Effective concentration of povidone iodine renal pelvis instillation in the treatment of chyluria

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DECLARATION

*I solemnly declare that this dissertation "**Effective concentration of Povidone Iodine renal pelvis instillation in the treatment of Chyluria"*** was prepared by me in the Department of Urology, Government Stanley Medical College and Hospital, Chennai under the guidance and supervision of **Dr.V.DHANAPAL.MCh,** Professor &HOD , Urology, Government Stanley Medical College, Chennai between 2004 and 2007.

This dissertation is submitted to the TamilNadu Dr. MGR Medical University, Chennai in partial fulfillment of the University requirements for the award of degree of MCh Genitourinary surgery.

Place : Chennai

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CERTIFICATE

*This is to certify that this dissertation entitled "**Effective concentration of povidone iodine renal pelvis instillation in the treatment of chyluria"***

is a bonafide record of the research work done by **Dr.R.Rajesh**. for the award of MCh Genitourinary surgery, under the supervision of **Dr.V.DHANAPAL.MCh** , Professor & HOD , Urology, Government Stanley Medical College, Chennai between 2004 and 2007.

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INTRODUCTION

Chyluria is the presence of chyle in the urine. This has been recognized since the time of Charak (300 BC) who described it as 'Shuklameha' Hippocrates recognized and described chyluria (1, 2). Following discovery of the lymphatic circulation by JEAN Pecquet in 1651, Moellenbrogii (13) ascribed chylous urine to an abnormal junction of the lymphatic and urinary systems. Nearly 100 years later Otto Wucherer, working in Brazil in 1866, found microfilaria in the urine of a patient with heamaturia. Wood in 1929 \first demonstrated pyelolymphatic backflow in retrograde pyelography.

KITTREDGE and Associates and others utilized lymphangiography to demonstrated the anatomic involvement seen in this condition.
It is not uncommon in the Asia especially in India, Japan, Hong Kong and Tai wan. It is rare in western countries. (4.11). It is believed to occur as a result of communication between the lymphatics and the renal collecting system. (3, 5, 6, 11) Al though not life threatening in most cases, it can be disturbing and sometimes debilitating if the chyle loss in urine is profuse.

The disease is largely the chronic stage of filarial disease and is therefore an endemic disease.(7) Management includes conservative measures like

avoidance of fat, anti filarial drugs etc; minimally invasive techniques like renal pelvic instillation of sclerosing agents and invasive procedures like renal decapsulation, retroperitoneoscopic nephrolympholysis etc. Instillation of 1% silver nitrate into the renal pelvis has been the initial treatment modality if conservative measures failed. However, this procedure may be associated with serious complications like acute renal failure (8), life threatening hemorrhage (9) and death (10).

Povidone iodine as a sclerosing agent has been shown to be effective and safe in the management of chyluria. Herein, we present our experience of treating chyluria with povidone iodine instillation in to the renal pelvis in the Department of Urology Stanley Medical College, Chennai, Tamilnadu, India.

2. REVIEW OF LITERATURE

Chyluria is believed to arise largely from parasitic infestation, especially *Wuchereria bancrofti*. Other non-parasitic causes such as malignant tumors of thoracic duct, trauma or pregnancy were occasionally seen. (44)
The parasitic infestation causes inflammation of the retroperitoneal lymphatics and therefore leads to obstruction, tortuous, dilatation and subsequent rupturing into pyelocaliceal system.

The level of communication between the lymphatics and pyelocaliceal system can be any where in the urinary tract, but it occurs most commonly in the renal pelvis.(45) The presentations are imperatively composed of milky white urine passage, in association with dysuria, hematuria, loss of protein and fat causing hypoproteinemia, weight loss, malnutrition and cachexia.

Classification of chyluria

Etiologically, chyluria has been classified into parasitic and nonparasitic forms:

1.Parasitic (primary-tropical)

Wuchereriabancrofti

Eustrongylusgigas

Taeniaechinococcus

Taenianana

Malarialparasites

Cereonomas hominis.

2. Nonparasitic(secondary:nontropical)

Congenital

Lymphangiomas of urinary tract

Megalymphatics with urethrvesicle fistula

Stenosis of thoracic duct

Retroperitoneal lympheangectasia

Traumatic lymphangio urinary fistula

Lymphatic obstruction due to tumor

Obstruction of deep retrperitonal lymphatics by other causes.

Pregnancy;

Diabetes;

Perniceous anaemia

Parasitic chyluria

A numbers of parasites besides Wuchereria bancrofti have been incriminated by various workers as a cause of chyluria eg. *Eustrongylus gigas, Taenia echinococcus,* and malarial parasite. *Taenia nana, Ascaris, S. Haematobium,* and *Ceronomas hominis* . It is not clear, however, as to whether these parasites are actually responsible or whether their presence is merely coincidental. By far the most important and the most common cause-effect relationship of chyluria is with Wuchereria bancrofti. The endemic occurrence of chyluria in filaria infested regions and demonstration of parasites in the blood, lymph or urine of chyluric individuals by various workers supports this view.(79)

Patrick Manson, known internationally as "the father of tropical medicine", while working in the remote Chinese port city of Amoy in 1877, first identified that mosquitoes were responsible for the transmission of lymphatic filariasis. Following the introduction in 1947 of the drug diethylcarbamazine (DEC) for the treatment of the disease, a number of countries (Japan, China, Malaysia, Korea and some islands in the Pacific)

made significant improvement in treatment of lymphatic filariasis.In 1993, an independent International Task Force for Disease Eradication identified LF as one of only six eliminable infectious diseases. Lymphatic filariasis was selected because of advances in treatment methods, both for controlling transmission and for managing the disease. (87)

The World Health Assembly (1997) adopted a resolution calling for the elimination of lymphatic filariasis as a public health problem worldwide.

The principal strategy for interrupting transmission of infection is to identify areas in which lymphatic filariasis is endemic and then implement community-wide programmes to treat the entire at-risk population. The goal of such treatment is to break the cycle of transmission between mosquitoes and humans.

There are six pathogenic nematodes (round worm) belonging to superfamily filariodea which develop to adult stage in humans .The adult female *W. bancrofti* is a pale, threadlike nematode measuring 6-10 cm in length and 0.2 mm in width . The male is smaller, at 4-6 cm in length and 0.1 mm width. Larvae (microfilarias) in the blood of human hosts are ingested when the insect vectors feed . Within the vector, the microfilarias migrate to specific sites and develop from first-stage larvae into infective third-stage larvae. The vector transmits the infective larvae into a human host when feeding. Mosquitoes deposit the larvae on the host skin adjacent to the

puncture site and the third stage larval (L3) parasites migrate through the venous system and lungs to eventually reside in the lymphatics.

In adolescent and adult men, there is a preference for the lymphatics of the spermatic cord. There they form nests occupied by male and female worms, and produce the first stage larvae or microfilariae by viviparous reproduction These larvae migrate from the lymphatics to the peripheral blood where mosquitoes ingest them. The developing microfilariae become third stage larva, L3, within the mosquito. Their lifespan of 5-10 years renders adult worms are more resistant to anti-infective agents than are microfilariae. Microfilariae may live up to several months. The diurnal periodicity of microfilaria distribution in the blood stream is not related to discharge from the mature female, but instead relies on a circadian rhythm related to mosquito feeding patterns, which is not well understood.

Nonparasitic chyluria

Nonparasitic conditions are rare causes of chyluria are usually associated with a process of stenosis or obstruction of the thoracic duct or retroperitoneal lymphatics.(80,81) The common causes are tuberculosis, reteroperitioneal abscess and neoplastic infiltration of retroperitional

lymphatics, trauma and pregnancy. A case of chyluria has been reported following an aortoiliac bypass graft and another in a patient following percutaneous nephrolithotomy.

PATHOGENESIS

CHYLURIA is an abnormal urinary condition in which intestinal chyle appears in the urine as a result of fistulous communications between the lymphatic path ways transmitting chyle) and the urinary tract at or beyond the level of the renal tubules either within the kidney, the renal pelvis or the urinary bladder.

LYMPHATICS OF THE KIDNEY

Fall into three groups.

1. Inter-Tubular lymphatics –within the substance of the kidney
2. Subcapsular lymphatics and
3. Perinephric lymphatics

Groups (2) and (3) communicate with each other and join the renal pelvic lymphatics to drain into the superior mesenteric nodes. The inter tubular lymphatics, coursing along and around the renal vascular pedicle and through the upper para-aortic nodes (viz) sup. Mesenteric and celiac nodes, terminate finally in the cisterna chyli .Many of the right renal lymphatics and a few from the left drain mainly into the descending intercostals trunk

which joins with the kidney drain mainly into the descending intercostal trunk which joins with the cisterna chyli.

The pelvic and para aortic lymphatic traverse the upper Para-aortic nodes draining into the cisterna chyli asright and left lumber trunks. The intestinal lymphatics carrying chyle also course through these nodes to terminate in cisterna chyli as gastro intestinal trunk. It may thus be noted that the three tributaries of the cisterna chyli(viz) the right left lumbar trunks and the gastrointestinal trunk course through the upper para-aortic nodes prior to their termination into cisterna chyli and these nodes also act as intermediary stations for the renal and renal pelvic lymphatics.Nonetheless, the renal lymphatics act as safety valves capable of balancing extra fluid loads under conditions of overload, as in renal pelvic or ureteral obstruction .In addition, intrarenal lymphatics play a role in maintaining a low interstitial oncotic presure, allowing the urine to become concentrated from the reabsorption of water and solutes through the lymphatic pathway.

Whenever there is a obstruction to the flow of chyle at the level of the upper para-aortic nodes (as happens in Filarial Chyluria due to fibrotic changes in the lymph nodes)- the intestinal chyle being unable to course through these nodes takes a deviated retrograde course along the renal and

renal pelvic lymphatics which become engorged with chyle and indue course the hydrostatic pressure in them increases to sufficient magnitude as to cause rupture into the renal tubles or into the renal pelvis with resultant escape of intestinal chyle into the urinary tract and its appearance in the urine. Kinmonth and associates have called attention to the fact that chyluria may occur as a part of the primary disease of the lymphatic system. (MEGALYMPHATICS or LYMPHATIC deficiency).The focus of "Rupture" into or communication with the urinary tract may apparently occur at any level (that is, calyces, pelvis ureter or ladder)

Pathophysiology

This has been explained by two theories

1. **Obstructive theory**

The parasitic infestation produces obliterative lymphangitis and lymphatic hypertension, which subsequently generate varicosity and collateral formation. Once lymphatics are dilated their valvular system fails adding to back flow and dilatation. This theory has been in vogue for nearly 100 years and appears partly contributory.

2. **Regurgitative theory**

The toxins released from dying filarial worms leads to some kind of weakness in the lymphatic wall ('ectasia'), which in turn leads to impairment

of valvular mechanism. Direct inflammatory damage of valves may cause additional effect. Thus, regurgitation of chyle from cisterna chyli or large lymphatic trunk into the other may lead to varicosity and subsequently chyluria by rupture of these varicosities/dilated lymphatics into renal calyces or pelvis.

The route from the intestinal to the renal lymphatics has been the subject of much speculation but it is agreed that chyle must first travel from the lacteals to the cisterna chili or thoracic duct. Then because of obstruction and/or insufficiency of the valvular system of lymph channels there is a reterograde flow to the upper lumbar lymph glands, which drain the renal lymphatics. Definite inadequacy of the lymphatic vessel valves exist since retrograde flow is frequently seen extending down the prevertebral and paravertebral regions on reterograde pyelography. It has been clinically observed and experimentally demonstrated that congestion in the lymphatics resulting from inflammation produces varix of its afferent vessels. It is believed that chyluria occurs because of retroperitoneal lymphatics receiving lymph flow from the intestinal lymphatics become obstructed secondary to fibrosis produced by parasitic infestation thus short-circuiting chyle from the intestinal lacteals to renal lymphatics, which rupture subsequently.

CLINICAL FEATURES OF CHYLURIA

The onset of chyluria may be insidious or sudden (11), is characteristically intermittent (1, 11,18), and usually occurs between the second and fifth decade of life (11), although it has been recorded in all age groups (1, 21) Chyluria may exist for years without materially compromising the health of the patient (1,11), No sex predominance exists (ORTIZ and associates). chyluria originating from the kidney may be unilateral or Bilateral. Secondary pyelonephritis develops in many patients. The only constant symptom is passage of urine that is opaque, white and of milky consistency (1); if blood is also present the urine may appear pink formation of fibrinous clot with its irritative effect in the genito-urinary tract accounts for the symptoms of backache, urgency, frequency, Dysuria, ureteric colic and rarely acute urinary retention.

Blood loss may lead to minimal or moderate iron deficiency anaemia (11) massive proteinuria may cause HYPROTEINEMIA and reversal of the albumin/globulin ratio (14). Loss of fat may lead to weight loss, which becomemanifest in the subcutaneous tissues and account for the peculiar, anxious,wizened facies so often seen in patients with CHYLURIA (11).Recurrences and exacerbationshave been attributed to such factors as posture, exercise,diet,menstruationand pregnancy (11). In the study of lymphatic Dynamics in Filarial chyluria by P.C.Rajaram and colleagues AP

Skiagrams of the kidney ureter Bladder area and chest were taken 15, 30, minutes, 1 1/2, 3, 6, and 9 hours after completion of the injection. The things were determined by the flow of contrast as assessed by fluoroscopy and by the first or second set of lymphograms. Each skiagram is studied for the appearance of contrast in the bladder before the patient is asked to empty the bladder, and he is instructed not to void urine till the next x-ray is taken. If the contrast is demonstrated in the bladder the patient is x- rayed also the next day Thereafter daily lymphograms are obtained. They have combined lymphography with excretory urography and Tomography in a few cases.

Follow through excretory urography in14 cases24 to 48 hour after lymphography has helped to assess renal function, to

study the calyceal pattern, to delineate the lymphatico-urinary fistulae in relationship with the calyces and renal pelvis and to demonstrate pyelolymphatic reflux which is evidenced by recopacification of lymphographic contrast by excretory urographich contrast in the renal lymphatic and adjacent para-aorticlymphatics and nodes.The outstanding finding in lymphangiography is a marked increase in the number, size and Caliber of pelvic and retroperitoneal lymphatic vessels. The vessels become tortuous.

Abnormal communication (URINARY LYMPHATIC FISTULA) with the urinary tract may e seen. These fistulas are large enough to allow opacification of the pelvicalyceal system by lymphangiographic contras medium in 40-50% of cases. A massively dilated vermiform plexus of lymphatic vessels has been demonstrated in the pelvis running medially and anterior from the iliac vessels towards the bladder

Most interesting is the demonstration of abnormal communications between the retroperitoneal and renal lymph vessel. These dilated, tortuous vessels appear to follow the collecting system and not infrequently a fine halo of lymph vessels can be seen surrounding the minor ealyees . The Lumbar lymph nodes are poorly visualized. They may appear to be almost entirely absent throughout the entire lilac and para aorticchai, but several are usually visualized and these are often enlarged.

It is though that lymph nodes fail to visualize because of obstruction,but KOELIER and associates visualized it and found it normal in 13of their15 cases. Dramatic anatomic demonstration have resulted from combining excretory urography on retrograde with chyluria has accumulated (23, 24).

Investigations

Chylous urine is best studied immediately after it has been voided. A fatty diet a day or night before has been used to enhance chyluria. On gross inspection, classic chylous urine is like milk, frequently containing a semisolid gel. Blood and fibrin clots are frequently observed in most of the samples. When kept in the test tube, it usually settles down into three layers, the fat being lighter gets deposited as the top layer, the fibrin clots from the middle layer and cells together with debris settle in the bottom layer.(62,63,64)

When equal part of the milky urine and ether are vigorously shaken for a few minutes, there is almost complete clearing of opacity with slight turbidity remaining in the lower nonether zone. Under the microscope the sediment is found to contain variable number of erythrocytes and lymphocytes. The latter when stained fresh with one or two drops of 1:1500 aquous solution of methylene blue reveals small lymphocytes floating single or in clumps. Fat droplets of varying size can be seen. Casts and cylindroids are usually absent.(62,63) Chylomicrons can be seen directly under microscope with dark ground illumination or stained with Sudan III. Oral ingestion of fat labelled with Sudan III (10 gm of butter with 100 mg of Sudan red III) causes orange pink colouration of urine in chylurics with in 2-6 h,(64) but Sudan III being expensive is not freely available.

The urine examination at the hands of various pathologists has been found to inaccurate number of times, particularly if chyluria is mild. This is partly due to less sensitively of ether test where only subjective methods are employed to see the resolution of turbidity.

Recently, focus is being shifted to biochemical as well as electrophoretic study to detect the lipid constituents of urine and recently urinary triglyceride have been demonstrated to be universally present even if the urine is clinically clear.(65) Whether chyluria is continuous/intermittent mild or severe, urinary triglycerides are invariably detected in morning samples.

Patients of UTI or phosphaturia are negative for the same. Estimation of urinary triglycerides is 100% sensitive and specific test for chyluria.

It is noninvasive and cost effective and is independent of manual error. The etimated values of chylomicrons, TGs and cholesterol in urine may point to the level of abnormal communication.

Similarly, urine albumin has been found in varying ranges from mild to nephrotic range(75) and immunoelectrophroresis has shown globulins of various types and apolipoprotein A 48 of intestinal origin in the urine. The urine may sometimes contain predominantly blood and sometimes, the severe haematochyluria in accompanied with a clot in bladder which is often confused as carcinoma bladder.

Localization of lympho-urinary fistulae

Urologic investigations to localise site of lymphatico-urinary fistulae and obstruction should include, cystourethroscopy, retrograde pyelography (RGP) and lymphography, in some patients.Intravenous urography is mostly normal, hence its routine use is questionable. It may rarely demonstrate dilated para-calyceal lymphatics particularly when ureteric pressure is applied.

Renal size may appear larger in severe lymphatic disease. It has poor sensitivity and often proves to be a costwaste. It is recommended if higher concentration of (Ag No3) is being planned for instillation.

Cystourethroscopy and retrograde pyelography

Cystourethroscopy (CPE) is very useful and often shows milky efflux from one or both ureteric orifices.

Rarely, chylous efflux may be seen from bladder or even posterior urethra. Particularly when irrigant flow is stopped and bladder in semi-filled. In mild chyluria, ureteric catherization and split urinalysis for chyle may be done.62, Retrograde pyelography with fluoroscopic control and spot films often demonstrates pyelolymphatic backflow. Earlier studies demonstrated this in most of the cases and believed it to be diagnostic of chyluria. Later studies revealed that it is not specific of chyluria and may be seen in normal kidneys particularly if contrast is injected under pressure. However, it is more likely to occur in chyluria and should be differentiated from pyelovenous reflux, which is rather rare.(66)

Lymphography

Lymphography shows lymphaticourinary fistulae. Numerous torurous dilated lymphatics around hilar region (lymphangiectasia) communicating with paravertebral lymphatics and contrast outling major/minor calyx. Contrast may enter pelvicalyceal system in 40% and may be followed into bladder.(67.68.69,70)Other associated findings may be; thoracic duct sometimes shows tortuosity and beading though mostly it is normal, round granular enlarged, nodes in para-aortic area, skipping of lymphatic chain in advance cases, dilated cisterna chylii may be demonstrated, abnormal lymphatics may be seen coursing down along line of ureter and transit of contrast medium from feet to thoracic duct is characteristically accelerated. Presently it is not recommended for routine use.

Lymphoscintigraphy

Recently, Radio-nuctide lymphoscintigraphy has been used to outline lymphatics in patients with various lymphatic disorders. (71, 72)A comparison is presented between the results of lymphangiography and lymphoscintigraphy in patients with chyluria and these are correlated well. Lymphoscintigraphy being less invasive has been promulgated as investigation of choice but is not available at all centers. A simple diagnosis-making algorithm is presented.

Elisa test for filariasis (fila test)

The ELISA test for filariasis is based on humoral immune response of the host to filarial antigen. The filarial ES antigen, immobilized on membrane is allowed to react with patients serum, followed by incubation with anti IgG enzyme conjugate. The presence of antibody is detected using a color change indicator system.(73) The specificity and sensitivity of this test has been reported to be 85 and 95%, respectively (Lymphatic filariasis fourth report of WHO expert committee of filariasis, 1984).

Renal biopsy

It is rarely done and mainly for research purpose. Light microscopic changes reported are; membranous nephropathy, mesangioproliferative nephropathy, endothelial cell proliferation; mild mononuclear cell interstitial infiltration. Ultrastructural changes reported are; immune complex type glomerulonephritis has been demonstrated in animal model, and also in human subjects. (74) How far these changes affect course of chyluria is not know because they are just the result of filariasis not of chyluria perse. Slight increase in renal size has also been reported in chyluria (? due to lymphatic obstruction).

Cloudy urine may be due to phosphates (and occasionally due to carbonates) precipitating in alkaline urine. The phosphates and carbonates redisolve when acetic acid is added. Uric acid and urates cause a white, pink or orange cloud in acidic urine and redissolve on warming to 60 degree. Ammonium urate occurs in neutral and alkaline urine and dissolve in acetic acid..

Leucocytes may form a white cloud similar to that caused by phosphates but in this case the cloud remains after the addition of dilute ascetic acid. The presence of leukocytes is confirmed by microscopic examination of the urine.

TREATMENT OF CHYLURIA

MEDICAL TREATMENT

The medical treatment of chyluria falls into three categories:-

1. Dietary restriction of fats.

2. Substitution of fat with medium-chain triglycerides and

3. Diethy carbazine for active filarial chyluria.

In the majority of patients Diethyicarbazine is capable of arresting mildly to moderatively active filarial chyiuria. The dosage used is 0.5 mg to 2 mg/kg three times daily for 1-3 weeks in some patients repeated courses of therapy are indicated. Because of secondary bacterial infections antibiotics have also proved helpful. Diethylcarbazine is only effective when active filarial disease is present. Once chyluriais is established Diethyicarbazine is of limited value. With non parasitic chyiuria dietary alteration is the only non- surgical therapy available.

This consists of reducing to the beneficial effect of

Medium- chain Triglyceride substitution. However, this effect is not universally accepted. Bed rest and the use of a tight-corset to raise intra abdominal pressure have been reported as successful in some Patients.

SURGICAL TREATMENT

The surgical options can be divided into six categories

1. Renal pelvic instillation sclerotherapy (RPIS) is a minimally invasive treatment modality in treatment of chyluria.
2. Renal Hilar Lymphatic stripping – open surgical.and laparoscopic
3. Hilar stripping coupled with renal decapsulation
4. Internal drainage by surgical means, and
5. Autotransplantation or nephrectomy

1. Renal pelvic instillation sclerotherapy (RPIS)

The various agents used as sclerosants are as follows:

1. silver nitrate
2. povidone iodine,
3. Sodium iodide,
4. Potassium bromide,
5. Dextrose (50%)
6. Urograffin76%,
7. Hypertonic saline (3%),
8. combination therapy.

Indications for sclerotherapy

Failure of conservative management-DEC therapy and dietary modifications.

Mechanism of action of the sclerosant

Injected sclerosant reaches lymphatics through the pyelolymphatic fistula where it induces an inflammatory reaction in the lymphatics. This leads to chemical lymphangitis and oedema of the lymphatic channels. Finally, healing occurs by fibrosis causing blockade of the offending lymphatics and communicating lymphatic fistula.

1. LAVAGE OF RENAL PELVIS WITH SILVER NITRATE

YAMAUCHI stated that silver nitrate was an effective therapeutic agent for chyluria. Of 888 cases of renal pelvic instillations. Therapy throughout JAPAN from1957 to 1961 silver nitrate solution was used in 585 965.8%) and better results were obtained than with the use of contrast medium or saline. The purpose of renal pelvic instillation.Therapy is to cauterize and obstruct the fistulas between the renal calices or pelvis and the renal lymphatics. When chyluria is severe with fibrin clots, therapy is done while the patient is placed on a fat restricted diet. Treatment is initiated with 0.1%silver nitrate to encourage patient tolerance to the therapy which causes backache and pain.The final concertration of silver nitrate is limited to 0.5%.Treatment is performed in the outpatient clinic using local anaesthesia. Chyluria stopped with instillation therapy in

almost 60% of the patients recurred in half of 45 patients followed for > 2 years (16 on the ipsilateral side). The results of renal pelvic instillation therapy in 217 patients between 1952 and 1973 were as follows:- Chyluria stopped in 129 patients (59.4%) .Of 45 Patients followed for < 2 years

relapse occurred on the ipsilateral side in 16 and from an undetermined side in7. Lavage of the renal pelvis using a sclerosing solution of 1% to 3% silver nitrate or 10% to 15% potassium lodide (if the kidney was the source of chyluria) has been used for many Years. (23)Endoscopic sclerotherapy with 1% silver nitrate has been associated with serious complications like acute renal failure, papillary necrosis, massive hematuria and even death.

LAVAGE OF RENAL PELVIS WITH BETADINE

In 1998, Shanmugam et al. described 0.2% povidone iodine instillation as safe and effective in curing chyluria.(10)

Bhat et al treated 20 patients with the same technique (51) (2ml of povidone iodine + 8 ml of distilled water a total of 10 ml).

Instillation of povidone iodine initially results in inflammatory edema and blockage of the lymphatics. Later, inflammatory fibrosis leads to permanent obstruction of the lymphatic channels and cure of chyluria.

Povidone iodine is iodine complexed with the non ionic surfactant

polymer polyvinyl pyrrolidone and has a local sclerosant action. As a sclerosant it has been used in the management of renal cyst (59) and lymphocele following renal transplanation(60) . However, it may be associated with serious iodine hypersensitivity reactions. Other agents that have been tried are 50% glucose, normal saline,10-25% sodium iodide and 15% potassium iodide. The reported success rate varies from 59-68% with recurrence rate of 51%(61).

The recurrence rate with this dose is high and there is no major study regarding the effective dose and the long term results. So we planned this study.

Combination therapy

It consists of mixture of two sclerosants in a hope to get a better and stronger fibrotic response. Nandy et al. used combination therapy for the renal pelvic instillation where they combined povidone iodine with 50% dextrose. They showed a response rate of 87% with a recurrence rate of 13% in their study of 46 patients which were followed up for 24 months.(78)

2. Renal Hilar lymphatic stripping

The surgical technique of stripping and interruption of the renal pedicle lymphatics was first reported by KATAMINE IN JAPAN in 1952.

OKAMOTO AND associates reported the results of the operation in 70 cases. Reports presented from outside Japan include those of TORRES and ESTRADA, CALLAHAN and associates,YU and associates and 22).

The purpose of the operation is to isolate the affected kidney and upper ureter from adjacent issues, and ligate and disconnect the renal pedicle lymphatics that accompany the renal pedicle lymphatics that accompany the renal vessels and ultimately link the cisterna chyli and the kidney. The operation interrupts renal lymphactics , preventing chylous lymph backflow
to the kidneu chyluria ceased immediately postoperatively in 98% of the patients so treated. Follow up studies indicated persistent excellent results. The reason for ipsillateral recurrence may be recanalisation of lymphatics but this occurred in only 6.2 % of the patients who were followed. Meticulous care should be taken not leave even the small lymphatics around the renal arteries uninterrupted ligation of the lymphatic with skill is also essential to discourage recanalisation.Chyluria developing in the opposite renal pedicle lymphatics, causing a reflux into the un operated kidney, contralateral chyluria occurred in8.1% of the followed patients. Operation is of benefit not only to relieve Dysuria owing to fibrin clots but also to
obviate dietary restrictions serum protein levels returned to normal postoperatively. Callahan and associates injected Methylene blue into some of thelarge visible lymphatics during operation so that they can be seen and stripped away.Karanjavala

adopted a new surgical technique of lymphatic Disconnection. Half on hour before the operation, the lympahatics were cannulaed on the dorsum of the foot, which was continued through out the operation. The lymphatic varies in the affected area was well demon started.

The kidney was approached through a standard renal incision, including resection of the 12th rib.Lymphatic tributaries around the renal vein artery are seem coming from the main lymphatic trunk near the venacave .These are severed and ligated. For the lower ureterand bladderlymphatic disconnection the oblique muscle-cutting exraperitoneal approach is adequate.

Laproscopic chylolymphatic disconnection

Chylolymphatic disconnection can be done by both open surgical technique and laparoscopy.(47) Cases have been reported via transperitoneal and extraperitoneal access.(46, 47, 48.49)

The success rate of open surgical technique has been reported up to 98% at follow up of 1 year.50 Laparoscopy in spite of being minimally ivasive has all the advantages of open surgery. Several authors have reported equally comparable results after laparoscopic chylolymphatic disconnection. (47, 48, 49) The advantages of retroperitoneoscopic chylolymphatic disconnection are; easy and straight access to the kidney, besides the other advantages of laparoscopy like magnified view for better identification of lymphatics, minimal morbidity, shorter hospital stay and lesser time off.

3 & 4. HILAR lymphatic stripping couples with renal decapsulation and NEPHRECTOMY

5. Autotransplantation or nephrectomy

Brunkwall *et a 52* reported a case of recurrent chyluria after failed initial surgical treatment, which consisted of stripping of the renal pedicle. Patient was successfully managed by renal autotransplantation. Before the advent of

sclerotherapy and chylolymphatic disconnection more formidable procedure like nephrectomy has also been described for recurrent chyluria.

Yamauchi has stated that nephrectomy, capsulectomy and the removal of perirenal lymph channels and a few regional nodes probably have no place in treatment of chyluria. Since dilated lymphatics were not seen in the peripheral area, this accounted for the failure of the operation of decapsulation.

IV. **INTERNAL DRAINAGE BY SURGICAL MEANS**

Dr. Cockettand Goodwin have advocated a shunt between a single varicose lymphatic and the testicular or ovarian vein for the relief of lymphatic hyoertension. A frequently reported cause for recurrence of chyluria, after renal hilar stripping, result from failure to fully ligate or disconnect all lymphatic channels. With an internal drainage procedure, the effect of incomplete stripping in minimized. Anastomosis of the lumbar lymphatic vessel to the spermatic vein is a technically difficult procedure. The anastomosis is performed with loupe

magnification.

Today a higher anastomotic patency rate is possible, with the use of an operating microscope to anastomose a lymphatic vessel with a venous tributary of similar size.

Lympho-venous anastomosis

This is the most physiological method of surgical correction for recurrent chyluria. (55.56,57,58) The procedure increases the drainage of lymph into venous system, which rapidly decreases the intralymphatic pressure. Thus facilitating the healing of pyelo-lymphatic fistulae. The procedure is technically cumbersome as lymphatics are difficult to identify, lymphatic channels are thin, brittle and liable to collapse, which requires microsurgical expertise.

Retro-peritoneal lympho-venous anastomosis

The technique was described by Cockett and Goodwin.(58) Jiang and Hu (1982) treated 29 patients of chyluria with retroperitoneal lympho-venous anastomosis (RPLVA). At a follow-up of 1-14 years, 24 patients were cured and four were improved. The shortcomings of RPLVA are deep seated operative field, risk of renal pedicle injury, risk of renal artery stenosis and renovascular hypertension. (58)

Trans-inguinal spermatic lympho-venous anastomosis

The procedure has been described in male patients with recurrent chyluria. Inguinal hernia incision is used. (57,58). About 1 ml of 1% methylene blue + 1% procaine injected in testis. Three large blue stained lymphatics and spermatic veins (of similar caliber) are dissected out. End-to-end interrupted anastomosis is done by 10-0 nylon. Xu *et al*. (55) described 64 patients in whom transinguinal spermatic lymphangiovenous anastomosis was performed. Follow up was 6 months to 11 years in 50 of the patients. Chyluria disappeared completely in 30 (60%). In another study by Zhao *et al*. (57) reported a success rate of 76.3%. The procedure has the advantage of a superficial operative field and is simple and less traumatic.

Inguinal lymph node-saphenous vein anastomosis

Here, a lymphnodo-venous anastomoses is made according to the principles of lymphovenous shunt. A conical tissue of lymph node close to the greater saphenous vein in the inguinal region is removed and the remaining tunnel-shaped node is anastomosed to the vein to drain the lymph into the venous system. Hou *et al (53)* treated 30 cases of chyluria and 21 cases were followed up for 6 months after the operation. Among them, 16 (76.2%) showed disappearance of chyluria and 2 (9.5%) were improved, giving an effective rate of 85.7%. The operation avoids damage to both the afferent and efferent lymphatic vessels and affords a large anastomotic stoma for free passage of the lymph into the vein. In another study by Ji *et al (54)* where in males a lymphatico-venous anastomosis of the spermatic cord was performed and in females the

lower inguinal lymph nodes were anastomosed to the branches of the greater saphenous vein. In patients with scrotal lymphangial fistulae, bilateral lymphatico-venous anastomosis was carried out after excision of the fistula and scrotoplasty. Thirty-seven patients were followed up for 1-9 years, 36 being cured by a single operation.

AIM AND OBJECTIVE

1. **To determine the percentage of Povidone Iodine required for cure of chyluria after single dose renal pelvis instillation.**

2. **To compare efficacy of percentage of Povidone Iodine versus side effects**

Materials and Methods

Between September 2004 and April 2007, all patients who presented with complaints of milky white colored urine (chylous) were evaluated. Patients were asked to bring freshly voided urine in a transparent bottle. After inspection Ether test was done to demonstrate chyluria.

Ether test

5cc of ether is added to 5 cc of urine added to see the solubility.

Urine - albumin

- Sugar

- Deposits

Urine culture and sensitivity

Blood – TC

- DC

- ESR

Blood smear for microfilaria

Blood urea

Sr.Creatinine

Blood sugar – fasting

- Post prandial

Ultrasound KUB

X ray KUB.

IVU done in selected cases who presented with

1. Haematuria

2. haemetochyluria.

3. Ultrasongram showing subtle changes in the kidney

4. Episodes of febrile illness

Dietary advice

To avoid saturated fatty acids fatty diet - avoiding ghee,butter,ground

nut oil.Advised to take sunflower oil.

Medical treatment

Diethylcarbazine (6 mg/kg Body weight) for - 3 weeks.

restriction of strenuous activity.

If urine culture was positive they were treated according to the

sensitive drugs before povidone iodine instillation.

The concentration of povidone iodine used

Group I	- 0.5 %	- 18 Patients
Group II	- 1 %	- 18 Patients
Group III	- 2.5 %	- 18 Patients
Group IV	- 5 %	- 18 Patients

The commercially available form povidone iodine is 5 %

It is diluted with distilled water to get the required concentration.

For each patient povidone iodine from a newly opened bottle was

used.Patients were selected according to registration in the order of

.5, 1, 2.5, 5 % concentration.

Procedure

On the day of procedure Patients were advised to take butter 25 gms with bread and if non vegetarian 2 boiled eggs 2-3-hours prior to cystoscopy. They were asked to collect urine and show it to us just before putting the patient on table. If the urine is clear then the procedure is postponed. If the urine is chylous Injection Cefataxime 1 gram is given IV after test dose.

Under local anasthesia with 20 F cystoscope withg 30 degree telescope was done with Normal saline for irrigation. The side of efflux was noted carefully. If reflux was found on both sides then right side is selected for treatment and the left side instillation after a period of 3 weeks with the same dose.

A 5 F ureteric catheter was passed into the selected ureter and Positioned in the pelvis. 5 - 7 ml of selected prepared concentration of povidone iodine was instilled into the renal pelvis slowly over a period of 1 to 2 minutes. During the procedure any pain or other

reaction was noted. Patients were observed for 24hours and discharged the next day.

At the time of discharge the following were noted

1. Fever

2. Loin pain

3. Haematuria.

4. Urine sample for culture.

At the time of discharge Tab Gatiflox 1 od was given for 5 days and Tab. Drotavarine sos.

All patients were reviewed after 3 weeks and if still symptomatic and the urine chyle is positive then the same procedure was repeated with the next higher concentration of povidone iodine on the same side in unilateral cases and in bilateral cases on both sides in 2 sittings with a time interval of 3 weeks.

The maximum concentration used was 5 % and if there was

no response then povidone iodine double wash was given i.e. 5 %

given as usual followed by another wash after a time interval of 6 to 8

hours.If still not responding then we group them as refractory.

All the cases were reviewed at 1, 3, 6 and 12 months.

OBSERVATION

A Total of 72 patients were included in this study, of these the maximum incidence of chyluria occurs between the third and fourth decade.

1 patient	-	less than 20 years
13 patients	-	20 to 30 years
25 patients	-	30 to 40 years
15 patients	-	40 to 50 years
12 patients	-	50 to 60 years
6 patients	-	60 to 70 years.

Of the total 72 patients

Females - 44 / 72 patients (61.11 %)

Male - 28 / 72 patients (38.88 %).

The sex incidence ratio was almost 1.6: 1.

The duration of complaints of passing milky urine varied from 1 month to 20 years and most of the patients had symptom free interval in between.

Haematochyluria was present in 8 patients and history of passing chylous clots was found in 11 parents. Obstructive voiding symptoms were found in 3 cases. Acute urinary retention was found in 3 cases.

Of the 28 male patients 2 has bilateral hydrocele and none of the 72 patient had filarial

limbs.

Ultrasound KUB showed normal upper tracts in all the cases and in 4 cases chylous balls were demonstrated in the bladder.

Intravenous urogram was normal in all (7 cases) in whom it was done.

Cystoscopy findings

chylous efflux On the right side - 27 cases

chylous efflux on the left side - 23 cases

chylous efflux bilateral - 22 cases.

Urine Culture- positive

Total - 7 cases

E.Coli - 5 cases

proteus - 1 case

klebsiella - 1 case

Renal function was normal in all patients.

Of the 72 patients 2 were diabetic and after povidone iodine instillation there was no significant side effects.

Disappearance of chyle after 3 weeks of Povidone Iodine instillation was noted as success.Appearance of chyle at any time during the study period was considered as

failure was noted as success.

Group I

Povidne iodine concentration - 0.5 %

Total number of cases - 18 cases

Success - 13 cases

Failure - 5 cases

Percentage of success - 72.22 %

Complications immediate - nil

Late - nil

Group II

Povidne iodine concentration - 1 %

Total number of cases - 18 cases

Success - 7 cases

Failure - 11 cases

Percentage of success - 33.33 %

Complications immediate - nil

Late - nil

Group III

Povidone iodine concentration - 2.5 %

Total number of cases - 18 cases

Success - 15 cases

Failure - 3 cases

Percentage of success - 83.33 %

Complications immediate - nil

Late - nil

Group IV

Povidne iodine concentration - 5 %

Total number of cases - 18 cases

Success - 17 cases

Failure - 1 case

Percentage of success - 94.44 %

Complications	immediate	- severe pain (38.8 %)
	Late	- nil

Of the 20 failures 8 cases had
bilateral reflux and 12 had unilateral reflux.

Failure was not influenced significantly by unilateral or bilateral reflux.

In our study of 72 cases no patient developed anaphylaxis following

povidone iodine instillation.

In our study 2.5 % concentration of povidone iodine has more success rate (83.33 %)

with no significant side effects.

Age distribution

Cystoscopy - Chyle efflux

DISCUSSION

Yamauchi (11) has reported the usual occurrence of chyluria between the second and fifth decade of life. In our study out of 72 patients 54 were in between the second and fifth decade of life. (75 %).

According to Torres and associates, no sex predominance exists (42).

In our study out of the 72 patients 44 were females and 28 were male.

The sex incidence ratio was 1.6: 1.

The duration of symptoms ranged from 2 month to 20 years.

Most of them had symptom free interval in between. The symptom free interval varies from months to years.

Shanmugam used single instillation of .2 % povidone iodine in five patients and there was no recurrence in 6 months follow up. (10)

Singh had studied two-types of dosage schedule in chyluria patients. In the first protocol, 8 h instillation of the povidone iodine was done for 3 days (total of nine doses) while in the second protocol weekly instillation of the povidone iodine was done for 6 weeks. The total number of patients included in the study was 27 in first protocol and 25 in the second protocol.

At median follow-up of 32 months in 8 h instillations group there was 85%

response rate with mean disease free duration of 27 months. While in weekly instillation group a response rate of 75% with disease free duration of 22 months were observed. (88)

Shailendra conducted a randomized prospective and comparative study to evaluate the efficacy and toxicity of 1% silver nitrate, 0.2% povidone iodine and 50% dextrose as RPIS for treating chyluria.

The dextrose treatment was discontinued at mid-term because of poor success. Of 85 patients, 44 received silver nitrate and 41 povidone iodine; both groups were well-matched and the mean follow-up was 28.4 and 23.3 months, respectively. 'Immediate clearance' was recorded in 91% and 98%, and recurrence in 21% and 22% of patients after the first course of RPIS, after silver nitrate and povidone, respectively; Kaplan-Meier estimates of 'disease-free duration' in the two groups (23.6 vs 20.1 months) were also similar ($P = 0.7906$). The cumulative success rate after two courses of RPIS was 82% (silver nitrate) and 83% (povidone; $P = 1.0$). Five (11%) patients in the silver nitrate and one (2%) in the povidone group had significant flank pain during treatment. He concluded that Povidone iodine 0.2% is as

effective for RPIS as 1% silver nitrate.

In our study 5 % Povidne iodine concentration (Group IV) had a Success rate of 94.44 % with severe pain as immediate Complication (38.8 %). with a recurrence rate of 5.6 %.

With 2.5 % Povidone iodine concentration (Group III) the Success rate was - 83.33 % with recurrence 16.67.

The manifestation of chyluria depends upon the site of involvement and the anastomotic variation of lymphatic system in the individual patient. The anastomotic variation primarily occurs at the cisterna chyli where the lumbar trunks and the intestinal trunks join. The classical cisterna chylii is seen in only about 47% of normal individuals, and the intestinal trunk in such cases drains in the lumbar trunks of one side or directly in the thoracic duct either as a single trunk or as multiple smaller ones. This may explain the presence of unilateral chylous oedema of only one extremity or unilateral chyluria. The unilateral findings are more common on the

left side.(76,77)

In our study of the 72 cases chylous efflux on the right side was for 27 cases and for the left side 23 cases and bilateral efflux in 22 cases with a ratio of the ratio Right : left - 1.17 : 1 with a slight shift to right side.

SUMMARY AND CONCLUSION

Between September 2004 and April 2007 all patients of chyluria were studied with single dose renal pelvis instillation of Povidone Idine

5 % Povidone Idine had the best success rate in clearing chyluria (94.4 %). The most common complication was severe pain which occurred in

38.8 %)

2.5 % Povidone Idine had a success rate of 83.33 % with no significant during and after the procedure.

1 % Povidone Idine had the most failure. The success rate was 33.33 %. which was worse than .5 % Povidone Idine. There was no significant complication.we cannot come to a conclusion why this variation happened.

.5 % Povidone Idine had a the sucess rate of 72.2 % with no significant complicating

We conclude that 2.5 % Povidone Iodine single pelvis instillation is the ideal dose, which gives good success with no major complications

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BJU International 94 (7), 1082–1085.

Tuberculoid Leprosy (TT):

Consent form

I am _____ willing to participate in the study titled “The Effect of
Levofloxacin in Paucibacillary Leprosy”. I am aware that I will be given a new drug, Levofloxacin instead of Ofloxacin in the ROM regimen for the treatment of the leprosy lesion which I am suffering from. The purpose and the advantage of the study has been explained in the mother tongue by the investigator. I am also aware that I can discontinue
from the study whenever I wished to do so.

Date;

Place; Signature of the Patient/Guardian

age group		
10 – 20	1	
20 – 30	13	
30 – 40	25	
40 – 50	15	
50 – 60	12	
60 – 70	4	
70 – 80	2	

Proforma- chyluria

Name

Age sex

Address

Complaints: duration
LUTS
Henatochyluria
Ureteric colic
AUR
H/O previous treatment

Examination: genitalia
Lower limb

Urine - albumin

- Sugar

- Deposits

Urine culture and sensitivity

Blood – TC

- DC

- ESR

Blood smear for microfilaria

Blood urea

Sr.Creatinine

X-ray KUB

USG- KUB:

Cystoscopy:

Treatment: betadine wash Side

% of betadine used

Complications: immediate

Late

Follow up; USG KUB;

Immediate

1 month

3 month;

6 month;

1 year:

Miscellaneous :