Journal of Drug Design and Medicinal Chemistry
2018; 4(4): 35-38
http://www.sciencepublishinggroup.com/j/jddmc
doi: 10.11648/j.jddmc.20180404.11
ISSN: 2472-355X (Print); ISSN: 2472-3576 (Online)

Report

The Examination of the Actual State of Autosomal Dominant Polycystic Kidney Disease Treatment at Our Hospital

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To cite this article:
Makoto Fukuda, Tsuyoshi Takashima, Keiichiro Matsumoto, Ken Yamaguchi, Takahiko Nakazono, Hiroyuki Irie, Motoaki Miyazono, Yuji Ikeda. The Examination of the Actual State of Autosomal Dominant Polycystic Kidney Disease Treatment at Our Hospital. *Journal of Drug Design and Medicinal Chemistry*. Vol. 4, No. 4, 2018, pp. 35-38. doi: 10.11648/j.jddmc.20180404.11

Received: December 12, 2018; **Accepted**: January 3, 2019; **Published**: February 18, 2019

Abstract: Autosomal dominant polycystic kidney disease (ADPKD) is the most common form of inherited kidney disease. Approximately half of ADPKD patients reach end-stage renal failure by 60 years of age. ADPKD can also cause severe complications, so continuous follow up is necessary. We aimed to develop a strategy for future ADPKD practice based on the current situation of ADPKD practice at our hospital . Methods: From February 2002 to April 2016, 81 cases with ICD-10 codes related to ADPDK were registered, based on the patients' medical records. The patients were divided into four groups according to the outcome after their introduction to our hospital . Various parameters at the first visit were compared and examined. We also investigated 19 patients who were newly introduced from May 2016 to September 2017. Results :We encountered to the fact that most ADPKD patients weren't introduced to our department (Division of Nephrology) until end stage renal failure, which unable both proactive treatment and evaluating severe complications. We coped with this problem and succeeded to have more ADPKD patients in the early stage. Conclusion: Now that we have more ADPKD patients in the early stage, we would like to treat ADPKD by proactive practices (i.e., introduce Tolvaptan treatment for adaptation cases) at the proper timing, and at the same time, offer them continuous medical follow ups for severe complications. Eventually, we hope to develop a sufficient strategy for future ADPKD practice which we could not reach this time.

Keywords: ADPKD, Radiologist, Tolvaptan

1. Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the most common form of hereditary kidney disease and is a disease requiring multidisciplinary treatment [1]. Approximately half of ADPKD patients reach end-stage renal failure by 60 years of age; it is underlyin disease in nearly 3% of dialysis-introduced patients in Japan [2]. Also, ADPKD can cause severe complications such as cerebral aneurysm and valvular heart disease, and so continuous follow up is necessary. Cystic kidney disease develops in patients of all ages from prenatal to adulthood. Although ADPKD is the most famous renal cystic disease, there are various other cystic kidney diseases, and the kidney specialist also needs knowledge about childhood kidney disease, its complications, genetic counseling and diagnosis method [3].

In Japan, it has been possible to use Tolvaptan (a vasopressin V2 receptor antagonist) to inhibit the increase in renal volume and the renal function decline in ADPKD, since 2014. Thus, ADPKD is actively treated using this drug throughout Japan. In contrast, Tolvaptan was indicated for few cases in our hospital in 2016. Also, most ADPKD patients weren't introduced to our department of kidney internal

medicine until they reach end-stage renal failure without evaluating complications. Thus, we aim to develop a strategy for future ADPKD practice based on the current situation of ADPKD practice at our hospital.

2. Method

From February 2002 to April 2016, 490 cases with ICD-10 codes related to ADPDK, nephron cysts, autosomal dominant polycystic kidney disease, and polycystic kidney disease were registered, based on the patients' medical records. From these, cases of multiple simple cystic renal cysts, acquired cystic kidney disease, and polycystic kidney were excluded. Finally, there were 87 cases that could be confirmed by imaging. Eighty-one subjects who did not have end-stage renal failure at the initial visit to our hospital were evaluated (6 of the 87 patients who had already developed end-stage renal failure at the time of the initial examination underwent renal replacement therapy).

The patients were divided into four groups according to the outcome after their introduction to our hospital: (1) dialysis introduction group (n=35), (2) hospital transfer group (n=21), (3) outpatient continuation group (n=18), (4) hospital self-discontinuation group (n=6). The age at the first visit, sCr at the first visit, eGFR at the first visit, family history (ADPKD or cerebral hemorrhage), complications (cerebral hemorrhage or unruptured cerebral aneurysm) were compared and examined. We also investigated 19 patients who were newly introduced from May 2016 to September 2017.

3. Result

The main introducers to our hospital included 36 general practitioners (internal medicine), 16 general hospitals, and 14 urology departments. Introductions from general hospitals included a large number of referrals for a second opinion on surgical procedures such as cyst fenestration (Figure 1).

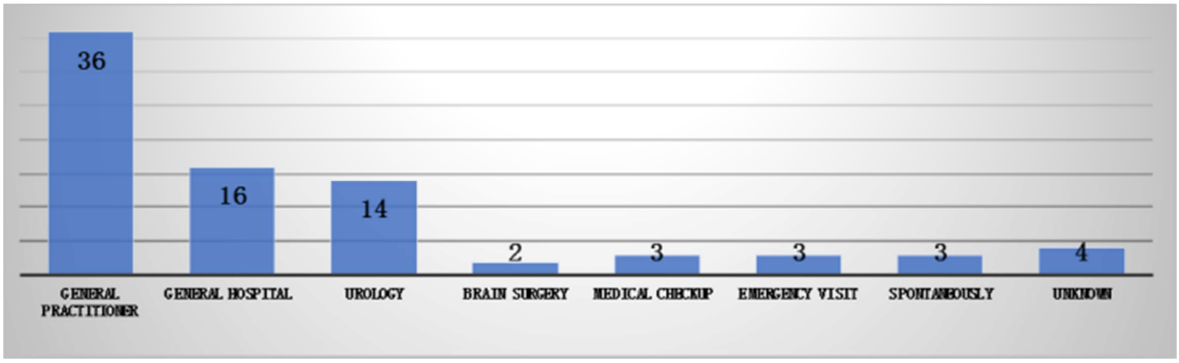

Figure 1. *Referring facility.*

The department at the first visit included the department of kidney internal medicine (n=39), the department of urology (n=15), and the department of general medicine (n=11) (Figure 2).

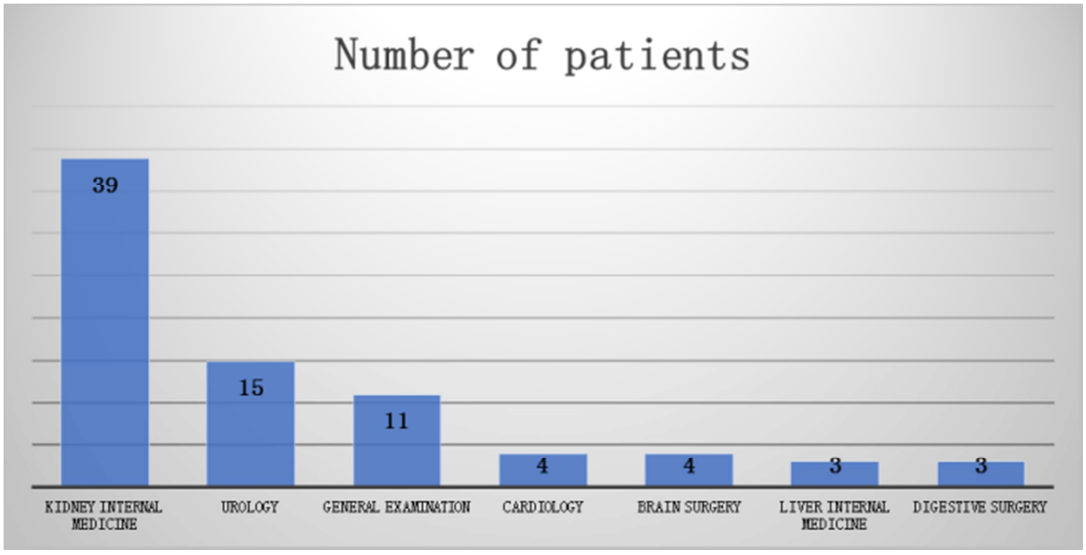

Figure 2. *Department at the first visit.*

The characteristics of the study population were as follows: mean age at the first visit, 55.6 ± 15 years; mean sCr at the first visit, 2.47 ± 2.2 mg/dL; mean eGFR at the first visit, 34.3 ± 27 ml/min/1.73 m^2; male, n=35; female, n=46; family history

(positive), 67%; and complication (positive), 21%. In the dialysis introduction group, the mean eGFR at the time of initial examination (17.5 ± 14.4 ml/min/1.73 m^2) indicated that advanced renal failure had already occurred; a family history was recognized in 77% of such patients and complications were confirmed in 31%. In the hospital self-discontinuation group, a family history was confirmed at 83% of the patients, the mean age at the first visit was 39.5 ± 13.8 years, and the eGFR at the first visit was 60.6 ± 15.1 ml/min/1.73 m^2; however, although the patients were introduced early, continuous follow up was not performed (Table 1).

Table 1. *Patient charactaristics.*

	Overall (n=81)	Dialysis introduction (n=35)	Hospital transfer (n=21)	Continuation (n=18)	Self-discontinuation (n=6)
Age (years)	55.6±15	57.8±11.6	59.6±17	51.7±16.7	39.5±13.8
sCr (mg/dl)	2.47±2.2	3.84±2.5	1.45±0.8	1.25±0.89	0.86±0.2
eGFR (ml/min/1.73m ^{2})	34.3±27	17.5±14.4	37.7±16.5	56.4±35.8	60.6±15.1
Male: Female	35 : 46	18:17	8:13	5:13	3:3
Family history (*1)	54/81 (67%)	27/35 (77%)	11/21 (52%)	11/18 (61%)	5/6 (83%)
Complications (*2)	17/81 (21%)	11/35 (31%)	4/21 (19%)	2/18 (11%)	0/6

*1 Family history: (PKD or cerebral hemorrhage).
*2 Complications: (SAH or Cerebral aneurysm).

On the other hand, among the 18 patients in the continuing hospitalization group, 10 patients visited the department of kidney internal medicine, and the CKD stage tended to be greater than G3b (Table 2).

Table 2. *Patients treated by the department of kidney internal medicine.*

Age (years)	Sex	eGFR (ml/min/1.73 m^2)	CKD Stage
30	F	77.4	G2A2
45	M	10.7	G5A2
71	F	18.1	G4A3
53	F	43.5	G4A2
40	F	88.6	G2A1
65	M	24.4	G5A2
45	M	40.1	G3bA1
58	M	39.9	G3aA2
61	M	34.8	G3aA1
72	F	16.2	G5A2
50	M	54.2	G3aA1
40	F	67.1	G2A2

None of the remaining 8 cases were introduced to the department of kidney internal medicine.

4. Discussion

Although previous treatment for ADPKD may have an impact on the rates of morbidity and mortality due to disease-related complications, it did not inhibit the progression of ADPKD. Cerebral aneurysm is well known as polycystic kidney complications. Zhou et al. Report that screening tests for intracranial aneurysms are recommended when there are family history of hemorrhagic stroke or intracranial aneurysm from Japan, China, Europe [4]. It has also been reported that the incidence of aortic dissection is high, and polycystic kidney patients are a high-risk group of cardiovascular event onset [5]. Since Tolvaptan was approved in Japan in 2014 it has become possible to delay the progression of the kidney volume increase and renal dysfunction in cases in which the renal function is relatively maintained [6]. A QOL survey of ADPKD patients conducted by Suwabe reported that abdominal distension accompanied by liver/kidney enlargement was closely correlated with a decrease in QOL, Tolvaptan is not a radical therapy, but can be expected to improve the QOL of patients with ADPKD [7].

In this study, even if diagnosis of ADPKD is made, the patients were often not introduced until they had reached end-stage renal failure—with the exception of patients who were introduced for complications. Efforts should be made to promote the introduction of patients to the department of kidney internal medicine from an early stage, which should be the core of ADPKD practice. Regarding ADPKD inside and outside the hospital—irrespective of the stage—for distinguishing ADPKD, it is thought to be necessary to inform the intervention of kidney internal medicine from the point of distinguishing ADPKD. The identification of cystic kidney lesions on imaging studies and diagnostic imaging by radiologists is thought to be effective for differentiating between infectious cystic kidney disease, acquired cystic kidney disease, and hereditary cystic kidney disease [8, 9]. Renal volume measurement is being performed to monitor the progress of polycystic kidney and to evaluate the effect of drug treatment. Sharma report that MRI examination is superior to CT examination, and in particular MRI examination requires expert operators to report it is necessary, and collaboration with radiologists is important [10].

For this reason, we thought that collaboration with radiologists who perform diagnostic imaging is necessary, and that that the radiology department should consult the department of kidney internal medicine for an interpretation of results when ADPKD is suspected based on imaging findings. Furthermore, in order to promote to introduction to the department of kidney internal medicine—irrespective of stage—we conducted lectures on chronic kidney disease as enlightenment activities for the department of urology and general practitioners inside and outside the hospital.

The two abovementioned efforts were started from May 2016. We also investigated 19 patients who were newly introduced from May 2016 to September 2017. The mean age of the 19 patients at the first visit was 51.8 ± 14 years; the mean Cr at the first visit was 1.53 ± 1.4 mg/dL, and the mean eGFR at the initial examination was 48.0 ± 23 ml/min/1.73 m^2.

Thus, the rate of early introduction was increased in comparison to the 81 cases that were treated between February 2002 and April 2016 (Table 3).

Table 3. *Comparison of the two study periods.*

Investigation period	Number of patients	Age (years)	sCr (mg/dL)	eGFR (ml/min/1.73 m^2)
2002.2–2016.4	81	55.6±15	2.47±2.2	34.3±27
2016.5–2017.9	19	51.8±14	1.53±1.4	48.0±23

Five of the 19 newly introduced cases were able to receive Tolvaptan treatment. Not only our efforts but also the availability of tolvaptan for ADPKD in 2014 became publicly known as time passed, which is also considered to be a factor.

The diagnostic criteria and nomenclature of cystic kidney disease were ambiguous; thus, it is likely that some of the cases that occurred during the study period were not identified.

5. Conclusion

Through this study, it became clear that the timing of intervention by the kidney specialist for ADPKD patients was delayed, and it was found that cooperation with other departments such as radiology department is important for improvement.

In order to develop a sufficient strategy for future ADPKD practice in our medical area which we could not reach in this research, we need to accumulate cases by conducting continuous collaboration and educational activities with other departments and other medical institutions.

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