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A PROSPECTIVE EVALUATION OF N-BUTYL CYANOACRYLATE FOR PERCUTANEOUS SCLEROTHERAPY OF SYMPTOMATIC SIMPLE RENAL CYST

AMR EL-DAKHAKHNY, TAREK SOLIMAN, AHMED M. AL-ADL, TAREK EL-KARAMANY

Urology Department, Benha University, Benha, Egypt.

Purpose: To assess the safety and efficacy of n-butyl cyanoacrylate (NBCA) and iodized oil mixture as sclerotherapy for symptomatic simple renal cysts under ultrasound guidance.

Materials and Methods: This prospective study conducted between June 2013 and October 2015, included 33 patients (22 males and 11 females) with 41 symptomatic simple renal cysts (> 5 cm). The mean age ± SD was 54.5 ± 11.4 (range 41 to 76) years. Before procedure, cyst volume was evaluated by US and non-contrast enhanced CT. Percutaneous real-time aspiration and injection of mixture of NBCA and iodized oil under ultrasound guidance was done. After the procedure, patients were followed up from 3 to 12 months with periodic US examinations. Primary endpoint is complete collapse or decrease in cyst diameter > 50% and elimination of symptoms. Failure was defined as decreased cyst volume < 50% and/or persistence of symptoms.

Results: The mixture of NBCA and iodized oil was technically successful as sclerosing therapy for managing symptomatic simple renal cysts. During median follow up period of 6 months (range 3 to 12), complete disappearance was detected in 27/41 (65.9%), reduced diameter and disappearance of symptoms in 11/41 (26.8) and failed procedure (due to recurrence) was detected in 3/41 (7.3%). In all the cases with failure, the pre-procedure cyst diameter was ≥10 cm. After sclerotherapy, fever (<38.5°C) developed in one patient, and microscopic hematuria was seen in two.

Conclusion: Percutaneous real-time aspiration and sclerotherapy with NBCA and iodized oil mixture under US guidance is simple, safe, and effective procedure for treating symptomatic simple renal cyst.

Keywords: N-butyl cyanoacrylate, sclerotherapy, cystic kidney.

INTRODUCTION

Simple renal cysts are acquired lesions of the kidney, which are common in aged adults, and it is estimated that half of adults above 50 years old have simple renal cysts.1-3 The prevalence of simple renal cyst detected by computed tomography (CT) was higher than the prevalence determined by ultrasonography (US).4 Most renal cysts are asymptomatic and discovered incidentally but may be symptomatic and cause flank pain, palpable mass, or back pressure.5 Treatment of renal cyst may be mandatory if cyst growth leads to symptoms such as flank pain, hematuria, hypertension, infection, or backpressure on the pelvicalyceal system.6 Open surgery, laparoscopy, or percutaneous aspiration with or without sclerosing material are options for intervention.7 Percutaneous aspiration and sclerotherapy have been described as safe and effective method for managing symptomatic simple renal cysts avoiding the morbidity and cost associated with conventional surgery and laparoscopy.8,9 Several sclerosing agents have been used for treatment of symptomatic simple renal cysts. Although good results have been reported by different agents and techniques, the optimal technique for treating renal cysts and the best agent for renal cyst sclerotherapy remain to be determined.10 N-butyl cyanocrylate (NBCA) (Histoacryl-Blue; Braun, Melsungen, Germany) intra-cystic injection is a sclerosing therapy for hepatic cyst and cysts in autosomal dominant polycystic kidney disease.11 This study was designed to evaluate the efficacy and safety of percutaneous ultrasound – guided NBCA for managing symptomatic simple renal cysts.

MATERIAL AND METHODS

In a prospective case-series study, 33 patients with 41 simple renal cysts selected from outpatient clinics of Benha University Hospital, underwent percutaneous cyst
ablation using NBCA in the period from June 2013 to October 2015. The study protocol was approved by the Research Ethics Committee at the Faculty of Medicine, Benha University (REC-FOMBU). The procedure and possible risks were explained thoroughly according to Declaration of Helsinki and an informed consent was obtained from each participant.

Patients presented with non-colic flank pain which was in the ipsilateral side of the cyst and not related to posture were considered eligible for the study provided that other causes of flank pain were excluded by urologic evaluation before referral to intervention. Patients with hematuria, bleeding tendency, urinary tract infection, morbid obesity, complex cysts and parapelvic cysts were excluded from the study.

Assessment was done by detailed history taking, general and local examination and laboratory investigations (urine analysis, serum creatinine, liver function tests, complete blood count, and coagulation profile). Radiological examination with pelvi–abdominal ultrasound and non-contrast CT was performed to demonstrate the volume, site, and size of the renal cyst. All cysts were Bosniak class I.12

**Procedure:**

The technique was performed as previously described for CT-guided aspiration and injection.13 The patients were kept fasting for 6 hours before the procedure. Insertion of a urethral catheter under complete aseptic technique was performed immediately before the procedure and after injection of 1 gm of ceftriaxone as a prophylactic antibiotic.

The patient was placed in the lateral decubitus or prone position according to the targeted cyst location (Figure 1). The puncture area was sterilized and 5% lidocaine hydrochloride as local anesthesia was applied to the puncture site for 5 minutes. The patient was asked to hold respiration for seconds while an US–guided 18–gauge needle was inserted into the cyst and aspirating about 1/2 of the estimated volume. Then 5 mL of methylene blue were injected in the cyst with observation of the urethral catheter for few minutes to exclude connection with the pelvicalyceal system. When ensuring a clear urine output in the urethral catheter, the remaining volume in the cyst was aspirated as completely as possible. Then, the needle was flushed with 2 mL of 5% dextrose water solution (D5W) to avoid contact of NBCA with the tissue fluid in the needle lumen. Half mL of NBCA and 1 ml of iodized oil (Lipiodol; Laboratoire Guerbet, Roissy, France) were injected in the cyst, then flush the needle with 1ml D5W to be sure that all the mixture entered the cyst. The needle was withdrawn carefully.

![Fig. 1: Ultrasound-guided Renal cyst aspiration.](image-url)
In patients with cyst diameter 10 cm or more, one ml of NBCA and two ml of iodized oil were used to ensure coverage of a large surface area.

Follow up using sequential US examination was done to evaluate the treated cyst diameter and assess recurrence, if any. Non-contrast enhanced CT was deferred to confirm the final outcome.

Primary end-point was considered once the cyst was totally collapsed or diameter was decreased more than 50% compared to initial diameter on ultrasonography (radiologic success) and symptomatic success was considered when pain was alleviated. Failure was considered when cyst recurred by more than 50% of the initial diameter with or without symptoms.

**Statistical analysis:**

Statistical analysis was done using SPSS statistical software (IBM Corp., Armonk, NY, USA). Results are expressed as the mean (SD, range) for quantitative data and number and percent for qualitative data. Kolmogorov-Smirnov test was used to assess normality of data. Student’s t–test for paired data was used to compare cyst diameter before and after intervention. Analysis of variance was done using ANOVA to compare cyst diameter regarding radiologic response. A p value < 0.05 was considered statistically significant. All statistical tests were two-sided.

**RESULTS**

The study population included 22 males and 11 females with a mean age ± SD of 54.5±11.4 (range 41–76) years. The pre-procedure demographic data of the study population are shown in table (1) where 41 cysts were found in the 33 cases. Bilateral lesions were found in one case and two lesions were found in 7 cases that were managed in the same session. The procedure time was about (10–15 minutes) from the start of puncture to the end. Cyst aspiration and injection of the sclerosing material was successfully performed in all cases without major bleeding or need for sedation. The median follow up was six months with a range from three to 12 months.

Radiologic outcome is shown in table 2, where 27 out of 41(65.9%) cysts were disappeared. While reduction in cyst diameter more than 50% of the original diameter was achieved in 11 (26.8%) cysts. Failed procedure due to recurrence during the follow up period was found in three (7.3%) cases. Those cases had pre-procedure cyst diameter of ≥ 10 cm.

Patients were further stratified per the symptomatic response. In 23 (69.7%) cases, symptomatic success with alleviation of symptoms was achieved (Table 3), while in 10 (30.3%) cases persistence of symptoms was found. Those patients had significantly larger pre-procedure cyst volume and diameter. In addition, the post-procedure diameter was larger in symptomatic cases. Symptomatic success rate in cases with single cyst and those with two cysts was statistically insignificant.

Recurrent cases (three, 7.3%) were associated with pain. They were treated successfully with laparoscopic cyst decortication.

Procedure-related complications were observed in 3 cases. In two cases, microscopic hematuria occurred due to incidental injury to the pelvicalycyeal system by the needle during the procedure. They were resolved spontaneously within 2 days. In another one case, fever less than (38.5°C) occurred 3 days after procedure due to UTI. It was treated adequately with antipyretic and antibiotic according to culture and sensitivity.

**DISCUSSION**

Simple renal cysts are common in general population. In a large Middle-Eastern population composed of 8551 individuals presented for a health-screening program, the prevalence of renal cysts detected by US was 4.2%, while in another recent study the incidence was 7.7% among a thousand of subjects. The prevalence increases with age as it was 0.6% in the third decade and about 30% at 80 years old. It was also more common in men (4.8%) than in women (2.6%). The major indications for surgical intervention are pain, infection, and obstructive uropathy.

Percutaneous aspiration and injection of sclerotherapeutic agents was described as a minimally invasive, safe, simple, and effective procedure for treating the symptomatic renal cysts in comparison with open surgery and laproscopy. High rate of recurrence (30–80%) was observed in simple renal cyst aspiration alone due to rapid accumulation of liquid from the epithelial cyst wall. Percutaneous aspiration with injection of sclerotherapy have high rate of success. Ethanol injection as the sclerosing substance for the treatment of symptomatic renal cysts was first described in 1981; since that time, various techniques for sclerotherapy have been proposed.
Table (1): Baseline Characteristics of 33 Patients with 41 Cysts.

<table>
<thead>
<tr>
<th>Demographic variables</th>
<th>54.5 ± 11.4 (41 – 76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>54.5 ± 11.4 (41 – 76)</td>
</tr>
<tr>
<td>Gender:</td>
<td>22 (66.7%)</td>
</tr>
<tr>
<td>Male</td>
<td>11 (33.3%)</td>
</tr>
<tr>
<td>Female</td>
<td>22 (66.7%)</td>
</tr>
<tr>
<td>Male</td>
<td>11 (33.3%)</td>
</tr>
<tr>
<td>BMI</td>
<td>28.7 ± 3.4 (23.5 – 35.9)</td>
</tr>
<tr>
<td>Cyst diameter (cm)</td>
<td>7.3 ± 1.9 (5 – 11)</td>
</tr>
<tr>
<td>Cyst volume (ml)</td>
<td>242.5 ± 189.7 (65 – 696.9)</td>
</tr>
<tr>
<td>Number of cysts:</td>
<td></td>
</tr>
<tr>
<td>One cyst</td>
<td>25 (75.8%)</td>
</tr>
<tr>
<td>Two cysts</td>
<td>8 (24.2%)</td>
</tr>
<tr>
<td>Laterality:</td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>32 (97%)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Clinical presentation:</td>
<td></td>
</tr>
<tr>
<td>Renal lump</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>Renal pain</td>
<td>30 (91%)</td>
</tr>
<tr>
<td>Cyst location:</td>
<td></td>
</tr>
<tr>
<td>Upper pole</td>
<td>7 (17%)</td>
</tr>
<tr>
<td>Middle</td>
<td>20 (49%)</td>
</tr>
<tr>
<td>Lower pole</td>
<td>14 (34%)</td>
</tr>
</tbody>
</table>

Variables are presented as mean ± SD (Range) or number (%) as appropriate. BMI: Body mass index

Table (2): Post Sclerotherapy radiologic outcome in 33 cases with 41 cysts.

<table>
<thead>
<tr>
<th>Radiologic success</th>
<th>Number of cysts</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disappeared</td>
<td>27</td>
<td>65.9</td>
</tr>
<tr>
<td>Reduced</td>
<td>11</td>
<td>26.8</td>
</tr>
<tr>
<td>Failed treatment</td>
<td>3</td>
<td>7.3</td>
</tr>
</tbody>
</table>

Table (3): Post Sclerotherapy symptomatic outcome in 33 cases with 41 cysts.

<table>
<thead>
<tr>
<th></th>
<th>Symptomatic success</th>
<th>Persistent symptoms</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated cyst volume</td>
<td>158.3 ± 109.1 (65 – 421.2)</td>
<td>435.9 ± 197.8 (179.6 – 696.9)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Pre-aspiration Diameter (cm)</td>
<td>6.5 ± 1.3 (5 – 9.3)</td>
<td>9.2 ± 1.5 (7 – 11)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Diameter at last follow-up (cm)</td>
<td>1.6 ± 0.4 (1 – 2.4)</td>
<td>4 ± 2 (2 – 7)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Number of cysts:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One cyst</td>
<td>18/25 (72%)</td>
<td>7/25 (28%)</td>
<td>0.673</td>
</tr>
<tr>
<td>Two cysts</td>
<td>5/8 (62.5%)</td>
<td>3/8 (37.5%)</td>
<td></td>
</tr>
</tbody>
</table>

Variables are presented as mean ± SD (Range) or number (%) as appropriate.

* Student t-test
  b Fisher’s exact test.

The most common sclerosing material used for cyst ablation was ethanol either 95% or 99%. It inactivates the secreting cyst cells rapidly and penetrate the fibrous capsule of the cyst within 4-12 hrs. Ethanol injection as a sclerotherapy has many factors for optimization which include the concentration (95% or 99%), the volume, the duration, the number of injections, and the continuous drainage before and after the injection. NBCA was used for treatment of wounds and for vascular embolization. NBCA glue lead to tissue fibrosis due to rapid polymerization as adhesive material. Recently, polycystic kidney disease was treated by NBCA. A mixture of NBCA and iodized oil was tried to decrease the NBCA exothermic reaction and to decrease the time of polymerization. It also gives radio-opacity of iodized oil in imaging. The mixture of NBCA to iodized oil is (1: 2). In the present study, we used the same ratio as that used in the previously mentioned studies and we observed that 0.5 ml of NBCA glue was sufficient for renal cyst ablation of a diameter less than 10 cm. For cysts with a diameter 10 cm or more the dose injected was doubled to ensure coverage of a large surface area. Doubling the dose in large cysts was previously described.28 Targeting the renal cyst percutaneously for aspiration and injection is usually done under ultrasound, fluoroscopy, or CT guidance. Ultrasound guidance provides easy access with less cost and avoids hazards of radiation, while the CT is preferred in the obese patients.
Using the more than 50% decrease in cyst diameter compared to pre-procedure diameter as a criterion of successful outcome in our cases series was previously used in treating polycystic kidney disease and simple renal cyst. In the current study the US-guided percutaneous sclerotherapy with NBCA and iodized oil mixture was effective in relieving symptoms (pain) and reducing the renal cyst size. The technique was successful showing complete ablation in 27 (65.9%) cysts, and more than 50% reduction of the original diameter in 11 (26.8%) cysts with 38/41 (92.7 %) overall success. Symptomatic success rate was (69.7%) with complete resolution of symptoms in 23 out of 33 patients. Our radiologic success rate was comparable to that obtained in the study of Baysal and Soylu that done using CT guidance. The authors found that the procedure was successful in 25 of 27 cysts (93%), they did not observe any complications related to the procedure. Another recent study used a similar technique, the authors found success rate of 98 out of 100 cysts (98%), demonstrated by follow-up CT. In that study, the only two failed cysts were larger than 10 cm in diameter and did not require any further treatment. These findings are comparable with the results of the present study. Symptomatic success in the present study did not run in parallel with the radiologic success. In the current study, two patients developed microscopic haematuria due to incidental injury of the pelvicalyceal system which resolved spontaneously while another patient developed pyretic UTI which was relieved with antibiotics.

CONCLUSION

Percutaneous sclerotherapy with NBCA is a simple, safe, and effective method for treating symptomatic simple renal cysts. Excellent results are expected to be encountered in patients with simple renal cysts less than 10 cm in diameter. However, further studies including larger number of patients and longer follow-up periods are required to verify our results.

REFERENCES


All correspondence sent to:

AHMED MAHMOUD AL-ADL, M.D.
Urology Department, Benha Faculty of Medicine, Benha, Egypt.