Is Single Dose Povidone Iodine Sclerotherapy Effective in Chyluria?
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ABSTRACT

Background
Chyluria is a chronic debilitating condition characterized by formation of pyelo-lymphatic connections. Renal pelvic instillation sclerotherapy is a minimally invasive treatment modality in treatment of chyluria. Various sclerosant with different regimen have been described in literature but there is no single consensus on this regard.

Objective
To evaluate the effectiveness and safety of single dose 0.2% povidone iodine renal pelvic instillation sclerotherapy for the treatment of chyluria.

Method
In a prospective study from August 2010 till July 2013, forty one patients presenting with milky urine were included. Apart from ether test, 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.

Result
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.

KEY WORDS
Chyluria, povidone iodine, sclerotherapy.
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. Chyle is composed mainly of albumin, emulsified fat and fibrin in varying proportions that are taken up by the lymphatics from the intestine. 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 like hematochyluria, colics etc. It also leads to nutritional deficiency and a state of compensated immunosuppression. Chyluria is endemic in South-east Asia, China, India, Japan, Taiwan, parts of Africa, Australia and South America. In endemic areas, approximately 10% of the population are infested, 10% of whom eventually develop chyluria.

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. Patients who do not respond to conservative management, renal pelvic instillation sclerotherapy (RPIS) is generally used to cause sclerosis of pyelolymphatic fistulae. Different sclerosing agents have been used since then for the treatment of chyluria. Although silver nitrate is one of the most commonly used agent it is associated with serious side effects even death. 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. It has been used either as a single instillation of diluted solution or as a 8 hourly instillation of total 9 doses or in combination with 50% dextrose twice a day for 3 days or with a contrast agent as single instillation. However, there is no consensus in dose and frequency of the sclerotherapy using povidone iodine solution till date.

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 haematochyluria were designated as grade III.

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.

A total of 41 patients were included in the study 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 the patients (10%) presented with hematochyluria with passage of chylous clots.

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 with the patient in Trendelenburg position. Povidone iodine 0.2% was prepared by adding 8ml 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 instillation(every eight hourly for three days) was given. All patients were discharged on the same day after 2 hours 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.

RESULTS

Figure 1. Distribution of patients according to age groups.
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, 7 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 for 9 doses 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 three 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 which required a single dose of parenteral analgesic.

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**Table 1. Comparison of results of povidone iodine as sclerosant**

<table>
<thead>
<tr>
<th>Study (Sclerosant used)</th>
<th>Total instillations</th>
<th>Response rate (%)</th>
<th>Mean Follow up (mo)</th>
<th>Recurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shanmugam et al 1998 0.2% Povidone iodine</td>
<td>1</td>
<td>5/5 (100)</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Nandy et al 2004 5% Povidone iodine + 50% dextrose solution</td>
<td>6</td>
<td>40/46 (87)</td>
<td>24</td>
<td>13.0</td>
</tr>
<tr>
<td>Sharma et al 2008 5% Povidone iodine + 76% Urografin</td>
<td>1</td>
<td>35/40 (87.5)</td>
<td>12</td>
<td>12.5</td>
</tr>
<tr>
<td>Ramana Murthy et al 2010 0.2% Povidone iodine</td>
<td>9</td>
<td>21/26 (81)</td>
<td>-</td>
<td>19</td>
</tr>
<tr>
<td>Our study 2013 0.2% Povidone iodine</td>
<td>1</td>
<td>34/41 (83%)</td>
<td>20</td>
<td>17</td>
</tr>
</tbody>
</table>

**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.\(^5\) Although it can be parasitic and non-parasitic, in tropical countries filarial parasitic infestation is the most common cause. Because chyluria is a late manifestation of filariasis, active microfilarial infestation is difficult to demonstrate, and it is often not possible to prove the association between the two.\(^5\) 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. Post prandial urinary lipids especially urinary triglycerides is a reliable marker in the evaluation of chyluria.\(^14\) Yamuchi in 1945 reported that estimation of urinary triglycerides is considered 100% sensitive and specific test for chyluria. It is non invasive and cost effective and is independent of manual error. Whether chyluria is continuous/intermittent, mild/severe urinary triglycerides are invariably present in morning samples.\(^15\) 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 oedema of the lymphatic channels and resultant blockade leads to immediate relief. Finally healing by fibrosis causes permanent remission.\(^16\)

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, papillary necrosis, acute renal failure and even death.\(^8,16-18\) Povidone iodine as sclerosant was found to have less of these side effects and was equally effective.\(^2\) It is nontoxic, a nonirritant, economical, and easily available. It has local sclerozing 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 remains unanswered.

In a study by Shanmugam et al, 0.2% povidone iodine was used in five patients, all considered successful at 6 months.\(^8\) 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 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 was comparable with the results of other series with extended instillations.\(^11\) Similarly, Murthy shared their experience of povidone iodine instillation. When total of 9 doses were given at 8-hour intervals for 3 days, 21 of 26 patients
showed complete clearance. In 4 patients, recurrence was noted and a repeat injection was given after 4 weeks, with success, in 2 patients.\textsuperscript{19} (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 like 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 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 is higher with this treatment modality.

In case of failure with initial instillation, similar dose can be repeated one more time after a duration of 6 weeks. Out of 7 patients who failed after first dose, 5 patients had clear urine after the second instillation and are symptom free till the last follow up. Only two patients in our series required 9 instillations, out of them one had persistence of chyluria even after nine doses. Open chylolymphatic disconnection was performed with good results in that patient. No serious side effects were noted in our series, however, flank pain was observed in two patients which was moderate to severe which subsided after a dose of parenteral analgesic.

**CONCLUSION**

In conclusion single dose 0.2\% povidone iodine sclerotherapy in chyluria has comparable efficacy to other regimens of RPIIS. 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.

**REFERENCES**