Cyst sclerotherapy with minocycline hydrochloride in patients with autosomal dominant polycystic kidney disease

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Abstract

Background. The enlarged cysts in autosomal dominant polycystic kidney disease (ADPKD) frequently cause abdominal discomfort. Cyst sclerotherapy with minocycline hydrochloride was performed to relieve this symptom.

Methods. Ten symptomatic ADPKD cases were recruited. As a sclerosant, minocycline hydrochloride solution (10 mg/dl) was used. This solution was instilled into the cysts under ultrasonographic control. Renal volume was calculated before therapy and at 6-month intervals thereafter. Renal function and blood pressure were regularly monitored. The effect of sclerotherapy on symptoms was also assessed at 6-month intervals.

Results. At 6 months, renal volume was statistically lower than the presclerotherapy, and was associated with improvement in chronic symptoms. However, such ameliorating effects were blunted at 12 months. Renal volume reduction at 6 and 12 months showed a significant positive correlation with the dose of minocycline injected. No significant influence in renal function and blood pressure was observed.

Conclusions. These results suggest that cyst sclerotherapy with minocycline hydrochloride is a valid treatment regime for the relief of chronic symptoms in ADPKD cases, although repeated application of this approach may be required to obtain a more long-term effect.

Key words: polycystic kidney disease; cyst sclerotherapy; minocycline hydrochloride

Introduction

In autosomal dominant polycystic kidney disease (ADPKD), the progressive enlargement of renal cysts is frequently associated with abdominal discomfort or lumbago. Without altering renal function [1,2], cyst reduction surgery can reduce this intolerable pain. In contrast, cyst fluid drainage by percutaneous puncture is a controversial procedure [3, our unpublished observation], due to the rapid refilling of fluid within the treated cysts. Thus, cyst contraction with a sclerosing agent may be more effective in lessening the symptoms associated with ADPKD.

We have recently shown the efficacy of minocycline hydrochloride (MH) for cyst regression in a small number of patients with ADPKD [4]. The current study presents a summary of the clinical observations made in 10 ADPKD patients undergoing such cyst sclerotherapy.

Subjects and methods

Ten patients with ADPKD were recruited for this study (Table 1). They complained of lumbago and/or abdominal discomfort derived from the enlarged cysts, but none of them required pain-relieving therapy.

The sclerosing technique has been reported previously [4] and is performed on an inpatient basis. MH is dissolved in distilled water at a concentration of 10 mg/dl and used as the sclerosing solution. The patient takes up either a prone or recumbent position. Following sterilization of the involved area, the ultrasonographic probe is applied to detect a pertinent cyst (usually >2 cm in diameter) and local anesthesia is applied to the puncture site. A 23-gauge needle is inserted into the cyst under ultrasonographic control and the cyst fluid is carefully aspirated until its presence is almost undetectable. Sclerosing solution of 1/4 to 1/2 volume of the aspirated fluid is injected. After irrigation, the cyst is drained and the same amount of sclerosing solution is instilled again. The needle is then withdrawn. During a session, lasting 1–2 h, 5–10 cysts of the kidney were treated and the cysts of the other side were similarly treated 1 week later. Periodic examination, including characterization of the symptoms and renal function, were performed on an outpatient basis before and after sclerotherapy.

Abdominal CT scans were performed before therapy and every 6 months thereafter, to determine renal volume, using a computerized planimeter (Planix 3000, Tamaya Corp., Tokyo, Japan). The mean volume of the normal right and left kidney calculated by this method (n=20) was 131±3.2 cm³ and 130±2.7 cm³ respectively.

The data are shown as mean±standard error (SE).
Statistical analyses were conducted with the Wilcoxon signed-rank test and the Mann–Whitney U test. The extent of correlation was determined by linear regression analysis. Significance was defined as a P value of less than 0.05.

Results

The average of punctured cysts and cyst fluid volume removed per patient were 26 and 421.2 ml respectively. The number of cysts on the right kidney (12 ± 3) did not differ from those of the left kidney (14 ± 3). In addition the aspirated volume from the right side (168.9 ± 37.4 ml) was not significantly different from that of the left side (252.3 ± 42.3 ml).

A typical example of cyst contraction by MH sclerotherapy is presented in Figure 1. The renal volume at 6 months (1722 ± 290 cm³) was significantly lower than the baseline volume (1982 ± 290 cm³) (P<0.01). However, the renal volumes at 12 months did not differ statistically from the initial volume (Figure 2). The right and left kidneys showed an identical profile to the above findings. By 6 months, but not at 12 months after treatment, there was a significant correlation between the aspirated volume and renal volume change. The correlation between the dose of MH injected into the cysts and renal volume reduction to the above findings. By 6 months, but not at 12 months after sclerotherapy, there was a significant correlation between the aspirated volume and renal volume change. The correlation between the dose of MH and volume reduction.

The right and left kidneys showed an identical profile to the above findings. By 6 months, but not at 12 months after treatment. In contrast, the reduction in renal volume at 6 and 12 months after sclerotherapy significantly correlated with the dose of MH instilled. Although the control study of sclerotherapy is lacking, MH can be regarded as an effective cyst sclerosant in polycystic kidney, when the rapid refilling of cysts after simple drainage [3, our unpublished observation] is considered.

Re-expansion of renal volume after sclerotherapy in polycystic kidneys may be caused by reaccumulation of fluid in the treated cysts, growth of the intact cysts, or newly developed cysts. The first possibility may be less likely, because of a significant correlation between the dose of MH and volume reduction.

With respect to the symptoms, we found that nine of 10 patients were free from chronic complaints at 6 months after sclerotherapy, while by 12 months two of 10 patients continued to be free of discomfort from increased volume.

Bennett et al. [5] reported that six of 11 symptomatic patients had recurrent symptoms within a mean of 2.5 months after cyst aspiration. Although we could not directly compare our present findings with their data, because of differences in the volume of fluid aspirated, our results suggested that cyst sclerotherapy is superior to aspiration during the first 6 months following treatment.

The present data may be consistent with those of Bennett’s group [1,5], who showed neither ameliorating nor deteriorating effect of cyst decompression surgery on renal function. In other words, the present cyst sclerotherapy was considered to be safe for the maintenance of renal function in ADPKD.

In ADPKD, hypertension is considered to be secondary to renal vascular abnormalities caused by the
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Observation period, month

(b)

Fig. 1. The CT scans without contrast in case 2. The enlarged cysts of the left kidney are shown in the upper panel and indicated by *. The corresponding cysts 6 months after therapy are shown in the lower panel and are apparently contracted.

Renal volume, cm³

0 6 12 Months

Fig. 2. Renal volume changes before (0) and at 6 and 12 months after cyst sclerotherapy. The horizontal bars at 0 and 6 months indicate the mean values of both kidneys in 10 patients, and that at 12 months indicates the mean of seven patients.

400 300 200 100

Minocycline hydrochloride, mg

Fig. 3. Relationship between the dose of minocycline hydrochloride instilled into the cysts and renal volume reduction at 6 months after sclerotherapy.

erg 300 200 100

Y = 38 + 0.20X
(t = 0.78, p<0.001)

enlarged cysts [6]. In fact, significant reduction in high blood pressure had been observed in some patients following the cyst reduction surgery [5,7]. This study, however, failed to elicit substantial changes in hypertension. This difference may be due to variable cyst volume reduction.

In summary, cyst sclerotherapy with MH in patients with ADPKD resulted in significant contraction of renal volume over 6 months and reduced the symptoms caused by the enlarged cysts. However, improvement of renal function and hypertension were not evident.

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References


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