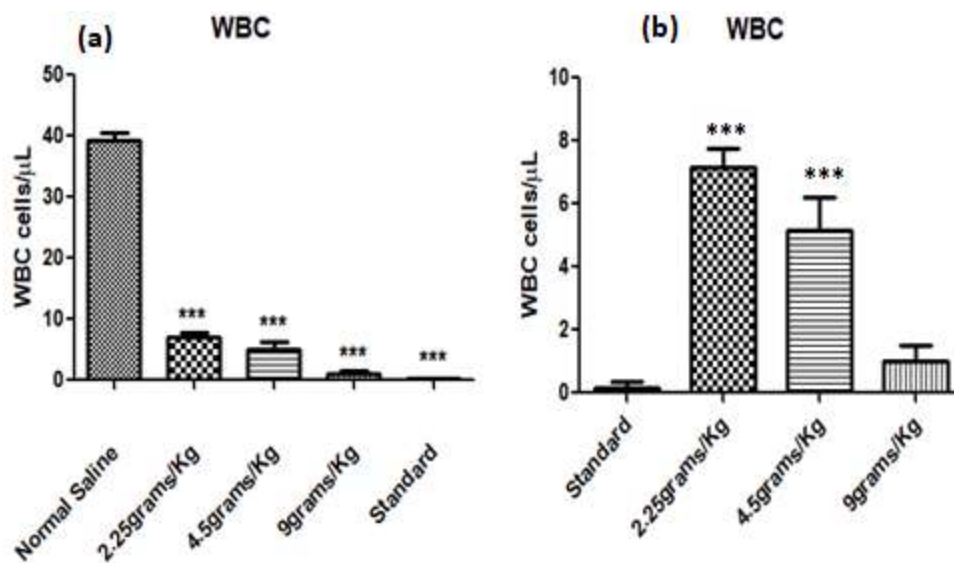


Chart 2. (a) The changes in urine WBC count in rats were measured in the control group (Normal Saline), Standard group (Levofloxacin), and QC groups. *** $P < 0.001$ compared with the control group. (b) The changes in urine WBC count in rats in the Standard group (Levofloxacin) and QC groups. *** $P < 0.001$ QC group 2.25gm/Kg and 4.5gm/Kg versus standard group.

Compared with the control group (Normal Saline), there was a significant reduction in the pH value after treatment with Standard group (Levofloxacin) and QC groups (*** $P < 0.001$) (Chart 3). There was nearly similar improvement in the pH values of both the standard and QC groups.

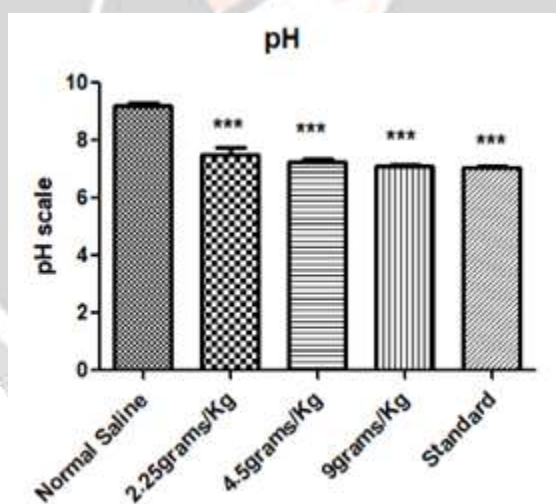


Chart 3. The changes in pH value in rats were measured in the control group (Normal Saline), Standard group (Levofloxacin), and QC groups. *** $P < 0.001$ compared with the control group.

The no. of rats with positive results for ketone bodies and nitrites were reduced in 2.25gm/Kg, 4.5gm/Kg, and 9 gm/Kg QC groups in a dose-dependent manner (Chart 4 and 5). Compared to the standard group, the 9 gm/Kg QC group showed nearly similar results in the reduction of ketone bodies and nitrites (Chart 4 and 5).

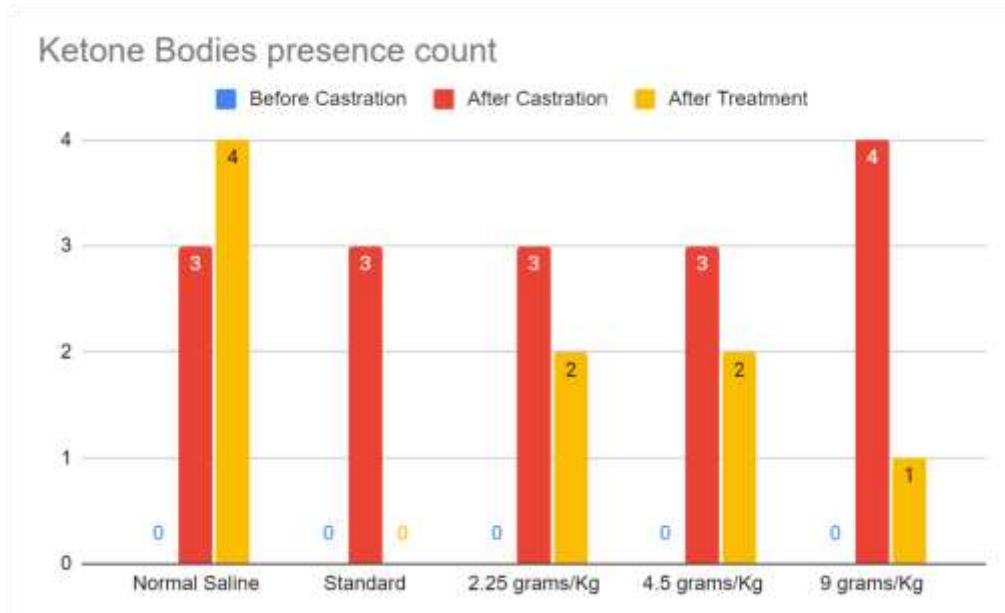


Chart 4. The no. of rats with presence of Ketone bodies in urine at three time points (before castration and 8 -10 days after castration and after end of treatment) were measured in the control group (Normal Saline), Standard group (Levofloxacin), and QC groups (2.25gm/Kg, 4.5gm/Kg and 9gm/Kg).



Chart 5. The no. of rats with presence of nitrites in urine at three time points (before castration and 8 -10 days after castration and after end of treatment) were measured in the control group (Normal Saline), Standard group (Levofloxacin), and QC groups (2.25gm/Kg, 4.5gm/Kg and 9gm/Kg).

All QC groups showed dose-dependent improvement in the no. of rats with turbid urine (Chart 6).

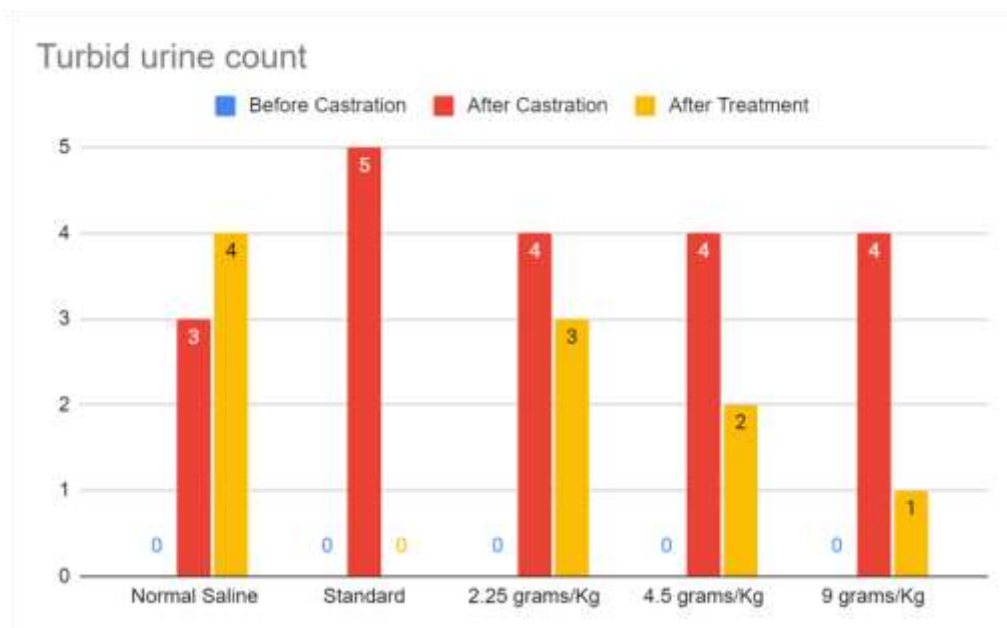


Chart 6. The no. of rats with turbidity in urine at three time points (before castration and 8 -10 days after castration and after end of treatment) were measured in the control group (Normal Saline), Standard group (Levofloxacin), and QC groups (2.25gm/Kg, 4.5gm/Kg and 9gm/Kg).

Urobilinogen and bilirubin were not detected in the urine sample of rats till the end of study.

3.3 Effect of Qianliening capsule (QC) on body temperature in castrated rats with Urinary Tract Infection (UTI).

Compared with the control group (Normal Saline), there was a significant reduction in the body temperature after treatment with Standard group (Levofloxacin) and QC groups (**P< 0.001) (Chart 7, a). There was nearly similar improvement in the body temperature of both the standard and 9gm/Kg QC group (Chart 7, b).

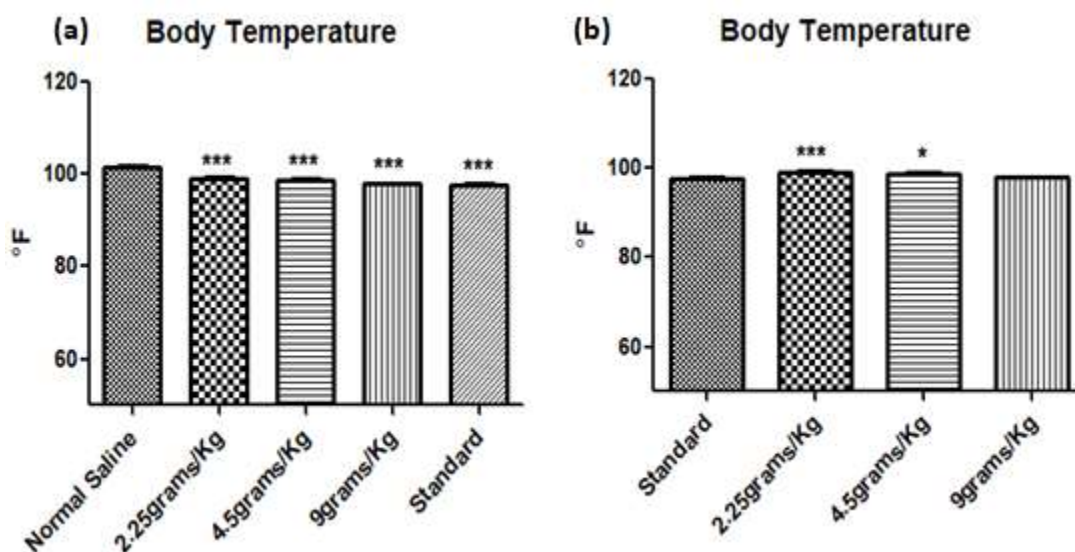


Chart 7. (a) The changes in body temperature in rats were measured in the control group (Normal Saline), Standard group (Levofloxacin), and QC groups. *** $P < 0.001$ compared with the control group. (b) The changes in body temperature in rats in the Standard group (Levofloxacin) and QC groups. *** $P < 0.001$ QC group 2.25gm/Kg versus standard group. * $P < 0.05$ QC group 4.5gm/Kg versus standard group.

4. DISCUSSION

An infection of the kidneys, ureters, bladder, and/or urethra is referred to as a urinary tract infection (UTI) [22]. UTIs are a major source of morbidity in women of all ages, elderly men, and infant boys. Frequent recurrences, pyelonephritis with sepsis, renal injury in children, preterm delivery, and problems brought on by repeated antimicrobial use, such as high-level antibiotic resistance and *Clostridium difficile* colitis, are examples of serious consequences [23].

Castration causes urethral stenosis (physical narrowing of the urethral channel), which ultimately led to the development of various urological problems in Eunuchs, such as urinary dribbling or retention and urinary incontinence (voiding difficulties) as well as urinary tract infection, and bladder stones [4, 6]. The normally harmless bacteria get an opportunity to multiply and produce urinary tract infection due to incomplete outflow of urine (urinary retention) [10]. The presence of structural defects such as urethral strictures/stenosis may predispose men to urinary tract infections while the rate of urinary tract infection was appeared to be higher in patients with urethral stricture disease [11,12].

UTI is now a challenge in medical practice because of its frequency, frequent recurrence, and growing antibiotic resistance [22]. Therefore, Traditional Chinese Medicine, which may be used to treat UTI, has drawn considerable interest. Because of its natural characteristics and minimal side effects, TCM offers proven advantages in treating UTI, particularly in chronic patients. TCM has less adverse effects than antibiotics, does not alter microflora, and is affordable and appropriate for long-term usage [24].

Qianliening capsule (QC) is a traditional Chinese medicine that has been used clinically in China for many years to treat BPH [17]. The chemical constituents of Rhubarb, Astragalus [19], Dodder [21] and Achyranthes [20] are reported to have well established efficacy against microbes. Additionally, QC can improve a series of LUTS (including frequency of urination, urinary urgency, thin urine flow and certain other voiding disorders) and boosts the urodynamic evaluation indexes in BPH patients [18]. Since, Eunuchs usually suffers from Urinary Tract Infection due to urinary retention caused by urethral stenosis (which was developed from castration), we evaluated the therapeutic effect of QC on Urinary retention and Urinary Tract Infection in a Castrated Animal Model.

Urinary tract obstruction may lead to decreased urine flow and urine output [25, 26]. Frequent urination in small amounts is one of the symptoms of chronic urinary retention [27]. In this study, increased micturition frequency and decreased total urine output in castrated rats confirmed the presence of Urinary Retention. The 9gm/Kg QC group showed statistically significant improvement in the micturition frequency and total urine output when compared to the control group (Normal Saline).

UTI patients are often evaluated by normal urine testing, and many of these signs have significant reference relevance. Urinary pH fluctuations are intimately associated with UTIs; a low pH is advantageous since it prevents bacterial development [28]. Adjusting the pH value is crucial for the prevention and treatment of UTI because urinary tract infection can readily spread if the urine has an alkaline pH [24]. There are several microorganisms that might cause UTIs. Some of these bacteria convert nitrates, a typical component in urine, into nitrites. Therefore, the presence of nitrites in urine indicates urinary tract infection [29]. In individuals with UTI symptoms, the nitrite test provides a direct proof of bacteria in the urine, which is a UTI by definition [28]. Although urine cultures are still the gold standard for diagnosing UTIs, they are time-consuming and expensive. The current standard of care for determining whether a person has a urinary tract infection relies heavily on the presence of symptoms as well as the results of a quick diagnostic nitrite strip test that reveals the presence of bacteria in the urine and a semi-quantitative measurement of the white blood cell count in the urine [30]. Fever is also considered as one of the UTI indicators. [31]. Dark, cloudy (turbid), or reddish colored urine may also be one of the symptoms of UTI [29]. Urethral stricture is reported to be one of the obstructive causes of urinary retention [32].

In case of voiding behavior study, 24 hour micturition frequency and total urine output was improved significantly only in the 9gm/Kg QC group. After treatment with QC, the pH value was significantly decreased. The contents of WBC in urine were reduced in castrated UTI rats. The no. of rats with positive results for nitrites and ketone bodies in urine were also reduced. There was a significant reduction in the body temperature after treatment with QC. All QC groups showed dose-dependent improvement in the turbidity of urine. These results indicate that QC has a great therapeutic effect in the treatment of UTI.

The technique of castration in eunuchs differs in different parts of the world and which are exhaustive [6]. We have used one of the methods of castration i.e. removal of both testis and penis in this study. Most of the literature mentioned removal of genitalia with a knife or a sharp cutter in one swift movement as a practice of castration followed traditionally. Occurrence of UTI which is induced by urinary retention due to castration could only be possible, if the castration procedure involved not only the removal of testis but also penis. The traditional methods of castration often reported removal of both testis and penis. Therefore, the findings of this study could be only applicable to the population who had their testis as well as penis removed. This is one of the limitations of the study.

5. CONCLUSIONS

Eunuchs after castration often suffer from urinary retention caused by narrowing of urethra. The normally harmless bacteria get an opportunity to multiply and produce urinary tract infection due to urinary retention. UTI is a frequent yet difficult condition with no comprehensive specific therapy. In this study, the Castrated Animal Model of UTI in rats was established to evaluate the effect of QC on UTI. The outcomes of the study demonstrate that QC has a remarkable therapeutic impact on UTI in castrated rats induced by urinary retention. The information offered in this study establishes the groundwork for future research into the treatment of UTI in the special population (Eunuchs) and offers a novel concept and approach.

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