Original Article

Factors associated with the normalization of blood pressure after unilateral adrenalectomy for primary hyperaldosteronism patients in Rajavithi Hospital

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Keywords:
Unilateral adrenalectomy, primary hyperaldosteronism

Abstract

Objective: To determine the factors associated with the resolution of hypertension after adrenalectomy for primary hyperaldosteronism in Rajavithi Hospital.

Material and method: Records of 44 patients who underwent adrenalectomy for primary hyperaldosteronism at Rajavithi Hospital between January 2005 and April 2015 were reviewed. Patients were divided in 2 groups according to whether blood pressure was normal without antihypertensive medication at 6 months postoperatively. Clinical and biochemical data were evaluated at baseline and after the follow-up at 6 months.

Result: At the 6 month follow-up, 21 patients (47.7%) were normotensive without antihypertensive medication and 23 patients (52.3%) were normotensive with antihypertensive medication. Female gender (P=0.005) and duration of hypertension less than 5 years (P=0.036) were associated with normotensive without antihypertensive medication. All patients had normal serum potassium.

Conclusion: About half of the patients were normotensive without antihypertensive medication, and all the patients had normal serum potassium after adrenalectomy. Factors associated with the resolution of hypertension after adrenalectomy for primary hyperaldosteronism were female gender and duration of hypertension less than 5 years.

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นิพนธ์ต้นฉบับ

ปัจจัยที่มีผลต่อการกลับสู่สภาวะปกติของความดันโลหิตหลังจากการผ่าตัดนำต่อมหมวกไตออกข้างหนึ่งในผู้ป่วยโรค ภาวะฮอร์โมนอัลโดสเตอโรนสูงแบบปฐมภูมิ ในโรงพยาบาลราชวิถี

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คำสำคัญ:
การผ่าตัดนำต่อมหมวกไตออกข้างหนึ่ง ภาวะฮอร์โมนอัลโดสเตอโรนสูงแบบปฐมภูมิ

บทคัดย่อ

วัตถุประสงค์: เพื่อประเมินปัจจัยที่มีผลความดันโลหิต ภายหลังการผ่าตัดต่อมหมวกไตข้างเดียวในผู้ป่วย ภาวะฮอร์โมนอัลโดสเตอโรนสูงแบบปฐมภูมิ ในโรงพยาบาลราชวิถี

ผู้ป่วยและวิธีการศึกษา: ทำการศึกษาแบบข้อมูลผู้ป่วย จำนวน 44 ราย ที่ได้รับการวินิจฉัยภาวะฮอร์โมนอัลโดสเตอโรนสูงแบบปฐมภูมิ และได้รับการผ่าตัดต่อมหมวกไต ที่โรงพยาบาลราชวิถี ระหว่าง มกราคม 2548 ถึง เมษายน 2558 โดยแบ่งผู้ป่วยเป็น 2 กลุ่ม ตามระดับความดันโลหิตและการได้รับยาลดความดันโลหิต ที่ 6 เดือนหลังผ่าตัด

ผลการศึกษา: เมื่อติดตามผลการรักษาที่ 6 เดือนหลังผ่าตัด พบว่าร้อยละ 47.7 มีความดันโลหิตอยู่ในระดับปกติ โดยไม่ได้รับยาลดความดันโลหิต และ ร้อยละ 52.3 ต้องได้รับยา โดยปัจจัยที่มีผลต่อกลุ่มไม่ได้รับยาลดความดันโลหิต คือ เพศหญิง (p=0.005) และระยะเวลาที่มีความดันโลหิตสูงน้อยกว่า 5 ปี (p=0.036) ผู้ป่วยทุกรายมีค่าปกติของค่าซีรัมโปแตสเซียม

สรุป: ผู้ป่วยที่ได้รับการผ่าตัดต่อมหมวกไต จากสาเหตุภาวะฮอร์โมนอัลโดสเตอโรนสูงแบบปฐมภูมิ ประมาณครึ่งหนึ่งมีระดับความดันโลหิตอยู่ในเกณฑ์ปกติ โดยไม่ได้รับยาลดความดันโลหิต โดยปัจจัยที่มีความเกี่ยวข้องกับการลดลงของระดับความดันโดหิต คือ เพศหญิง และระยะเวลาที่มีความดันโลหิตสูง น้อยกว่า 5 ปี

ผู้นิพนธ์หลัก: พีรดนย์ สาเพิ่มทรัพย์ หน่วยศัลยกรรมระบบปัสสาวะ กลุ่มงานศัลยกรรม โรงพยาบาลราชวิถี กรุงเทพฯ
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Introduction

Primary hyperaldosteronism (PHA) is one of the most common causes of secondary hypertensionwhich is correctable by surgery. About 11-20% of patients with hypertension resist to medical management[1]. Target organ damage is the complication caused by long-standing hypertension. Untreated hypertension can cause irreversible cardiovascular and renal damage[2,3,4] and increase the risk of cardiovascular event[5].

PHA is characterized by drug-resistant hypertension and hypokalemia caused by a renin-independent overproduction of aldosterone. Adrenal producing adenoma is one cause of primary hyperaldosterone. It was first reported by Jerome W. Conn in 1955[6]. The most common causes of PHA are unilateral aldosterone producing adenoma (APA) and bilateral adrenal hyperplasia (BAH), which together account for about 95 % of cases[7-9].

Patients may suffer from complications of uncontrolled hypertension that affect quality of life and cause morbidity and mortality, such as cardiovascular disease, cerebrovascular disease, and renal failure. Other symptoms of PHA, such as muscle weakness, arrhythmias, paresthesia, constipation and fatigue, are caused by hypokalemia.

Unilateraleral adrenalectomy is the treatment of APA. Hypokalemia subsides in more than 90% of patients, but hypertension had complete resolution in about 30 % of patients after surgery[10,11]. Previous studies found that factors associated with the complete resolution of hypertension consist of using fewer than 3 antihypertensive medications, shorter durations of hypertension, presence of family history of hypertension in first-degree relatives, younger age, female gender, body mass index and pathologic findings[10-16].

In our institute, there had been no study conducted about the factors to predict outcomes after surgery; therefore, the object of our study was to determine the factors associated with the resolution of hypertension after adrenalectomy for primary hyperaldosteronism in Rajavithi Hospital.

Material and method

Medical records of patients who underwent unilateral adrenalectomy for PHA from January 2005 to April 2015 in Rajavithi Hospital were retrospectively reviewed. All patient shad proven imaging of adrenal adenoma. Incomplete information, no adrenal adenoma from imaging, suspected adrenocortical carcinoma from imaging or bilateral adenoma were excluded from the study. Institutional ethics committee review boards approved the study.

PHA was diagnosed by an endocrinologist based on plasma aldosterone concentration (PAC), plasma renin activity (PRA),and aldosterone-ratio (ARR). In our study we used ARR >20 to screen for PHA and then confirmed the diagnosis with saline loading test. APA was diagnosed after PHA when imaging showed adrenal adenoma. All imaging results were interpreted by radiologists. Histopathology after adrenalectomy was reported by pathologists. Hypertension was defined as systolic blood pressure more than 140 mmHg and diastolic blood pressure more than 90 mmHg. Hypokalemia was defined as serum potassium less than 3.5 mEq/L.

We collected data including patient demographics, biochemical testing, antihypertensive medications, pathology, imaging, and blood pressure measurements from medical records. Clinical and biochemical data were evaluated at baseline and at 6 months' follow-up after surgery. To determined factor associated with normotensive after surgery, patients were divided in 2 groups according to whether blood pressure was normal with or without antihypertensive medication at 6 months postoperatively. The first group was the cure group which was defined as not requiring antihypertensive medication after surgery and blood pressure within the normal limit. The second group required antihypertensive medication after surgery. We studied main favorable factors appearing in the literature[10-16] to find relations with outcome after surgery in Rajavithi Hospital, which consisted of female gender, use of antihypertensive less

than or equal to 2 drugs, age less than 50 years old, duration of hypertension less than 5 years, no family history of hypertension, chronic kidney disease, and BMI less than 25 kg/m^2.

After collecting data and dividing the patients into 2 groups to determine the favorable factors after surgery, we analyzed the data with statistical analysis software, SPSS 17.0. Descriptive statistics are shown as a number, percentage, mean, median, minimal and maximal value. For inferential statistics and quantitative information comparisons we used the Student T-test with normal distribution data and the Mann-Whitney U test with non-normal distribution. Chi-square test was used for qualitative information comparisons. Factor associated with the normalization of blood pressure after unilateral adrenalectomy for primary hyperaldosteronism were identified with univariate analysis, followed by multivariate analysis. P-value less than 0.05 was considered to indicate statistical significance.

Result

After reviewing medical records, we found 44 patients who met our inclusion criteria. The general characteristic data and biochemical data are shown in Table 1. Most of the patients were female [n=31 (70.5 %)], all patients had hypokalemia before surgery, most pathological findings were adrenal adenoma [n=37 (84.1%)], and after surgery all of the patients had normal serum potassium.

In 44 patients, we found that 21 (47.7%) patients were cured from hypertension and 23 (52.3%) patients still required antihypertensive medication after surgery. In the group that required antihypertensive medication after surgery, 18 (78.3%) patients could control blood pressure after surgery while the remaining 5 (21.7%) had poorly controlled blood pressure. Overall, 39 patients (88.6%) could control blood pressure with or without antihypertensive medication.

Overall, 44 patients were analyzed to identify factors associated with cure after surgery. In Table 2, the univariate analysis shows that the favorable factors were female gender (p=0.005) and duration of hypertension less than 5 years before surgery (p=0.036). Multivariate analysis (Table 3) shows female gender (p=0.012) and duration of hypertension less than 5 years before surgery were significant factors associated with cure after surgery (p=0.049).

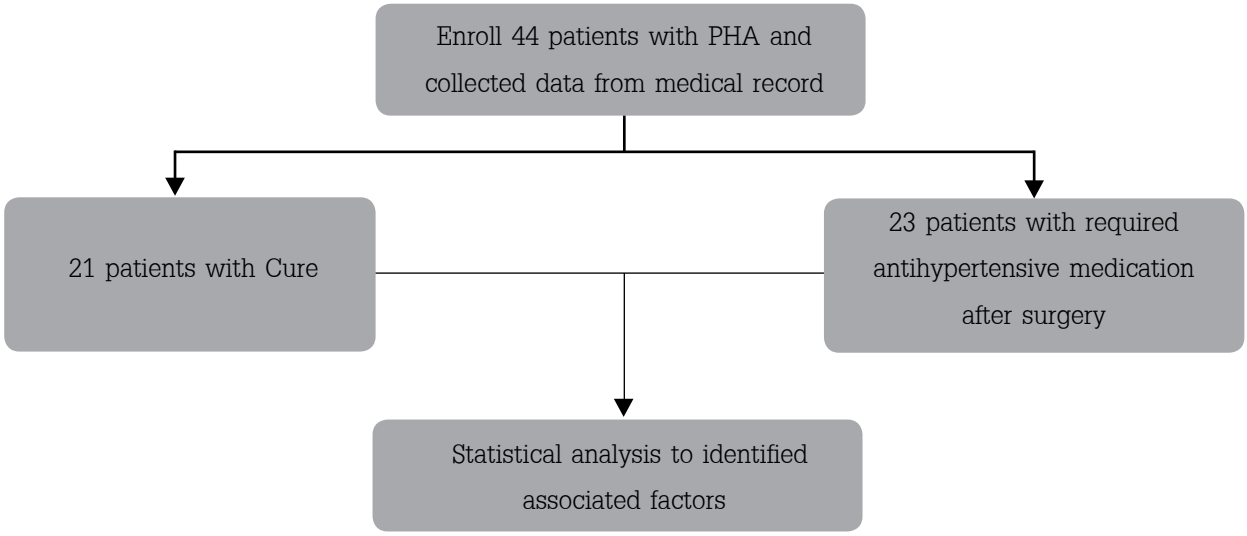

Figure 1. Protocol flow chart

Table 1. General characteristic data

Characters	Number	Stat
Age (years old)	46.3±12.1	Mean±SD
Gender		
male	13 (29.5%)	
female	31 (70.5%)	
Duration of hypertension (months)	60 (2-360)	Median
BMI (kg/m^2)	25.1±5.1	Mean±SD
Family history of hypertension		
yes	21 (47.7%)	
no	23 (52.3%)	
Number of antihypertensive medication before surgery	3±1.2	Mean±SD
Blood pressure before surgery (mmHg)		Mean±SD
SBP	167.4±20.4	
DBP	96.5±12.2	
Serum potassium before surgery (mEq/L)	2.4±0.5	Mean±SD
Serum creatinine (mg/dL)	1.0±0.3	Mean±SD
ARR	164 (30-82850)	Median
PAC	65.05 (11.6-2270)	Median
PRA	0.35 (0.02-1.75)	Median
Final pathology		
Adenoma	37 (84.1%)	
Hyperplasia	7 (15.9%)	
Side of adrenal gland		
Left	23 (52.3%)	
Right	21 (47.7%)	
Size of adrenal mass (mm)	18±7.2	Mean±SD
Blood pressure after surgery (mmHg)		Mean±SD
SBP	128±11.4	
DBP	80.3±7.5	
Serum potassium after surgery (mEq/L)	4.3±0.3	Mean±SD
Number of antihypertensive medications after surgery	1 (0-3)	Median

Table 2. Univariate analysis

Variable	Cure N=21	required medication N=23	P value
Gender			0.005
male	2 (9.5%)	11 (52.2%)	
female	19 (90.5%)	12 (47.8%)	
Family history of hypertension			0.068
yes	7 (33.3%)	14 (60.9 %)	
no	14 (66.7%)	9 (39.1 %)	
Side of adrenal gland			0.537
Left	12 (57.1%)	11 (47.8%)	
Right	9 (42.9%)	12 (52.2%)	
Final pathology			1.000
Adenoma	18 (85.7%)	19 (82.6%)	
Hyperplasia	3 (14.3%)	4 (17.4%)	
Number of antihypertensive medication before surgery			0.138
≤2 medication	10 (47.6%)	6 (26.1%)	
>2 medication	11 (52.4%)	17 (73.9%)	
Age (Years old)			0.062
<50	15 (71.4%)	10 (43.5%)	
≥50	6 (28.6%)	13 (56.5%)	
Duration of hypertension (Years)			0.036
<5	13 (61.9%)	7 (30.4%)	
≥5	8 (38.1%)	16 (69.6%)	
BMI			0.190
<25	15 (71.4%)	11 (47.8%)	
≥25	6 (28.6%)	12 (51.2%)	
Blood pressure before surgery (mmHg)			
SBP	166.5±20	168.3±21.9	0.773
DBP	98.3±13	94.9±11.7	0.358
Serum potassium before surgery (mEq/L)	2.4±0.4	2.4±0.5	0.864
Serum creatinine (mg/dL)	0.9±0.3	1.0±0.3	0.121
Size of adrenal mass (mm)	16.7±7.8	19.1±6.8	0.273

Table 3. Multivariate analysis

Multivariate analysis				
Factor	**Crude OR (95%CI)**	**P value**	**Adjusted OR (95%CI)**	**P value**
Female gender	8.71 (1.64-46.31)	0.011	9.49 (1.63-55.31)	0.012
duration of hypertension less than 5 years	3.71 (1.06 -12.98)	0.040	4.11 (1.01-16.76)	0.049

Discussion

In our study we found that female gender and duration of hypertension less than 5 years before surgery were significant factors associated with normalized blood pressure and without requiring antihypertensive medication after unilateral adrenalectomy in APA patients in Rajavithi Hospital. No family history of hypertension and age less than 50 years old tend to be favorable factors after surgery. After surgery, 21 patients (47.7%) were cured, 18 patients (40.9%) could control blood pressure with reduction of antihypertensive medication, and 5 patients (11.4%) continued to have poor blood pressure control. Our study found that 88.6% of patients had positive effects with blood pressure after surgery, which corresponds with published studies[17-19].

Previous studies have shown that independent factors for the resolution of hypertension after adrenalectomy are female gender, use of antihypertensive less than or equal to 2 drugs , age less than 50 years old, duration of hypertension less than 5 years, no family history of hypertension, chronic kidney disease, and BMI less than 25 kg/m[10-16]. Our study shows that the independent factors were female gender and duration of hypertension less than 5 years before surgery. Negative family history of hypertension and age less than 50 years old tend to be favorable factors after surgery. Due to the small sample size in our study, some factors did not reach statistical significance.

PHA can cause drug resistant hypertension. Unilateral adrenalectomy in PHA patients can provide resolution from hypertension and hypokalemia, but not all cases of PHA will have resolution from hypertension. Hypertension is influenced by many factors, including PHA. Most patients were diagnosed with essential hypertension the first time. Some patients have coexisting PHA and essential hypertension. Patients in this group after surgery may require antihypertensive medication because they have essential hypertension. Therefore, essential hypertension relates to persistent hypertension after surgery. BMI more than 25 kg/m^2, age more than 50 years old, duration of hypertension more than 5 years, family history of hypertension, and chronic kidney disease: these factors all relate to essential hypertension. For that reason, after we performed adrenalectomy in patients who had essential hypertension coexisting with PHA, there was no resolution after adrenalectomy. Essential hypertension can be controlled by antihypertensive medication after surgery. However, some patients in this group may continue to have poor control of blood pressure because essential hypertension has many factors that cause poor blood pressure control. Five patients in our study showed poor blood pressure control, 3 of them were more than 50 years old, 4 patients were exposed to hypertension more than 5 years, 3 patients had a family history of hypertension, and 3 patients had BMI more than 25 kg /m^2. All patients took more than 2 antihypertensive medications; these were unfavorable factors after surgery. Another factor associated with outcome is microadrenal adenoma on the other side of the adrenal gland Patients in this group require further investigation in order to rule out microadrenal adenoma in the remaining adrenal gland.

Serum potassium was within the normal limit after surgery in all the cases in our study. Our institution does not check serum PAC and PRA routinely after surgery; hence we could not use ARR as an outcome after surgery. The final pathology in our study shows that most pathologic findings were adenoma (84.1%), because we selected cases of APA to be enrolled in our study.

The limitations of this study should be highlighted. First, due to its retrospective design, some data were missing, which caused some medical record to be excluded and thus the sample size was too small. Second, due to the small sample size, correlation of some variables could not reach statistical significance; if more patients had been included, statistical significance could have been reached. Third, a large multicenter prospective study is mandatory to ensure adequate collection of data in order to perform multivariate analyses in a larger number of patients, providing external validation of our results.

Conclusion

About half of the patients were normotensive without antihypertensive medication and all the patients had normal serum potassium after adrenalectomy. Factors associated with the resolution of hypertension after adrenalectomy for primary hyperaldosteronism were female gender and duration of hypertension less than 5 years.

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