Single-dose instillation of povidone iodine for chyluria: A safe and effective therapy

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Abstract

Introduction: Management of chyluria with initial conservative approach and then using endoscopic sclerotherapy is a mainstay approach. However, a wide range of sclerosants are available with differential success rates and complication rates. This study evaluated the safety and efficacy of a single-dose instillation of 1% povidone iodine for the treatment of chyluria.

Materials and Methods: This was a prospective, observational study conducted on patients with chyluria who did not respond to conservative management with dietary restriction and diethylcarbamazine. The site of chyle efflux was identified by cystoscopy. A 6 Fr ureteral stent was inserted into effluxing side, diluted contrast was injected to delineate the pelvicalyceal system and the pyelolymphatic connection (arborization of the pelvicalyceal system), and a single-dose of 1% povidone iodine was instilled. Patients were observed for loin pain, fever, and disappearance of milky urine postinstillation and followed up at intervals of 3 months for a total duration of 1 year.

Results: Of a total 50 patients included, 35 were men and 15 were women, with a mean age of 37 years. Pyelolymphatic connections were noted in 48% of the patients. All patients showed an immediate disappearance of milky urine. During 1-year follow-up, 92% of the patients were symptom-free till the last follow-up while only 8% of the patients experienced recurrence of chyluria which were treated with other treatment modalities. The mean duration of recurrence was 8 weeks.

Conclusion: Single dose of 1% povidone iodine was effective in immediate clearance of milky urine and well tolerated in patients with chyluria during 1-year follow-up.

Keywords: Conservative management, endoscopic sclerotherapy, pyelolymphatic connections, sclerosant agents, silver nitrate

INTRODUCTION

Chyluria is the medical condition with the presence of chyle in urine, resulting in a milky-white appearance of urine. Etiology of chyluria includes parasitic, generally due to Wuchereria bancrofti, a thready filarial parasite lodged in the lymphatic system, or nonparasitic infections. It indicates the presence of an abnormal communication between intestinal lymphatics and the urinary tract. Chyluria is more commonly encountered in the tropical and subtropical
regions such as India, Southeast Asia, Sub-Saharan countries, and South America and rare in Western countries. Chyluria is caused by the obstruction of the lymphatic flow, which occurs due to chronic lymphourinary reflux via fistulous communications secondary to lymphatic stasis, which allows for the passage of white blood cells, fats, and fat-soluble vitamins into the urine. It also leads to nutritional deficiency and a state of compensated immune suppression.[2,3]

Management of chyluria involves various types of treatment options, including conservative methods, endoscopic sclerotherapy, surgical lymphatic disconnection, and microsurgery. Generally, the first line of treatment used in such patients is a conservative method in the form of bed rest, use of abdominal binders, high fluid intake, low-fat diet, high-protein diet, and antifilarial drugs such as diethylcarbamazine.[3] In some patients with chronic conditions, conservative measures show empiric effects.

Endoscopic sclerotherapy is one of the promising management strategies used to cure chyluria after failure of conservative treatments. It involves use of instilled sclerosant that induces an inflammatory reaction and blocks the lymphatic channels, resulting in immediate cure with permanent remission.[4-6] However, higher concentrations of sclerosant agents can lead to patient’s death. Hence, to overcome these effects, agents such as povidone iodine and radiographic contrast media were introduced. Renal pelvic instillation sclerotherapy (RPIS) is a minimally invasive endoscopic sclerotherapy used frequently to treat chyluria. Silver nitrate and povidone iodine are the most commonly used RPIS agents. However, silver nitrate is discontinued due to its multiple side effects.[5,7-12]

Although previous studies have established similar efficacy of povidone iodine and silver nitrate in the management of patients with chyluria, the lack of randomized clinical trials assessing safety and efficacy of different sclerosants is a major hurdle in providing a clear evidence, regarding superiority of the single dose of povidone iodine instillation in RPIS.[13-15] The present study aimed to evaluate the safety and efficacy of single dose of 1% povidone iodine instillation in the management of patients with chyluria.

**MATERIALS AND METHODS**

This was a prospective observational study, conducted in accordance with the principles of the Declaration of Helsinki. The study was conducted at the Department of Urology, SCB Medical College and Hospital, Cuttack, India, between October 2017 and October 2018, enrolling patients with chyluria who did not respond to conservative management with dietary restriction and diethylcarbamazine. Patients with bilateral efflux, comorbidities, and chronic kidney conditions were excluded from this study. Written informed consent was obtained from all the patients.

All eligible patients were given heavy fatty meal the night before the procedure. The patients were placed in lithotomy position, and the site of chyle efflux was identified by diagnostic cystoscopy. In all patients, a 6 Fr ureteral stent was inserted into effluxing side and diluted contrast was injected to delineate the pelvicalyceal system and the pyelolymphatic connection identified by arborization of the pelvicalyceal system [Figure 1]. In all patients, single dose of 1% povidone iodine was instilled into the effluxing side manually by syringe. The sclerosant agent was prepared with 1 ml 10% povidone iodine diluted with 10 ml of distilled water and was instilled till the patient experienced flank pain. The ureteric catheter was left open till 30 min and removed after that. In three cases, bilateral chyle efflux was identified and both sides were instilled with a gap of 1 month. In five cases, the pelvis was moderately large and extrarenal where the volumetric evaluation was made with the help of computed tomography intravenous urogram, and the amount of solution instilled into the pelvicalyceal system was around 17–20 ml. All patients were observed for loin pain, fever, urinary tract infection (UTI), evidence of acute kidney injury (AKI), and disappearance of milky urine after the procedure. All patients were followed up at intervals of 3 months for a total duration of 1 year, and examinations included symptoms, routine urine analysis to look for urinary chyle, and ether test.

**RESULTS**

A total of 50 patients with chyluria were included in this study and followed up for 1 year. Among them, 35 were...
men and 15 were women. The mean age of the patients was 37 years ranging from 25 to 49 years [Table 1].

Pyelolymphatic connections were noted in 48% of patients, which was diagnosed by retrograde instillation of contrast. Three patients had bilateral chyle efflux. None of the patient suffered from any allergic reaction. All patients showed an immediate disappearance of milky urine after procedure. During 1 year of follow-up, 92% (n = 46) of the patients were symptom-free till the last follow-up while only 8% (n = 4) of the patients experienced recurrence of chyluria [Table 1]. Of the three patients with bilateral efflux, one patient experienced recurrence. The mean duration of recurrence was 8 weeks. In patients with pyelolymphatic flow who were cured with 1% povidone iodine instillation, follow-up retrograde pyelography showed disappearance of arborization pattern. In all patients with recurrence, a second dose of 1% povidone iodine instillation was done. Of these eight patients, four were cured of their disease. After povidone iodine instillation, three out of 50 patients (6.6%) developed UTI which was managed with antibiotics. None of the patients showed signs of AKI.

**DISCUSSION**

The present study evaluated the safety and efficacy of single-dose instillation of povidone iodine in the management of chyluria. Overall observations demonstrated that single dose of 1% povidone iodine was effective in causing immediate disappearance of milky urine after procedure, thereby causing obliteration of pyelolymphatic communications in patients. Further, absence of any allergic reaction in all patients and symptom-free survival in majority of the patients (92%) suggest that 1% povidone iodine was well tolerated in the present study patients.

There are several previous studies that established the efficacy and safety of different sclerosant agents in the cure of chyluria. These include 0.5% silver nitrate solution, 0.2%-5% povidone iodine, 50% dextrose, 3% hypertonic saline, 10%-25% potassium iodide, and contrast media used in radiology.[1,8,15,16] Currently, the use of povidone iodine is considered superior to other sclerosants due to minimal complication rate associated with povidone iodine. Povidone iodine has been used alone or in combination with other drugs. The commonly used sclerosing agent is a combination of 5% povidone iodine and 50% dextrose instilled through a ureteric catheter and reported the cure rate of 90% when used for 6 months duration.[6,9,17] Using silver nitrate as a sclerosing agent in the instillation into renal pelvis demonstrated 80% success rate.[8] However, associated side effects cannot be ignored. Some of the complications reported were flank pain, nausea, vomiting, interstitial nephritis, chemical cystitis, papillary necrosis, arterial hemorrhage, pelvicalyceal system cast formation, ureteric strictures, acute renal failure, and even death.[5,10-12]

A study by Goel et al. assessed and compared the efficacy and toxicity of 1% silver nitrate, 0.2% povidone iodine, and 50% dextrose in RPIS for chyluria. They demonstrated similar efficacy of 0.2% povidone iodine and 1% silver nitrate for RPIS, suggesting povidone iodine as an alternative to the use of silver nitrate.[13] Another study from India used 2 ml of 5% povidone iodine dissolved in 8 ml of distilled water instilled every 8 h into the renal pelvis for 3 days for the treatment of patients with chyluria. They observed 88% of success rate with complete clearance of chyluria in 21 patients and complications in four patients (hematuria, n = 2; and acute pyelonephritis, n = 2) which were treated with conservative approach. Overall observations indicated that instillation of povidone iodine as a sclerosant into the renal pelvis was safe, effective, and associated with minimal morbidity.[14] These observations are in concordance with the present study results and indicate the use of povidone iodine as a substitute sclerosant to silver nitrate in the management of chyluria. A similar study conducted by Shrestha et al. evaluated the effectiveness and safety of single dose 0.2% povidone iodine RPIS for the treatment for chyluria. They reported immediate clearance of symptoms in all patients and recurrence in 7 (17%) with mean disease-free duration of 18 months. In addition, two patients experienced moderate-to-severe flank pain which subsided after a single dose of parenteral analgesic. Therefore, they concluded that single dose 0.2% povidone iodine sclerotherapy is a safe and effective treatment for chyluria. In addition, as it also offers treatment on a daycare basis, continuous ureteral and urethral catheterizations can be avoided.[17] These observations accord with the present study.

| Parameter                        | Total (n=50) |
|----------------------------------|-------------|
| Age (years), mean                | 37          |
| Sex                              |             |
| Male                             | 35 (70)     |
| Female                           | 15 (30)     |
| Pyelolymphatic connections       | 24 (48)     |
| 1-year follow-up                 |             |
| Symptom free                     | 46 (92)     |
| Recurrence                       | 4 (8)       |
| Duration of recurrence (weeks), mean | 8           |
| Urinary tract infection          | 3 (6.6)     |
| Evidence of AKI                  | 0           |

Data shown as n (%), unless otherwise specified. AKI: Acute kidney injury
Previous study by Suri et al. retrospectively assessed various modes of presentation of chyluria, treatment options available, and associated complications in a total of 600 patients. They found that instillation of povidone iodine was as effective as silver nitrate showing immediate clearance in 91% of the patients in the silver nitrate and 98% in the povidone group. The recurrence of chyluria was observed in 21% and 22% in two groups, respectively, and the cumulative success rate after two courses of sclerotherapy was 82% in the silver nitrate and 83% in the povidone group. Side effects were much less with povidone iodine treatment. However, they did not observe any complication in nearly 500 patients over 16 years with the use of silver nitrate. It could be due to strict adherence to guidelines and taking utmost precautions during the instillation procedure.[19]

A recently published study assessed the parameters that affect outcomes of endoscopic sclerotherapy for filarial chyluria and demonstrated that the choice of sclerosing agent (silver nitrate 1% versus povidone iodine 0.1%) had no difference in success rate; however, silver nitrate had slightly higher complications rate (25% vs. 20%). A higher number of instillations (>3) was associated with better success rate. Majority of the complications were either Clavien Grade 1 or 2. The factors predicting recurrence were higher clinical grade, higher number of pretreatment courses, and high urinary TG and cholesterol.[18]

A case report of an 8-year-old boy presented to a pediatric nephrologist for the evaluation of passing cloudy white urine for 1 year demonstrated that repeated sclerotherapy with 1% povidone iodine solution successfully resolved the symptoms of an idiopathic chyluria.[19] A study by Seleem et al. compared the safety, efficacy, and complications of single versus multiple instillations of povidone iodine (0.2%) and urographin (76%) for the treatment of chyluria. They reported comparable success rate between patients with single instillations (85.2%) and multiple instillations (88.9%). The recurrence rates in both groups were 14.8% with a disease-free duration of 4–15 weeks and 11.1% with a disease-free duration of 6–18 weeks. However, authors emphasize on the use of single instillation protocol of sclerosing agents due to its cost-effectiveness and advantage of a shorter hospital stay.[20]

The limitations of this study include lack of randomized trials involving comparative assessment with other sclerosant agents, small sample size, and shorter follow-up period.

CONCLUSION

Overall observations of this study suggest that single-dose instillation of 1% povidone iodine sclerotherapy is an effective, well-tolerated, inexpensive, minimally invasive method for the management of chyluria. However, further comparative studies are needed to establish its efficacy better.

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Conflicts of interest
There are no conflicts of interest.

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