

Percutaneous Treatment of Renal Cysts with OK-432 Sclerosis

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Purpose: The aim of this study was to demonstrate OK-432 sclerotherapy efficacy for treatment of simple renal cysts. **Materials and Methods:** Twenty patients with 25 symptomatic or large simple cysts were treated by ultrasonography (US)-guided percutaneous aspiration and injection of OK-432 (8 men and 12 women, mean age 63.6 years, SD 9.5). Six patients presented with flank pain, 14 presented with renal mass; renal cyst location was right, left, or bilateral sided in 9, 8, and 8 kidneys, respectively. Patients were evaluated by clinical assessment, US, or CT scan 3 months following the procedure. Complete and partial success was defined as symptom resolution with either total cyst ablation or greater than 70% reduction, respectively. Failure was defined as 30% of cyst size recurrence and/or persistent symptoms. **Results:** Average reduction was 93.0%. Complete and partial resolution occurred in 11 (44.0%) and 13 (52.0%) cysts, respectively. One case was defined as failure, with a 64.2% size reduction from 10.9 cm to 3.9 cm (volume reduction rate 95.4%). Renal pain improved in all patients, regardless of complete or partial resolution. Minor complications occurred in 3 patients, 2 developed leukocytosis and 1 had mild fever (< 38.5 °C) following aspiration and sclerotherapy. Successful treatment was achieved with conservative measures and NSAID therapy. **Conclusion:** Percutaneous treatment of simple renal cysts with OK-432 sclerotherapy was found to be a safe, effective and minimally invasive procedure.

Key Words: Renal cyst, percutaneous sclerotherapy, OK-432

INTRODUCTION

Simple renal cysts involve the cylindrical epithelium and are histologically benign.¹ They are

quite common and usual incidental findings in elderly patients. In one study, incidence at 40 and 60 years was reported at 20% and 33%, respectively.²

Simple renal cysts are usually clinically silent and do not require treatment, however, can be associated with flank pain, hypertension, hematuria, and collecting system obstruction. When symptoms and/or urinary tract obstruction is detected, a treatment modality should be considered. Symptomatic renal cysts can be managed by a variety of surgical and percutaneous methods, including percutaneous aspiration (with or without sclerosing agent), percutaneous marsupialization, and open and laparoscopic cyst unroofing.³⁻⁸ Percutaneous drainage with single or multiple-session sclerotherapy has been successfully performed with high success rates. However, in terms of recurrence, better results have been reported with multiple-session sclerotherapy.^{1,5,9-12}

OK-432 intracystic injection is a new sclerosing therapy for cystic hygroma, lymphangioma, haemangioma, and malignant pleural effusion.^{13,14} In this study, we made the first attempt to use OK-432 sclerotherapy in management of simple renal cyst, and aimed to demonstrate its efficacy and safety.

MATERIALS AND METHODS

Twenty patients (8 male, 12 female) with 25 simple cysts underwent percutaneous sclerotherapy treatment between October 2005 and February 2006. The study was performed on patients with flank pain, dyspepsia, other related symptoms, or cyst size greater than 4 cm. Symptomatic

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omatic cysts occurred in 6 patients (30.0%) and large sized cysts in 14 (70.0%). All cysts were type I Bosniak cysts.¹⁵ Location was right, left, or bilateral sided in 9, 8, and 8 kidneys, respectively. Mean age was 63.6 (range 40-73) years (Table 1). Baseline ultrasound (US) or CT scan was obtained on all patients; cyst dimensions were measured to calculate initial volume prior to treatment. Detailed information on presence and severity of symptoms was collected. Complaints and blood pressures were closely documented before and after treatment.

Procedures were performed by US and fluoroscopy guidance on a 1 day inpatient basis. Patients were placed prone and cyst location confirmed by US. Puncture site was selected and infiltrated with Lidocaine; 18 G puncture needle under US guidance was used for initial cyst puncture. The first 10 mL of aspirate was sent for cytological and biochemical examination. Subsequently, all fluid was aspirated and 0.1 mg of OK-432 per 10 mL of cystic fluid was administered. Maximum injected volume was 1 mg.

Patients were evaluated after 3 months by clinical assessment, US, or CT scan. Success was defined as complete or partial when there was total ablation or greater than 70% reduction with resolution of symptoms, respectively. Failure was defined as less than 70% reduction and/or persistent symptoms.

RESULTS

Mean cyst size was 6.8 cm (4.9 - 10.9 cm) (Table 1). Average reduction was 93.0%. 11 (44.0%) cysts showed complete resolution (Fig. 1) and 13 (52.0%) had partial resolution (Table 2). One case was defined as failure, with 64.2% size reduction from 10.9 cm to 3.9 cm (volume reduction rate 95.4%). No cyst had malignant cells on cytological examination. Renal pain improved in all patients, regardless of complete or partial resolution.

Minor complications occurred in 3 patients, 2 developed leukocytosis and 1 had mild fever (< 38.5 °C) the first few days after aspiration and sclerotherapy. Patients were treated successfully by conservative measures and NSIAD therapy.

Table 1. Characteristics of Patients and Cysts

	No. of case
No. of patients	20
Age (yrs)	63.6 (40 - 73)
Sex ratio (M/F)	8/12
No. of renal cysts	25
Laterality (Rt./Lt./Bil.)	9/8/8
Cyst size (cm)	
< 6	14
6 - 10	8
≥ 10	3
Mean size (cm)	6.8 (4.9 - 10.9)
Cyst volume (mL)	
< 200	17
200 - 500	5
≥ 500	3
Mean volume (mL)	201.6 (61.6 - 677.7)

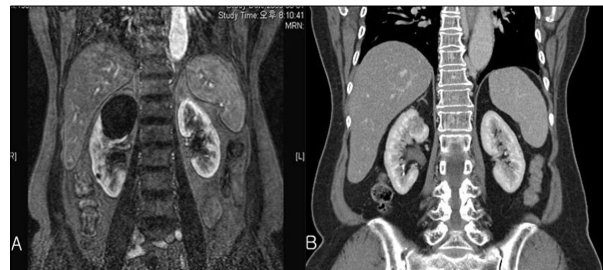


Fig. 1. Imaging of a 47-year-old woman with flank pain. (A) Coronal MRI shows a simple right renal cyst with diameter of 5.8 cm. (B) 3 months after percutaneous sclerotherapy with OK-432, CT image shows no remnant of cyst.

DISCUSSION

With new advances in endourology and interventional radiology, attractive alternatives to open surgery have been suggested for treatment of simple renal cysts. Appropriate procedure selection depends on clinical goal in addition to considerations of patient safety, comfort, and cost.

Simple drainage without sclerotherapy is associated with recurrence of 30-80%.^{5,16} The percu-

Table 2. Characteristics of Treatment and Follow-Up (n=25)

	No. (%)
Renal cyst reduction rate	
Successful treatment	24 (96.0)
Disappearance (100%)	11 (44.0)
\geq 90%	4 (16.0)
90 - 80%	8 (32.0)
80 - 70%	1 (4.0)
Failed treatment (< 70%)	1 (4.0)
Complications	
Mild fever (< 38.5°C)	1 (4.0)
Leukocytosis	2 (8.0)
Examination of cystic fluid	
Biochemical profile	all normal
Cytologic studies	all negative

taneous approach with a sclerosing agent provides more satisfactory results than aspiration alone, where fluid almost always re-accumulates because of a viable cyst wall.^{5,17} Several sclerosing agents including ethanol, glucose, phenol, chlorohydroxylate, pentopaque, acetic acid, povidone iodine, tetracycline, bismuth phosphate, and ethanolamine oleate have been used to injure the epithelial cells of the wall.^{1,5,6,18-22} Ethanol has been commonly used for hepatic cysts, hydatid cyst, and lymphoceles.²³⁻²⁵ As ethanol penetrates the fibrous capsule after 4-12 h, epithelial cells lining the cyst may be completely destroyed without damaging adjacent renal parenchyma.²⁵

However, current reports suggest lower rates of 10-68% complete resolution with 1 alcohol injection.^{5,6,22} The difference between early and recent reports may be attributed to longer follow-up in recent studies. However, several current studies showed improved results in modified alcohol sclerotherapy. Complete cyst resolution improved to 73-100% when injection was repeated 2 or more times over several days.^{6,8,16} Others reported good results using continual 24 h cyst drainage by pigtail catheter, either before or after 1 injection.^{5,10} Also, prolonged cyst wall contact with alcohol

was reported to produce better results.^{11,26}

OK-432 is a lyophilized mixture of a low virulence Su strain of *Streptococcus pyogenes* which has been incubated with penicillin G (Chugai Pharmaceuticals Co, Tokyo, Japan).²⁷ Injection of OK-432 into lymphangioma cyst immediately evokes inflammation and infiltration of inflammatory cells (including neutrophils and macrophages) causing extensive production of IL-6.²⁷ Intralesional injection has been reported as an alternative treatment for lymphangiomas and cystic hygromas.^{13,27} In addition, intracavitary injection in patients with malignant pleural or peritoneal effusion has resulted in resolution in approximately 90% of patients.^{27,28}

In our preliminary data, 24 of the 25 renal cysts had complete or partial resolution after OK-432 sclerosing therapy. No significant complications were observed in follow up.

Many define success as reduction greater than 50% original cyst volume and failure as recurrence of greater than 50% volume. However, we defined success as reduction greater than 70% original size and failure as recurrence greater than 30%. Volume reduction is more wide difference changes than size reduction. Our results were very effective, we therefore chose size reduction rather than volume reduction in our definition. We experienced failure in 1 case, however if we had used volume reduction rate, our failure case would be defined a success.

In conclusion, we have shown that single-session OK-432 sclerotherapy is a safe, effective, well-tolerated, and minimally invasive procedure for management of simple renal cysts and has a low recurrence rate comparable to other forms of sclerotherapy.

REFERENCES

1. Paananen I, Hellstrom P, Leinonen S, Merikanto J, Perala J, Paivansalo M, et al. Treatment of renal cysts with single-session percutaneous drainage and ethanol sclerotherapy: long-term outcome. *Urology* 2001;57:30-3.
2. Laucks SP Jr, McLachlan MS. Aging and simple cysts of the kidney. *Br J Radiol* 1981;54:12-4.
3. Amar AD, Das S. Surgical management of benign renal cysts causing obstruction of renal pelvis. *Urology* 1984; 24:429-33.

4. Guazzoni G, Montorsi F, Bergamaschi F, Consonni P, Bellinzoni P, Centemero A, et al. Laparoscopic unroofing of simple renal cysts. *Urology* 1994;43:154-9.
5. Hanna RM, Dahniya MH. Aspiration and sclerotherapy of symptomatic simple renal cysts: value of two injections of a sclerosing agent. *AJR Am J Roentgenol* 1996;167:781-3.
6. Holmberg G, Hietala SO. Treatment of simple renal cysts by percutaneous puncture and instillation of bismuth-phosphate. *Scand J Urol Nephrol* 1989;23:207-12.
7. Hulbert JC, Hunter D, Young AT, Castaneda-Zuniga W. Percutaneous intrarenal marsupialization of a perirenal cystic collection-endocystolysis. *J Urol* 1988;139:1039-41.
8. Okeke AA, Mitchelmore AE, Keeley FX, Timoney AG. A comparison of aspiration and sclerotherapy with laparoscopic de-roofing in the management of symptomatic simple renal cysts. *BJU Int* 2003;92:610-3.
9. Bozkurt FB, Boyvat F, Tekin I, Aytakin C, Coskun M, Ozkardes H. Percutaneous sclerotherapy of a giant benign renal cyst with alcohol. *Eur J Radiol* 2001;40:64-7.
10. Chung BH, Kim JH, Hong CH, Yang SC, Lee MS. Comparison of single and multiple sessions of percutaneous sclerotherapy for simple renal cyst. *BJU Int* 2000;85:626-7.
11. Gasparini D, Sponza M, Valotto C, Marzio A, Luciani LG, Zattoni F. Renal cysts: can percutaneous ethanol injections be considered an alternative to surgery? *Urol Int* 2003;71:197-200.
12. Ozgur S, Cetin S, Ilker Y. Percutaneous renal cyst aspiration and treatment with alcohol. *Int Urol Nephrol* 1988;20:481-4.
13. Ogita S, Tsuto T, Nakamura K, Deguchi E, Iwai N. OK-432 therapy in 64 patients with lymphangioma. *J Pediatr Surg* 1994;29:784-5.
14. Ogita S, Tsuto T, Tokiwa K, Takahashi T. Treatment of cystic hygroma in children with special reference to OK-432 therapy. *Z Kinderchir* 1987;42:279-81.
15. Bosniak MA. The current radiological approach to renal cysts. *Radiology* 1986;158:1-10.
16. Stevenson JJ, Sherwood T. Conservative management of renal masses. *Br J Urol* 1971;43:646-7.
17. Raskin MM, Poole DO, Roen SA, Viamonte M Jr. Percutaneous management of renal cysts: results of a four-year study. *Radiology* 1975;115:551-3.
18. Brown B, Sharifi R, Lee M. Ethanolamine sclerotherapy of a renal cyst. *J Urol* 1995;153:385-6.
19. Mohsen T, Gomha MA. Treatment of symptomatic simple renal cysts by percutaneous aspiration and ethanol sclerotherapy. *BJU Int* 2005;96:1369-72.
20. Ohkawa M, Tokunaga S, Orito M, Shimamura M, Hirano S, Okasho A, et al. Percutaneous injection sclerotherapy with minocycline hydrochloride for simple renal cysts. *Int Urol Nephrol* 1993;25:37-43.
21. Phelan M, Zajko A, Hrebinko RL. Preliminary results of percutaneous treatment of renal cysts with povidone-iodine sclerosis. *Urology* 1999;53:816-7.
22. Seo TS, Oh JH, Yoon Y, Lim JW, Park SJ, Chang SG, et al. Acetic acid as a sclerosing agent for renal cysts: comparison with ethanol in follow-up results. *Cardiovasc Intervent Radiol* 2000;23:177-81.
23. Akhan O, Cekirge S, Ozmen M, Besim A. Percutaneous transcatheter ethanol sclerotherapy of postoperative pelvic lymphoceles. *Cardiovasc Intervent Radiol* 1992;15:224-7.
24. Akhan O, Ozmen MN, Dincer A, Sayek I, Gocmen A. Liver hydatid disease: long-term results of percutaneous treatment. *Radiology* 1996;198:259-64.
25. Bean WJ, Rodan BA. Hepatic cysts: treatment with alcohol. *AJR Am J Roentgenol* 1985;144:237-41.
26. Falci-Junior R, Lucon AM, Cerri LM, Danilovic A, Da Rocha PC, Arap S. Treatment of simple renal cysts with single-session percutaneous ethanol sclerotherapy without drainage of the sclerosing agent. *J Endourol* 2005;19:834-8.
27. Ogita S, Tsuto T, Nakamura K, Deguchi E, Tokiwa K, Iwai N. OK-432 therapy for lymphangioma in children: why and how does it work? *J Pediatr Surg* 1996;31:477-80.
28. Kasahara K, Shibata K, Shintani H, Iwasa K, Sone T, Kimura H, et al. Randomized phase II trial of OK-432 in patients with malignant pleural effusion due to non-small cell lung cancer. *Anticancer Res* 2006;26:1495-9.