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ENDOSCOPIC TREATMENT OF CHYLURIA USING POVIDONE IODINE WITH CONTRAST AGENT – A PRELIMINARY EXPERIENCE

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Objective: To evaluate the safety and efficacy of povidone iodine with contrast agent as a sclerosant for the endoscopic treatment of chyluria.

Patients and Methods: From December 1999 to October 2003, a total of 22 patients having chyluria were treated. After their baseline evaluation they were subjected to endoscopic instillation therapy. The sclerosing agent was prepared by using povidone iodine with contrast agent diluted with sterile water in the ratio of 1:1:3. The side with chylous efflux was identified via cystoscopy. Using a bulb tip ureteric catheter the sclerosing solution was instilled in the pelvicalyceal system. Unilateral instillation was performed in 13 cases; eight on the left and five on the right side. In the remaining nine cases that had bilateral chylous efflux instillation was performed on both sides in the same session. Fluoroscopy was used to see the complete filling of the pelvicalyceal system. The sclerosing solution was kept in the system for five minutes and the ureteric catheter was then withdrawn.

Results: All patients were cured from chyluria in the immediate post operative period. Relapse occurred in three patients, but retreatment by instillation therapy resulted in cessation of chyluria also in these cases. The longest follow up was three years, the shortest two months. Fifteen patients were lost to follow up after nine months. None of the cases but the three mentioned previously had relapse during the follow-up period.

Conclusion: Povidone iodine is a very safe and efficacious agent for the endoscopic treatment of chyluria by instillation therapy. Using a contrast agent along with it helps to know, under fluoroscopic guidance, the exact amount of sclerosing agent to be instilled to completely fill the pelvicalyceal system. Thus overfilling of the system is avoided and the complications occurring due to pyelointerstitial backflow of the sclerosant are prevented.

Key Words: chyluria, hematochyluria, povidone iodine

INTRODUCTION

Chyluria is basically a urological manifestation of lymphatic system disease, occurring as a result of communication between the lymphatics and the renal pelvis[1]. Although not life threatening, it often causes morbidity due to its presentations like hematochyluria, colics etc. It also leads to nutritional deficiency and a state of compensated immunosuppression[2-4]. Various treatment modalities have been used to tackle chyluria. The outpatient procedure commonly used is endoscopic instillation of silver nitrate into the chylous effluxing ureter, where it acts as a sclerosant. Although the procedure enjoys wide popularity, it can be associated with serious side effects. In order to avoid the problems associated with the use of silver nitrate and at the same time to achieve an effective treatment of chyluria, we applied a combination of povidone iodine with contrast agent as a sclerosing solution.

PATIENTS AND METHODS

From December 1999 to October 2003, 22 patients (14 males and 8 females) were treated for chyluria at our center. The majority of patients were in the 20-30 years age group (Table 1). All patients presented with a history of passage of milky white urine.

Table 1: Age Distribution

Age in Years	No. of Patients
< 20	1
20 – 30	12
30 – 40	7
> 40	2

The associated symptoms were hematuria in 13, flank pain in three, dysuria in two, passage of chylous clots in seven and fever in two patients. The duration of the symptoms ranged from four months to three years. Fourteen patients had received a course of diethylcarbamazine before. Those who had not received the course were started on diethylcarbamazine and asked to take the complete course. One patient had previously undergone endoscopic instillation therapy with silver nitrate but had no relief of symptoms.

The diagnosis of chyluria was made by the ether test in all patients. Routine biochemical parameters and renal parameters, i.e. serum creatinine and blood urea levels, were examined in all patients and were found to be normal. Abdominal ultrasound performed as a protocol in all patients did not reveal any abnormalities. Intravenous urography was done in 12 patients and was essentially normal. Pyelolymphatic communication was not seen on any of the IVU. Lymphangiography was not done in any case.

All patients underwent cystoscopy under general anesthesia. They were asked to have some butter in their dinner the night before the procedure. This was very helpful in seeing the chylous efflux. In 13 cases the chylous efflux was unilateral; eight from the left ureteric orifice and five from the right ureteric orifice. The efflux was seen bilaterally in nine patients. All the sides showing chylous efflux were subjected to endoscopic instillation therapy.

The sclerosant solution was prepared by using povidone iodine 5%, contrast agent (urografin 76%) and sterile water in the ratio of 1:1:3. A bulb tip ureteric catheter was used to instill the sclerosant in the pelvicalyceal system. Imaging in the form of C-arm fluoroscopy was used in all cases to visualize the complete filling of the pelvicalyceal system. The pelvicalyceal system was filled until blunting of the fornices was seen. Thus, over-distension of the system and the consequent risk of pyelointerstitial backflow of the sclerosant were avoided. The ureteric catheter was kept at the ureteric orifice to prevent the sclerosant from getting drained in the bladder. The other end of the ureteric catheter was blocked to prevent the sclerosant from dripping out. The sclerosant remained in the pelvicalyceal system for five minutes. The ureteric catheter was then removed.

In patients with bilateral chylous efflux both sides were treated in the same session.

All patients were followed up by doing urine tests for chyle one month after the treatment. Serum creatinine was evaluated in those patients who had undergone bilateral instillation of the sclerosant. Intravenous urography was done after one month in the first five patients but was not done in the subsequent patients.

RESULTS

Of the 22 patients, 19 showed clear urine and had no relapse. Three patients experienced recurrence one month (n=1) and three months (n=2) after sclerotherapy on the side that had been previously treated (two on the right and one on the left). All were retreated in the same way as described above. No relapse was noted after retreatment.

The patient who had had a previous history of sclerotherapy with silver nitrate did not show any relapse after sclerotherapy with povidone iodine and contrast agent.

The post-treatment period was uneventful in all patients except for minimal pain and minimal dysuria reported by some of the patients. Post-treatment intravenous urography was done only in five patients - three of them had undergone bilateral instillation therapy – and was found to be normal in all patients. In view of this finding and the minimal theoretical risk of renal damage or ureteric strictures using this sclerosing agent, subsequent patients were not advised to undergo intravenous urography. Serum creatinine was normal in the follow-up studies of all patients who had undergone bilateral instillation therapy.

None of the patients except the three cases mentioned above showed relapse of chyluria during follow-up. The longest follow-up period was three years, the shortest two months. Fifteen patients were lost to follow up after nine months.

DISCUSSION

Chyluria is a common problem in developing countries and usually affects the lower socio-economic classes. Although a variety of parasitic and non parasitic factors can cause chyluria[5,6], it is generally agreed that it should be considered as filarial unless proved otherwise, particularly in areas where lymphatic filariasis is or was endemic[7]. As observed by Tan et al.[8], non-parasitic causes such as malignant tumors of the thoracic duct, pregnancy, trauma etc. are rare. None of these causes were seen in this study. Congenital causes do exist[2], but such patients present at an early age, while filarial chyluria usually presents after the second decade[9].

Parasitic infection causes obstruction to the retroperitoneal lymphatics, leading to dilatation, proliferation and subsequent rupture of the lymphatics into the pelvicalyceal system[10]. Recent observations suggest that the extensive lymphangiectasia observed in Bancroftian filariasis is secondary to lymphatic dysfunction caused by cytokines liberated by adult filarial worms and by the host immune responses to the parasite[11,12]. Although chyluria can occur anywhere in the urinary tract, chyluria of renal origin is the most common[13]

The diagnosis of chyluria can be made simply by observing the urine sample and by doing the ether test. Lymphangiography has been advocated to localize the pyelolymphatic communications[14]. But routine use of lymphangiography is neither found to be useful[15] nor cost effective[16]. Intravenous urography, as observed by Sabnis et al.[15], is not helpful in delineating pyelolymphatic leaks. We had a similar observation in all 12 patients who were subjected to IVU. It would be highly debatable not to advise IVU to be done routinely in chyluria patients, but in view of its limited efficacy to alter the management, it certainly is a point worth considering and studying.

Amongst the treatment modalities recommended for chyluria are renal decapsulation[17], lymphatic venous anastomosis[18], hilar clearance of the lymphatics[10] and even nephrectomy[19]. More recently, Hemal et al. and Chiu et el. have described retroperitoneoscopic and laparoscopic nephrolympholysis, ureterolympholysis, hilar vessel stripping and fasciectomy as treatment modalities for chyluria[20-22]. Open surgical disconnection of lymphorenal communications[23], bilateral excision of perinephric fat and fascia (Gerota's fasciectomy)[24] and microsurgical inguinal lymphangiovenous and lymph node venous anastomosis[25,26], have been suggested as surgical modalities for the treatment of chyluria.

Non-operative treatment described for chyluria includes reduction of fat in the diet or a diet containing medium chain triglycerides[27]. The use of somatostatin for the treatment of posttraumatic chyluria has also been described[28]. Chyluria is debilitating and causes morbidity but not mortality. Hence, the treatment of chyluria should be safe, effective and minimally invasive. The most popular form of treatment for chyluria has been endoscopic instillation therapy. The basic principle of this particular form of treatment is to instill a sclerosant in the renal pelvis where it induces an inflammatory reaction in the lymphatics. This causes chemical lymphangitis and edema of the lymphatic channels; the resultant blockage leads to immediate relief. Subsequent healing by fibrosis results in permanent remission. The most commonly used sclerosant has been silver nitrate[8,15,16]. Okamoto and Ohi used it in a concentration of 0.1%[9]; Tan et el used 0.5% concentration[8]; while Sabnis et al.[15] and Dalela et al.[16] used a 1% concentration of silver nitrate. All these investigators reported satisfactory results. But this popular form of endoscopic instillation therapy has been associated with the following problems:

- Most of the patients complain of significant flank pain, nausea and vomiting.
- Various investigators instill it with variable frequencies. While Sabnis et al. advocated instillations every half hour for two hours[15]; Dalela et al. described weekly instillations for four weeks[16] and Okamoto and Ohi used instillations two to three times a week for 10 or more times[9].
- There is a significant failure rate ranging from 22.7% to 30%[8,16].
- Serious side effects like interstitial nephritis and ureteric strictures may occur. Renal

failure is known to occur if a concentration of more than 1% is used and the instillation is bilateral. Pelvicalyceal cast formation has been described[29]. Life-threatening complications like arterial hemorrhage due to intrarenal aneurysm formation and even death have been reported following silver nitrate instillation[30,31].

Povidone iodine is an iodine complex with the non-ionic surfactant polymer polyvinyl pyrrolidone. It is water-soluble and releases iodine slowly. The use of 0.2% povidone iodine as a sclerosant for the treatment of chyluria has been described by Shanmugam et al.[32]. They treated five patients using 5% povidone iodine diluted with distilled water using 1:5 dilutions to get a concentration of 0.2%. They used 8-10 ml of 0.2% solution, which was instilled in the pelvicalyceal system via a ureteric catheter. All their patients were free of symptoms over six months of follow up.

In all these studies using various sclerosing materials, two things have never been answered:

1. Which amount of sclerosant should be instilled in the pelvicalyceal system?

2. For how long should the sclerosant remain in the pelvicalyceal system?

As the capacity of the pelvicalyceal system varies from individual to individual it is but logic that the amount of sclerosant needed to fill the pelvicalyceal system would vary from patient to patient. It might be argued that pre-treatment RGP can help to determine the exact amount needed to achieve a pyelolymphatic backflow of the instilled sclerosant. The problem with this is that pyelolymphatic backflow is not seen in all cases. In the study done by Ko Ko et al., such a communication was seen on RGP in only 50% of cases[33]. Also, pyelolymphatic backflow is not specific to chyluria and is difficult to be distinguished from pyelovenous backflow[13]. On the other hand, to determine the amount of sclerosant needed by pre-treatment RGP and then to instill the sclerosant means repeating the procedure.

In order to be able to answer these questions and to achieve a minimally invasive endoscopic instillation therapy for chyluria we decided to study the efficacy of the combination of povidone iodine with contrast agent (urograffin 76%) as a sclerosing agent.

Povidone iodine has the following advantages:

- It provides a non-toxic, non-irritating, non-volatile and non-staining form of iodine.

- It exerts a local sclerosant action as well as antiseptic, anti-bacterial and anti-fungal actions.

- It is cheap, easily available and it is easy to dilute to the required concentration.

The sclerosing solution was prepared by using 5% povidone iodine, contrast agent and sterile water in a ratio of 1:1:3. Due to the presence of contrast media the exact amount of sclerosing solution needed to fill the pelvicalyceal system could be decided by performing the endoscopic instillation therapy under fluoroscopic control. The contrast agent would also demonstrate any pyelolymphatic communication. We failed to see any such communication in all but six cases. This observation did not come as a surprise. Our aim was to completely fill and optimally distend the pelvicalyceal system so that the sclerosant enters the pyelolymphatic channels and induces chemical lymphangitis. Over-distension of the pyelocalyceal system would be associated with the risk of pyelointerstitial and pyelovenous backflow and its attendant complications. The commonest site of the lymphatico urinary communication is at the fornices. Hence, the sclerosing solution was instilled until blunting of the fornices was seen.

The optimum time for which the sclerosing agent should be in the pelvicalyceal system is not known. But we feel that the sclerosing agent should be in contact with the pyelolymphatic channels for a sufficient duration; long enough to induce chemical lymphangitis and edema of the lymphatic channels. Hence we kept the sclerosing solution for five minutes. We feel that this is better than instilling it repeatedly at half hourly or weekly intervals. Whether instillation of the sclerosing agent for a shorter duration would be equally effective can be ascertained only by a separate study.

All the patients in our series tolerated the procedure well. There was minimal pain. No major side effects or complications were noted. Even when the sclerosant was used bilaterally no side effects were seen. Of the 22 patients, 19 did not have any relapse. The three patients

who had a relapse also responded very well to the second session of instillation therapy.

We feel that the use of povidone iodine is safe as a sclerosant for treatment of chyluria. The use of a contrast agent along with it helps to determine the exact amount of sclerosing solution that should be used. Thus, pyelointerstitial backflow and its resultant complications are avoided which otherwise would occur if the sclerosant was instilled in random amounts exceeding the capacity of the pelvicalyceal system. At the same time under-filling of the system and the resultant failure of the therapy is avoided.

Though the number of patients in this preliminary study is small and the maximum follow-up is only up to three years, we feel that this is a safe, cheap, minimally invasive and very effective treatment of chyluria.

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Editorial Comment:

This article is a valuable contribution to the scant literature on the topic of minimally invasive treatments for chyluria. The author has given a thorough consideration of the technique and useful suggestions for safe application. The follow-up is relatively short. However, re-application could conceivably be done if necessary prior to consideration of more extreme measures such as ureterolympholysis. And it is much safer than other endoscopic techniques, such as silver nitrate application.

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RESUME

Traitement endoscopique de la chylurie utilisant povidone iodine avec produit de contraste – expérience préliminaire

Objectifs: Évaluer l'innocuité et l'efficacité de la povidone iodine avec produit de contraste comme produit sclérosant dans le traitement endoscopique de la chylurie. **Patients et Méthodes**: De décembre 1999 à octobre 2003, un total de 22 patients présentant une chylurie ont été traités. Après une évaluation de base ils ont subi une instillation thérapeutique sclérosante par voie endoscopique. L'agent sclérosant a été préparé en utilisant de la povidone iodine avec un agent de contraste dilués avec de l'eau stérile dans une proportion de 1:1:3.Une montée de sonde urétérale à ballonnet après un repérage du méat urétéral à l'origine de la chylurie par voie endoscopique a été réalisée. Une solution de produit sclérosant a été instillée dans le système pyélocaliciel. Dans 13 cas l'instillation était unilatérale; huit du côté droit et cinq du côté gauche. Les neuf cas restants avaient une chylurie bilatérale, l'instillation a été entreprise bilatéralement pendant la même séance. La fluoroscopie a été utilisée pour suivre le remplissage complet pyélocaliciel. La solution sclérosante a été gardée dans le système pendant cinq minutes et la sonde urétérale a été alors retirée. **Résultats**: Un arrêt de la chylurie a été constaté chez tous les patients en post opératoire immédiat. Une rechute observée chez trois patients a été traité par la même procédure résultant en cessation de la chylurie dans ces cas. Le plus long suivi est de trois années et le plus court est de deux mois. Quinze malades ont été perdus de vue après neuf mois de suivi. **Conclusions:** La povidone iodine est un agent sûre et efficace pour le traitement de la chylurie par instillation endoscopique. Utiliser un agent de contraste permet d'estimer, sous fluoroscopie, la quantité d'agent sclérosant à injecter pour remplir complètement le système pyélocaliciel et donc de prévenir un trop-plein et ses complications en particulier un passage pyelo-interstitiel du produit sclérosant.

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