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Acetic Acid as a Sclerosing Agent for Renal Cysts: Comparison with Ethanol in Follow-Up Results

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Abstract

Purpose: To compare follow-up results of sclerotherapy for renal cyst using 50% acetic acid with those using 99% ethanol as sclerosing agents.

Methods: Eighty-one patients underwent sclerotherapy and 58 patients, 23 males, 35 females, aged 6–76 years, having a total of 60 cysts, were included in this study; the others were lost to follow-up. The renal cysts were diagnosed by sonography, computed tomography (CT), or magnetic resonance imaging (MRI). Sclerotherapy was performed using 50% acetic acid for 32 cysts in 31 patients and 99% ethanol for 28 cysts in 27 patients. Under fluoroscopic guidance, cystic fluid was aspirated as completely as possible. After instillation of a sclerosing agent corresponding to 11.7%–25% (4–100 ml) of the aspirated volume, the patient changed position for 20 min and then the agent was removed. Patients were followed up by sonography for a period of 1–49 months. The volume of the renal cyst after sclerotherapy was compared with that of the renal cyst calculated before sclerotherapy. Medical records were reviewed to analyze complications.

Results: The mean volume after sclerotherapy of the 17 cysts followed for 3–4 months in the acetic acid group was 5.1% of the initial volume, and for the 14 cysts in the ethanol group it was 10.2%. Complete regression during follow-up was shown in 21 cysts (66%) in the acetic acid group; the mean volume of these cysts before the procedure was 245 ml. The mean volume of the nine (32%) completely regressed cysts in the ethanol group was 184 ml. Mild flank pain, which occurred in three patients in each group, was the only complication and resolved the next day.

Conclusion: Acetic acid was an effective and safe sclerosing agent for renal cysts, tending to induce faster and more complete regression than ethanol.

Key words: Kidney, cysts—Sclerotherapy—Cyst, percutaneous drainage

The simple renal cyst is the most common benign mass of the kidney in an adult. Most are asymptomatic and detected incidentally on an imaging study, but large cysts cause pain or manifest as palpable masses and may cause complications [1, 2]. Surgical resection had been the treatment of choice for renal cysts, but has been replaced by aspiration of cystic fluid using a Chiba needle to arrive at a correct diagnosis and treatment. However, renal cysts treated by aspiration frequently recur since they are lined by secretory epithelium [3, 4]. Sclerotherapies using various sclerosing agents to destroy the secretory epithelium have been tried in order to prevent cyst recurrence after aspiration, and ethanol has generally been a safe and effective sclerosing agent. However, complications from ethanol were pain, fever, or drunken state and its effectiveness decreased by dilution from the remaining cystic fluid [5, 6].

Acetic acid was used effectively in the treatment of small-sized hepatocellular carcinoma [7] and we performed an experimental study on the urinary bladder of the rabbit using acetic acid as sclerotherapy for renal cysts [8]. The purpose of this study was to compare the follow-up results of sclerotherapy for renal cysts using 50% acetic acid as a sclerosing agent with those using 99% ethanol.

Materials and Methods

Eighty-one patients underwent sclerotherapy from March 1994 to September 1998. Informed consent was obtained after the nature of the disease and procedure had been fully explained to all patients. The chief complaint was intermittent flank discomfort without

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Table 1. Mean volume of renal cysts, aspiration, and sclerosing agents

	Acetic acid	Ethanol
Volume of cysts before sclerotherapy	301 ml (32–1651 ml)	209 ml (24–697 ml)
Volume of aspirated fluid	245 ml (40–523 ml)	172 ml (24–450 ml)
Percent of aspirated volume to calculated volume	81.4% (61–111%)	82.3% (62–100%)
Volume of sclerosing agent	56 ml (4–100 ml)	40 ml (6–100 ml)
Percent of agent volume to aspirated volume	22.9% (11.7–25%)	23.2% (21.8–25%)

disturbance of daily life in 39 patients, continuous flank pain in 15 patients, and palpable mass in 11 patients. Renal cysts were found incidentally on abdominal imaging for evaluation of other disease in 16 patients; these 16, from an innumerable number of patients with incidentally diagnosed renal cysts, wanted to be treated because of the psychological stress of knowing they had a lesion in their body. Sclerotherapy in patients who complained of intermittent flank discomfort was selectively performed, excluding those who refused treatment or had cysts without mass effect.

This study included 58 patients with 60 renal cysts and excludes 23 patients who were lost during follow-up because of relocation or the patient's poor cooperation. There were 23 males and 35 females aged 6–76 years (mean 57 years). Forty-nine renal cysts in 47 patients were diagnosed by sonography (ATL Ultramark 9, Bothell, WA, USA; HDI 3000, HDI, Bothell, WA, USA; 128xP/10, Acuson, Mountain View, CA, USA; SSA-250A, Toshiba, Tokyo, Japan), eight other cysts by CT (Somatom plus4, Siemens, Erlangen, Germany), and three others by MRI (1.5 Tesla Magnetom Vision, Siemens). The diagnostic criteria for the renal cysts were well-demarcated and smooth margin, round or oval shape, location at least partly within the renal contour, and homogeneously anechoic lesions with posterior acoustic enhancement on sonography, homogeneous low attenuation on CT scan, and low signal intensity on T1-weighted and high signal intensity on T2-weighted MRI without enhancement after administration of contrast media. Volumes of renal cysts were calculated from images before the procedure with the method described by Pedersen et al. [9]. The volume of a lesion was calculated as $V = \pi d^3/6$; for a spherical lesion d = diameter of the cyst, and for a nonspherical lesion $d = (l \times w \times d)/3$ where l, w, and d are the geometrical mean length, width, and depth of the cyst, respectively. The mean volume of the renal cysts on the initial images before the procedures was 301 ml (32–1651 ml) in the acetic acid group and 209 ml (24–697 ml) in the ethanol group (Table 1).

One gram of ceftezole Na (Samjin Pharm, Seoul, Korea) was injected intravenously as a prophylactic antibiotic at 10 and 2 hr before the procedure. Piprinhydrinate 3 mg (Plakon, Yungjin Pharm, Seoul, Korea) and pethidine HCL 50 mg (Guju Pharm, Seoul, Korea) were injected intramuscularly 30 min before the procedure. Sclerotherapy was performed with the method reported by Bean [4] for the treatment of renal cysts with alcohol. Fifty percent acetic acid was used as a sclerosing agent for 32 cysts in 31 patients from June 1996 to September 1998 and 99% ethanol in 28 cysts for 27 patients from March 1994 to May 1996. The concentration of 50% acetic acid was determined based on the results of a previous experimental study in the bladder of rabbits [8], and was made with 99% acetic acid (Duksan Pure Chemicals, Ansan, Korea) diluted with normal saline. With the patient in a prone position, after determination of the puncture site and needle angle with sonography (SPA-1000, Diasonic, Milpitas, CA, USA), antiseptic preparation and local anesthesia with 2% lidocaine hydrochloride (Daeheung Pharmacy, Seoul, Korea) were performed and a small puncture wound was made. Under fluoroscopic guidance (Integris C-2000, Philips, Best, The Netherlands), the cyst was punctured with a 21 G Chiba needle (Cook, Bloomington, IN, USA) or a 19 G Seldinger needle (Soo Ho Meditech, Seoul, Korea). A hair wire (0.018″ guidewire; Cook) and a Cope needle set (Cook) were used when the puncture was done with a Chiba needle. A J guidewire (0.035 inch × 150 cm, Terumo, Tokyo, Japan) was placed through the needle into the cyst and the needle was removed; a 6 Fr pigtail catheter with side holes (Soo Ho Meditech) was placed into the cyst. Cystic fluid was aspirated as completely as possible through the catheter. The mean of the ratio of aspirated volume to volume calculated on the initial images, was 81.4% in the acetic acid group and 82.3% in the ethanol group (Table 1). Contrast material (Meglumine iothalamate, Ilsung Pharmacy, Seoul, Korea) was injected into the cyst to confirm that there was no evidence of leakage into the peritoneal cavity or the adjacent organs and then removed. The aspirated fluid was analyzed.

A sclerosing agent corresponding to 11.7%–25% (4–100 ml) of aspirated volume was administrated through the catheter into the cyst (Table 1) and left in for a duration of 20 min. The patient was rolled into supine, prone, and lateral decubitus positions at 5-min intervals to increase contact between all surfaces of the cyst and the sclerosing agent. The amount of sclerosing agent was determined as 25% of the aspirated volume. However, for a large cyst with volume greater than 400 ml, the amount of sclerosing agent was limited to 100 ml to prevent systemic side effects. In a 6-year-old girl, 40 ml was used even though 25% of the aspirate volume was 85 ml because her body weight was 22 kg. After treatment, the sclerosing agent and debris were removed and irrigation with normal saline was performed. Procedures were performed once for each cyst.

In order to evaluate changes in the size of the renal cysts and complete regression, patients were followed up with sonography for a period of 1–49 months. The volumes of renal cysts calculated on follow-up sonography were compared with those calculated before sclerotherapy. Complete regression was defined as no remaining cyst to be measured on sonography with or without a scar at the renal cortex. Recurrence was defined as an increased cyst volume when compared with that before sclerotherapy; cysts having no change of calculated volume were excluded from recurrence. Sonography follow-up was scheduled for 3-month intervals after the sclerotherapy until complete regression of the cyst was found, but the timing was variable for several causes. The medical records of the patients were reviewed for procedure-related complications such as pain, bleeding, infection, and formation of urinoma or arteriovenous fistula. The number of cysts followed up in each period is shown in Table 2.

Results

At 1–2-month follow-up the mean volume of the cysts remaining in the acetic acid group was 6.9% of the initial volume calculated before sclerotherapy and the mean volume of the 14 cysts in the ethanol group was 12.4%; these values were 5.1% and 10.2%, respectively, at 3–4-month follow-up. The mean volume of the remaining renal cysts

Table 2. Number of cysts followed up and regressed to less than 10% on sonography

		1–2 mo.	3–4 mo.	5–6 mo.	7–12 mo.	>12 mo.	Total
Acetic acid	Followed up	7	17	9	4	5	42
	Regressed to <10%	4 (57%)	15 (88%)	9 (100%)	4 (100%)	5 (100%)	
Ethanol	Followed up	4	14	4	15	8	45
	Regressed to <10%	1 (25%)	9 (64%)	4 (100%)	13 (87%)	7 (88%)	

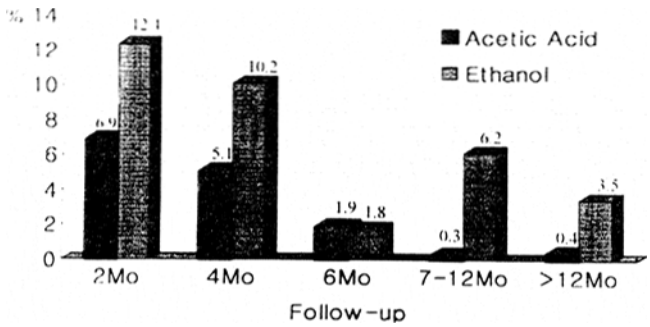

Fig. 1. Ratio of mean volume of remaining renal cysts on follow-up sonography to calculated volume on initial imaging.

was smaller in the acetic acid group than in the ethanol group at almost all periods of follow-up except the 5–6-month period (Fig. 1). The percent of cysts which regressed to less than 10% of the initial volume was 57% in the acetic acid group at 1–2 months and 25% in the ethanol group; these values were 88% and 64%, respectively, at 3–4 months. All cysts followed up after 5 months in the acetic acid group had regressed to less than 10% of the initial volume (Table 2). Complete regression of renal cysts during the entire follow-up period was shown in 21 cysts (66%) of the acetic acid group and in 9 cysts (32%) of the ethanol group (Table 3). The mean volumes before the procedure of those cysts that completely regressed were 245 ml (40–523 ml) for the acetic acid group and 184 ml (24–458 ml) for the ethanol group.

Aspirated fluids in all cysts were transudate without malignant cells on analysis. A review of the medical records showed no clinically significant sclerotherapy-related complication occurred during or after the procedure, such as gross hematuria, hemorrhage, or necrosis of the soft tissue by leakage of the sclerosing agent into the parenchyma of the kidney or soft tissue around the tract; one minor exception was mild flank pain which occurred in three patients of each group and was resolved with analgesics in all patients by the next day. On follow-up sonography, complications such as urinoma, arteriovenous fistula, infection of the remaining cyst, or enlargement of the cyst were not seen in either group.

Discussion

The pathogenesis of renal cysts is not evident, but obstruction of a convoluted tubule and ischemia at the obstructive site [10] and a number of diverticula on the tubule, increasing with age [11], are hypothesized. Renal cyst is asymptomatic in most patients and is usually diagnosed incidentally on an imaging study such as sonography, CT, or MRI, but if the cyst is large, it causes pain or manifests as a palpable mass. Infection, hypertension, and obstruction of the ureter may be associated with renal cyst [1, 2].

Table 3. Number of cysts with complete regression on follow-up sonography

		1–2 mo.	3–4 mo.	5–6 mo.	7–12 mo.	>12 mo.	Total
Acetic acid	$n = 32$	0	8	6	3	4	21
	R/T[a]	0	25%	18%	9%	13%	66%
Ethanol	$n = 28$	1	0	2	2	4	9
	R/T	4%	0	7%	7%	14%	32%

[a]R/T = cysts with complete regression/total cysts

The treatment of choice for complicated cysts had been surgical resection, but operative morbidity and complications existed. In the mid-1970s, aspiration of a renal cyst using a Chiba needle under sonography or CT guidance was performed for precise diagnosis and treatment, but the effectiveness was temporary and the recurrence rate was high because the wall of a renal cyst is lined by secretory epithelium [3, 4]. Destruction of the secretory epithelium of the cyst was necessary to prevent the recurrence and adjuvant sclerotherapies with various sclerosing agents after aspiration of the cystic fluid were tried. Glucose [12], phenol [13], iophendylate [14], pantopaque [15], and minocycline hydrochloride [16] were among the agents used, and ethanol has been used as a safe and effective sclerosing agent since the report by Bean et al. [4]. However, ethanol caused pain, fever, or a drunken state in cases treated with large amounts, and the effect of the sclerotherapy decreased due to dilution by the remaining fluid in the cyst. Recurrence was reported in over 30% of cases and sclerotherapy using over twice the amount of the sclerosing agent (up to 40% or 50% of aspirated volume) or repeat procedures were needed to compensate for the decreased effect. Catheters have been placed in renal cysts for 3 or 4 days for complete drainage of transudate by sclerotherapy [5, 6].

Ethanol had been used for sclerotherapy of renal cysts from March 1994 to May 1996 in our hospital without serious complications during the procedure or enlargement of the renal cyst during follow-up. However, several cysts retained a volume of over 20% of the calculated pre-therapy volume after 6 months follow-up or showed an arrest of regression on repeat follow-up sonography; therefore we investigated another sclerosing agent.

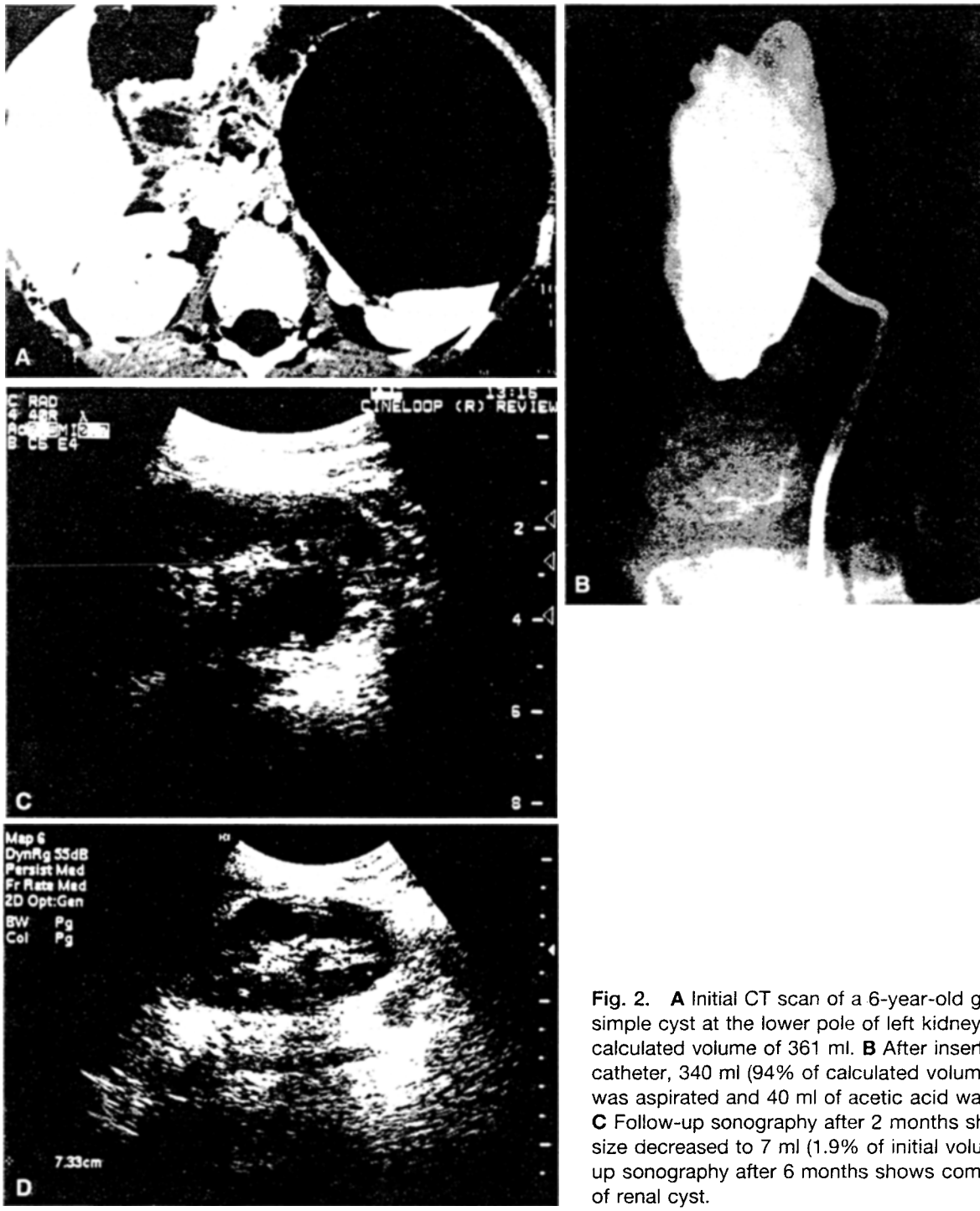

Fig. 2. **A** Initial CT scan of a 6-year-old girl shows a simple cyst at the lower pole of left kidney with a calculated volume of 361 ml. **B** After insertion of a catheter, 340 ml (94% of calculated volume) of cystic fluid was aspirated and 40 ml of acetic acid was administered. **C** Follow-up sonography after 2 months shows renal cyst size decreased to 7 ml (1.9% of initial volume). **D** Follow-up sonography after 6 months shows complete regression of renal cyst.

Ohnishi et al. [7] used acetic acid as the sclerosing agent in rat livers [7]. They reported that the desiccating action of the acetic acid on protein induced coagulation necrosis and the area of necrosis was significantly greater than when ethanol was used, if the concentration of acetic acid was over 20%. The effect reached a plateau when 50% acetic acid was used. In sclerotherapy of a hepatocellular carcinoma, it is necessary to increase the amount of ethanol in each procedure in order to decrease the number of procedures, but this may increase the frequency of complications such as portal vein thrombosis or sclerosing cholangitis. Furthermore, necrosis of the tumor may be incomplete. However, it is possible to decrease the amount of the sclerosing agent and the frequency of the procedure when acetic acid is used. An effective reduction in the size of the tumor and a complete regression are induced without recurrence in follow-up.

Kim et al. [8] reported histopathologic changes in the epithelium of the urinary bladder of rats after administration

of acetic acid in a preliminary study using acetic acid for sclerotherapy of renal cysts. Acetic acid in concentrations of 10%, 20%, 30%, 40%, and 50% were instilled into the urinary bladder and removed after 5 min. The rabbits were sacrificed after 2 days and pathologic specimens were taken. Using 10% acetic acid, mild vascular congestion of the bladder wall on gross specimen and microscopic finding of a normal epithelial cell layer were shown. Using 20% acetic acid, destruction of the epithelium and partial or complete denudation were induced on microscopic examination, and infiltration of acute inflammatory cells and interstitial edema were associated. Thickening of the bladder wall and discoloration were shown on gross specimen. Acetic acid with a concentration of 30% revealed an excellent capability for complete destruction and denudation of all layers of the epithelium on microscopic examination. Microscopic findings in specimens using acetic acid with a concentration of 40% or 50% were similar to findings in the 30% group.

The concentration of acetic acid for sclerotherapy of renal cysts in humans was set at 50% to prevent decrease in effectiveness when acetic acid is diluted by the cystic fluid remaining within the renal cyst because of incomplete aspiration; the concentration is then decreased to under 30%.

In our study, the volume (as a percent of the initial volume) of the remaining cysts that were followed up in the first 4 months after sclerotherapy using acetic acid was one-half that of the ethanol group (Fig. 1). The number of cysts that regressed to under 10% of the initial volume in the acetic acid group was greater than in the ethanol group. This means that acetic acid induces faster regression of a renal cyst than ethanol. The rate of complete regression in the acetic acid group was approximately twice that of the ethanol group and the mean volume before the procedure of completely regressed renal cysts was larger in the acetic acid group than in the ethanol group. This also means that acetic acid is more effective as a sclerosing agent. The suggestive mechanism is that unless the concentration of acetic acid was decreased to under 30%, it showed destructive action to the epithelium of the renal cyst. Acetic acid was effective in spite of dilution by the remaining fluid in the cysts after incomplete aspiration, contrary to ethanol whose effect was decreased by incomplete aspiration, as reported previously.

Acetic acid was convenient and economical because the therapy was completed with a single procedure; a repeated procedure to compensate for the decreased effect caused by dilution was not needed. Acetic acid was a safe sclerosing agent; no procedure-related complications occurred, except for mild flank pain relived with analgesics. It was possible to decrease the systemic effect of the sclerosing agent using a large dose and to prevent infection of the cyst by placing the catheter in the cyst for 3 or 4 days. Acetic acid was especially effective on cysts with a volume greater than 400 ml, in which the sclerosing agent used was less than 25% of the aspirated volume.

One limitation of this study was the irregular follow-up of patients. Many cysts were found incidentally in patients whose chief complaint was intermittent flank discomfort without disturbance of daily life or who had no complaint, and almost all patients were asymptomatic after sclerotherapy. Therefore, the patients did not return for follow-up at a recommended date and refused sonographic evaluation. If the cyst was decreased on follow-up sonography after 1 year or more without a serial follow-up, there was a discrepancy between the time of regression and detection. The other limitation was the small number of cases and the variation in the size of the remaining cysts. This resulted in no statistical significance because of a large standard deviation in spite of the fact that the volume of the remaining cysts in the acetic acid group is half of that in the ethanol group. Further study with more cases and regular follow-up is needed.

Acetic acid was an effective and safe sclerosing agent for renal cysts, tending to induce faster and more complete regression than ethanol, without recurrence on follow-up in spite of dilution by the remaining fluid in the cyst.

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