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Is single dose povidone iodine sclerotherapy effective in chyluria?

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Abstract
Purpose To evaluate the effectiveness and safety of single dose 0.2 % povidone iodine renal pelvic instillation sclerotherapy for the treatment for chyluria.
Methods In a prospective study from August 2010 till July 2013, 41 patients presenting with milky urine were included. Apart from ether test, the presence of lymphocytes in urine and urine triglycerides levels were also done to confirm chyluria. On a day care basis under local anesthesia, 5F open-ended ureteric catheter was introduced in the ureteric orifice of affected side. Freshly prepared 7–10 ml of 0.2 % povidone iodine solution was instilled with the patient in Trendelenburg position.
Results Total of 41 patients were enrolled (27 males and 14 females; mean age 40 years, SD 8.9, range 19–61) with a mean follow-up of 20 months. Immediate clearance was seen in all patients and recurrence in 7 (17 %). Mean disease-free duration was 18 months. Two patients had moderate to severe flank pain.
Conclusion Single dose 0.2 % povidone iodine sclerotherapy is safe and effective treatment for chyluria. As it offers treatment on a day care basis, continuous ureteral and urethral catheterizations can be avoided.

Keywords Chyle · Chyluria · Povidone iodine · Sclerotherapy

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Introduction

Chyluria is a chronic condition characterized by passage of milky appearing chylous material in urine due to abnormal pyelolymphatic communications. It is a condition with spontaneous remissions and exacerbations [1]. Chyle is composed mainly of albumin, emulsified fat and fibrin in varying proportions that are taken up by the lymphatics from the intestine [2]. The symptoms are usually of sudden onset and mostly occur in young adults. Although not life threatening, it often causes morbidity due to its presentation such as hematochyluria and colics. It also leads to nutritional deficiency and a state of compensated immunosuppression [3]. Chyluria is endemic in South-east Asia, China, India, Japan, Taiwan, parts of Africa, Australia and South America [4]. In endemic areas, approximately 10 % of the population are infested, 10 % of whom eventually develop chyluria [5].

Treatment with high-protein and low-fat diet is offered in most of the cases but is effective only in some patients, whereas antifilarial drugs are not helpful in this late manifestation of parasitic infestation by Wuchereria bancrofti [6]. In patients who do not respond to conservative management, renal pelvic instillation sclerotherapy (RPIS) is generally used to cause sclerosis of pyelolymphatic fistulae. Wood in 1929 noted the incidental disappearance of chyluria after retrograde pyelography [7]. Different sclerosing agents have been used since then for the treatment for chyluria. Although silver nitrate is one of the most commonly used agents, it is associated with serious side effects even death [8]. Because of these side effect profiles of silver nitrate, safe but effective sclerosing agent is being sought.

After Shanmugan et al. reported their experience with povidone iodine as a sclerosant in 1998, various studies

have been conducted to study the dose, efficacy and side effect profiles of this agent [1, 4, 9–12]. It has been used either as a single instillation of diluted solution [10] or as a 8-h instillation of total 9 doses [1] or in combination with 50 % dextrose twice a day for 3 days [9] or with a contrast agent as single instillation [11]. However, there is no consensus in dose and frequency of the sclerotherapy using povidone iodine solution till date.

Methods

From August 2010 till July 2013, forty-one patients presenting with milky urine were prospectively included in the study. Written informed consent was taken before the initiation of treatment. Chyluria was confirmed with ether test, microscopic visualization of lymphocytes in urinary sediment (lymphocyturia) and by estimating triglycerides in urine samples. After a detailed clinical history taking, all the patients underwent routine hematological investigations, renal function tests, routine urine test and culture and sensitivity testing of urine. Ultrasound of abdomen and pelvis was done as a part of the protocol in all the patients.

Chyluria was graded according to symptoms severity into 3 grades. Grade I—patients passing milky white urine, grade II—milky white urine associated with whitish clots or episodes of clot retention and patients with hematochyluria were designated as grade III.

Patients were assessed by cystoscopy under local anesthesia. All the patients were advised to take a fatty meal the night before to help lateralizing the chylous efflux. A 5F open-ended ureteric catheter was introduced into the ureteric orifice of the affected side and passed up to the renal pelvis. Freshly prepared 7–10 ml of 0.2 % povidone iodine solution was instilled via a ureteric catheter over a minute with the patient in Trendelenburg position. Patients remained in same position for 5 min with ureteric catheter in situ to prevent sclerosant from being drained into the bladder. Povidone iodine 0.2 % was prepared by adding 8 ml of distilled water in 2 mL of 5 % povidone iodine solution.

Clearance of chyluria after RPIS up to the last follow-up was considered as success, whereas failed therapy is the persistence of chyluria. Relapse of the milky urine after an initial clearance of chyluria was recorded as recurrence. The interval between instillation and recurrence or last follow-up (if the patient is recurrence free) was documented as the disease-free duration (DFD). Patients with recurrence were treated with a second course of RPIS after 6 weeks of initial therapy. If there was recurrence after second dose of treatment, nine doses of instillation (every eight hourly for 3 days) was given. All patients were discharged on the same day after 2 h of observation on oral antibiotics and analgesics except those requiring 9 instillations. Patients were followed up the next day to assess the persistence or clearance of milky urine and thereafter at 3 monthly intervals.

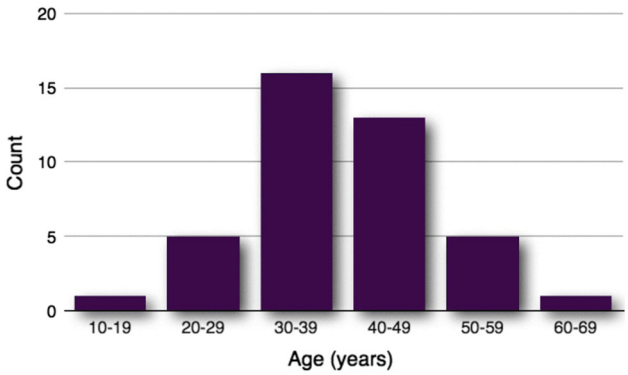

Fig. 1 Distribution of patients according to age groups

Results

A total of 41 patients presented with chyluria during the study period. Out of them, 65.9 % were male (M:F = 27:14). Majority of the patients were in the 4th and 5th decades of their lives (Fig. 1). Mean age of presentation was 39.93 years (±8.94) with a range of 19–61 years. Two-third (66 %) of the patients in our study had grade I chyluria. Four of 41 patients (10 %) presented with hematochyluria with passage of chylous clots.

All the patients had immediate clearance. Out of 41 patients, 34 (82.9 %) had complete disappearance of milky urine after single dose and were symptom free till the last follow-up, whereas seven patients required additional course of RPIS, which was given after 6 weeks of initial instillation. Two patients developed recurrence even after the second dose of sclerotherapy and were subjected to 9 doses of instillations. Chyluria persisted for a few days after the 9th instillation in one patient but it subsequently stopped, and the patient is symptom free in the last follow-up of 9 months. Another patient had persistence of symptom and underwent open chylolymphatic disconnection and nephropexy.

Mean DFD was 17.95 months (range 3–36 months), whereas those patients who experienced recurrence had a mean DFD of 10.57 (±5.59) months only. The earliest recurrence was seen at 3 month follow-up in one patient who underwent second instillation after 6 weeks of initial course.

No serious complications were noted in any of the patients during the study period. All the patients were discharged on the same day. Two patients had moderate to severe flank pain lasting for 1–2 h, which subsided after a single dose of parenteral analgesic.

Discussion

Chyluria usually does not affect the general health. However, when there is excessive loss of fat, the patient may suffer from weight loss, hypoproteinemia and immunologic disorders from severe proteinuria. Chyluria occurs after rupture of lymphatic vessels into the urinary system as a result of increased intralymphatic pressure due to obstruction [13].

Goel et al. had reported that ether test failed to confirm chyluria in 73 (69 %) of 106 patients in whom it was later confirmed by the presence of lymphocytes in urinary sediments. Therefore, lymphocyturia was a more sensitive tool to confirm the diagnosis of chyluria than the ether test [1]. In our study, ether test was positive only in 25 % of the patients. However, lymphocyturia was present even in the patients with a negative ether test. Postprandial urinary lipids, especially urinary triglycerides, are a reliable marker in the evaluation of chyluria [14]. Urinary triglycerides were routinely done in all our patients, and it was positive in 40 out of 41 (97.5 %) patients.

Chyluria is not a life-threatening disease. Hence, the treatment should be safe, minimally invasive and at the same time effective also. RPIS is widely being used because it is minimally invasive and effective. Injected sclerosant induces inflammatory reactions after reaching lymphatics through the pyelolymphatic fistula. This leads to chemical lymphangitis and edema of the lymphatic channels, and resultant blockade leads to immediate relief. Finally, healing by fibrosis causes permanent remission [15].

Silver nitrate as a sclerosant has been used by most and is often associated with a number of serious side effects, including sepsis, interstitial nephritis, pyonephrosis, ureteral strictures, arterial hemorrhage, chemical cystitis, acute renal failure and even death [8, 15, 16]. Povidone iodine as sclerosant was found to have less of these side effects and was equally effective [1]. It is nontoxic, a nonirritant, economical and easily available. It has local sclerosing action as well as antiseptic, antibacterial and antifungal actions, and it is easy to prepare in desired concentration [10]. To date, the problems regarding best dose, frequency and total number of instillation and concentration of povidone iodine RPIS remain unanswered.

In a study by Shanmugam et al. [10], 0.2 % povidone iodine was used in five patients, all considered successful at 6 months. Although there were few patients and a short follow-up, these initial results prompted others to use povidone iodine as an alternative to silver nitrate. In another study, a combination of 5 ml povidone iodine with 5 ml of 50 % dextrose was used, which was instilled twice a day for 3 days. Observed results were complete remission in 87 %, persistence in 13 % and noted recurrence in 2 out of 47 patients [9]. Sharma et al. [11] reported the efficacy of single instillation of combination of 5 % povidone iodine with contrast agent (Urografin 76 %) diluted with sterile water in a ratio of 1:1:3. They had a success rate of 87.5 % and were comparable with the results of other series with extended instillations. Similarly, Murthy shared their experience of 9 doses of povidone iodine instillation at 8-h intervals for 3 days, and 21 of 26 patients showed complete clearance [17] (Table 1).

After the initial study by Shanmugam, almost all other studies using povidone iodine as sclerosant have used either multiple doses or combination with other agents such as dextrose solution or contrast agents. Since Shanmugam achieved complete response with this new agent, though the number of cases and follow-up duration was short, we decided to study the efficacy of single dose 0.2 % povidone iodine in the management of patients with chyluria. The success rate of 83 % with single dose povidone iodine sclerotherapy in our study is comparable to the result of

Table 1 Comparison of results of povidone iodine as sclerosant

Study (sclerosant used)	Total instillations	Response rate (%)	Mean follow-up (month)	Recurrence (%)
Shanmugam et al. [10] 0.2 % Povidone iodine	1	5/5 (100)	6	–
Nandy et al. [9] 5 % Povidone iodine + 50 % Dextrose solution	6	40/46 (87)	24	13.0
Sharma et al. [11] 5 % Povidone iodine + 76 % Urografin	1	35/40 (87.5)	12	12.5
Ramana Murthy et al. [11] 0.2 % Povidone iodine	9	21/26 (81)	–	19
Our study 2013 0.2 % Povidone iodine	1	34/41 (83)	20	17

other studies using mostly 9 doses or combination sclerotherapy. Single dose sclerotherapy has certain advantages over 9 dose regimens. Single dose protocol does not require admission for subsequent instillations and also keeps patients catheters and tubes free. So, it is performed as a day-care procedure with good results. For this reason, cost effectiveness and patients' satisfaction are higher with this treatment modality.

In case of failure with initial instillation, similar dose can be repeated one more time after duration of 6 weeks. Out of seven patients who failed after first dose, five patients had clear urine after the second instillation and are symptom free till the last follow-up. Only two patients in our series required nine instillations, out of them one had persistence of chyluria even after nine doses. Open chyllymphatic disconnection was performed with good results in that patient.

In conclusion, single dose 0.2 % povidone iodine sclerotherapy in chyluria has comparable efficacy to other regimens of RPIS. It offers the treatment on a day care basis so continuous ureteral and urethral catheterizations are not necessary. However, randomized control studies will confirm its efficacy better. In addition, split function test before and after the therapy would better clarify the impact of this regimen on renal function.

Conflict of interest None.

References

1. Goel S, Mandhani A, Srivastava A, Kapoor R, Gogoi S, Kumar A et al (2004) Is povidone iodine an alternative to silver nitrate for renal pelvic instillation sclerotherapy in chyluria? BJU Int 94(7):1082–1085. doi:10.1111/j.1464-410X.2004.05108.x
2. Hemal AK, Gupta NP (2002) Retroperitoneoscopic lymphatic management of intractable chyluria. J Urol 167(6):2473–2476
3. Date A, John TJ, Chandy KG, Rajagopalan MS, Vaska PH, Pandey AP et al (1981) Abnormalities of the immune system in patients with chyluria. Br J Urol 53(4):384–386
4. Suri A, Kumar A (2005) Chyluria-SGPGI experience. Indian J Urol 21(1):59–62. doi:10.4103/0970-1591.19554
5. Zhang X, Ye ZQ, Chen Z, Chen ZQ, Zhu QG, Xin M et al (2003) Comparison of open surgery versus retroperitoneoscopic approach to chyluria. J Urol 169(3):991–993. doi:10.1097/01.ju.0000045090.45767.56
6. Brunkwall J, Simonsen O, Bergqvist D, Jonsson K, Bergentz SE (1990) Chyluria treated with renal autotransplantation: a case report. J Urol 143(4):793–796
7. Okamoto K, Ohi Y (1983) Recent distribution and treatment of filarial chyluria in Japan. J Urol 129(1):64–67
8. Mandhani A, Kapoor R, Gupta RK, Rao HS (1998) Can silver nitrate instillation for the treatment of chyluria be fatal? Br J Urol 82(6):926–927
9. Nandy PR, Dwivedi US, Vyas N, Prasad M, Dutta B, Singh PB (2004) Povidone iodine and dextrose solution combination sclerotherapy in chyluria. Urology 64 (6):1107–1109; discussion 1110. doi:10.1016/j.urology.2004.07.035
10. Shanmugam TV, Prakash JV, Sivashankar G (1998) Povidone iodine used as a sclerosing agent in the treatment of chyluria. Br J Urol 82(4):587
11. Sharma G, Chitale V, Karva R, Sharma A, Durug AB (2008) Fluoroscopy guided instillation therapy in chyluria using combination of povidone iodine with contrast agent. Is a single instillation sufficient? Int Braz J Urol 34(3):270–275 discussion 275–276
12. Singh K, Srivastava A (2005) Nonsurgical management of chyluria (sclerotherapy). Indian J Urol 21(1):55–58. doi:10.4103/0970-1591.19553
13. Maged A (1967) Renal chyluria. Br J Urol 39(5):555–559
14. Peng HW, Chou CF, Shiao MS, Lin E, Zheng HJ, Chen CC et al (1997) Urine lipids in patients with a history of filariasis. Urol Res 25(3):217–221
15. Sabnis RB, Punekar SV, Desai RM, Bradoo AM, Bapat SD (1992) Instillation of silver nitrate in the treatment of chyluria. Br J Urol 70(6):660–662
16. Kulkarni AA, Pathak MS, Sirsat RA (2005) Fatal renal and hepatic failure following silver nitrate instillation for treatment of chyluria. Nephrol Dial Transplant 20(6):1276–1277. doi:10.1093/ndt/gfh790
17. Ramana Murthy KV, Jayaram Reddy S, Prasad DV, Purusotham G (2010) Povidone iodine instillation into the renal pelvis in the management of chyluria: our experience. Urol Int 84(3):305–308. doi:10.1159/000288233