The role of increased plasmatic renin level in the pathogenesis of arterial hypertension in young adults

MANUELA STOICESCU1), C. CSEPENTO1), GABRIELA MUŢIU2), S. BUNGĂU1)

1)Department of Internal Medicine, County Hospital, Oradea
2)Department of Histology, Faculty of Medicine and Pharmacy, University of Oradea

Abstract

Introduction: Plasma renin level is an important marker of hypertension in the young adults. The purpose of this study was to determine the role of increased levels of plasmatic renin in the pathogenesis of hypertension in young adults and to highlight the main conditions underlying the pathogenesis of hypertension in young people in these circumstances. Patients and Methods: The group of patients taking part in the study was made of 121 young hypertensive adults (selected from a group of 321 young hypertensive adults), with ages between 18 and 35 years, with elevated blood pressure exceeding 140/90 mmHg in at least three repeated measurements at intervals of one week to exclude white coat phenomenon, or had a blood pressure value greater than 170/100 mmHg at the first measurement and increased plasma renin levels above 4.3 ng/mL. Results and Discussion: Of the 121 young hypertensive patients with increased plasma renin levels, 49 were cases of renal artery stenosis representing 40.50% (p<0.001), eight cases were represented by small unilateral kidneys representing 6.61% (p<0.001), renal cell carcinoma (previously known as “hypernephron” – Grawitz tumor) was responsible for the younger group of patients studied (four cases) representing 3.30% (p<0.001) of the cases of hypertension in the young adults, and 60 cases representing 49.59% were represented by pheochromocytoma. Conclusions: The results show the role of plasma renin dosing as being particularly important in the pathogenesis of secondary hypertension in young adults.

Keywords: renin, arterial hypertension, young adults.

Introduction

Renin is an enzyme secreted by the juxtaglomerular apparatus to maintain electrolyte balance and blood pressure in the appropriate limits. Plasma renin level is an important marker of hypertension in young adults. The purpose of this study was to determine the role of increased levels of plasma renin in the pathogenesis of hypertension in young adults and highlight the main conditions underlying the pathogenesis of hypertension in young adults with increased plasmatic renin. The main diseases which had increased plasma renin levels were: renal artery stenosis, pheochromocytoma, congenital unilateral small kidney, primary reninoma (renal cell carcinoma or Grawitz tumor), situations in which renin is secreted in excess, the highest values being in cases with renal cell carcinoma – 320 ng/mL.

Patients and Methods

The group of patients taking part in the study was made of 121 hypertensive young adults, with ages between 18 and 35 years, with elevated blood pressure over 140/90 mmHg in at least three repeated measurements at intervals of one week to exclude white coat phenomenon frequently encountered in the young, or had a severely increased blood pressure of >170/100 mmHg on the first measurement and plasma renin levels greater than 4.3 ng/mL.

The parameters for the assessment of the diseases, which had increased plasma renin levels, were clinical, radiological, biological and histopathological. The study was performed after the diagnosis of hypertension and staging according to WHO. All patients were clinically investigated and fully analyzed paraclinically.

They agreed to participate in the trial after they were explained the criteria of professional, scientific ethics, and the terms of confidentiality. All patients participating in the study had plasmatic renin levels over 4.3 ng/mL.

The statistical analysis was performed with the help of the EPIINFO software, version 6.0, software of the Center for Disease Control and Prevention-CDC in Atlanta, suitable for processing of medical statistics. Averages, frequency ranges, standard deviations, were calculated for the parameters and the statistical significance was assessed using the Student t-test and χ²-test.

The positive diagnostic criteria for the diseases included in the study were:

For renal artery stenosis:
• increased value of diastolic blood pressure over 110 mmHg;
• paraumbilical systolic murmur;
For congenital small kidney:
- values of blood pressure over 140/90 mmHg;
- arteriographic evidence of the small kidney;
- abdominal MRI;
- increased plasmatic renin level >4.3 ng/mL.

For renal carcinoma (Grawitz tumor):
- unilateral lumbar pain;
- loss of appetite;
- weight loss;
- macroscopic hematuria (blood in the urine);
- the value of plasma renin level increased >4.3 ng/mL, mentioning that in this situation the plasma renin values reached the highest values, up to 320 ng/mL;
- abdominal MRI;
- renal biopsy.

For pheochromocytoma:
- paroxysmal outbursts of severe blood pressure over 220/120 mmHg;
- headache;
- tremor of extremities;
- nervousness;
- increased serum catecholamine levels above 260 pg/mL;
- increased urinary catecholamine values above 7.4 mg/24 hrs;
- increased plasmatic renin level >4.3 ng/mL;
- abdominal MRI used in the detection of adrenal tumors.

Table 1 – Diagnostic criteria

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. of cases</th>
<th>Diagnostic criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular pathology</td>
<td>49</td>
<td>24 cases – 4 of 4</td>
</tr>
<tr>
<td>Renal artery stenosis</td>
<td>8</td>
<td>25 cases – 3 of 4</td>
</tr>
<tr>
<td>Renal parenchymatous pathology</td>
<td>4</td>
<td>2 cases – 7 of 7</td>
</tr>
<tr>
<td>Congenital small kidney</td>
<td>4</td>
<td>2 cases – 6 of 7</td>
</tr>
<tr>
<td>Renal carcinoma (Grawitz tumor)</td>
<td>4</td>
<td>38 cases – 8 of 8</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>60</td>
<td>12 cases – 7 of 8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 cases – 6 of 8</td>
</tr>
</tbody>
</table>

Results

In the group of young hypertensive patients with ages between 18 and 35 years, with elevated blood pressure >140/90 mmHg, with increased plasma renin levels over 4.3 ng/mL. We found 49 cases of renal artery stenosis representing 40.50%, eight cases of congenital small kidney representing 6.61%, 4 cases of Grawitz tumors (renal cell carcinoma) representing 3.30% and 60 cases of pheochromocytoma representing 49.59% (Table 2).

Of the group of young hypertensive patients studied with increased plasma renin activity, 49 of the cases were renal artery stenosis representing 40.50% (p<0.001). The parameters of the clinical assessment were the increased value of diastolic blood pressure over 110 mmHg, puraumbilical systolic murmur and the arteriographic imaging (Figure 1).

In the group of young patients included in the study, we found eight cases of unilateral small kidney representing 6.61% (p<0.001). The pathogenic mechanism of hypertension was ischemic, thus the arterial high blood pressure evolved along with hyper-reninemia in all congenital unilateral small kidney cases. The early diagnosis of renal disease is very important, before the hypertension causes severe nephro-angiosclerosis on the contralateral kidney, leading to nephrectomy, which then can lead to the disappearance of hypertension.

The assessment parameters in this case were the clinical blood pressure values above 140/90 mmHg, the imaging methods highlighting the small kidney – arteriography (Figure 2) abdominal MRI (Figure 3), and biological increased plasmatic renin activity >4.3 ng/mL.

Renal cell carcinoma (renal carcinoma, previously “hypernephroma” – Grawitz tumor) was responsible for the group of four younger patients studied, representing 3.30% (p<0.001) of the HBP young cases. All had severely elevated blood pressure values over 200/100 mmHg. The diagnostic was based on clinical parameters which were unilateral lumbar pain, loss of appetite, weight loss, but only two cases had macroscopic hematuria (blood in the urine), the biological parameters – value of increased plasma renin level >4.3 ng/mL, mentioning that in this situation the plasma renin values reached the highest values up to 320 ng/mL.

Imaging parameters were represented by the abdominal MRI (Figure 4). Histopathologic parameters were highlighted in all the four cases, in which renal biopsy was performed. Two cases were clear cell renal carcinoma based on the histopathology results after renal biopsy (Figures 5 and 6). The other two cases of renal carcinoma are showed in the Figures 7 and 8.

Hypertension in the young patients with renal cell carcinoma took the form of severe paroxysmal HBP=200/110 mmHg or above in all four cases, due to excessive secretion of renin produced in large quantities by the tumor and it was the one form which attracted most the clinical attention when it did not manifest by macroscopic hematuria. From the group of hypertensive young adults studied, 60 of the cases were of pheochromocytoma representing, 49.59%.

The diagnostic criteria used in this clinical situation were: paroxysmal outbursts of severe blood pressure values over 220/120 mmHg accompanied by headache, tremor of extremities, nervousness, biological parameters represented by increased serum catecholamine levels above 260 pg/mL, increased urinary catecholamine values above 7.4 mg/24 hrs, imaging parameters which were used in the detection of adrenal tumors by performing an abdominal MRI (Figure 9).

Table 2 – The main conditions present in the group of young hypertensive patients with increased plasma renin levels

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular pathology</td>
<td>49</td>
<td>40.50</td>
</tr>
<tr>
<td>Renal artery stenosis</td>
<td>8</td>
<td>6.61</td>
</tr>
<tr>
<td>Renal parenchymatous pathology</td>
<td>4</td>
<td>3.30</td>
</tr>
<tr>
<td>Congenital small kidney</td>
<td>60</td>
<td>49.59</td>
</tr>
</tbody>
</table>
The role of increased plasmatic renin level in the pathogenesis of arterial hypertension in young adults

Figure 1 – Arteriography of the right renal artery stenosis (M.I., 21-year-old, with HBP=170/120 mmHg).

Figure 2 – Arteriography evidence the congenital small left kidney (D.R., 19-year-old, with HBP=165/110 mmHg).

Figure 3 – MRI scan with contrast substance showing the left renal hypoplasia (D.R., 19-year-old, with HBP=165/110 mmHg).

Figure 4 – MRI with bilateral renal tumor (F.R., 34-year-old, with malignant hypertension, HB=220/130 mmHg, worked with pesticides).

Figure 5 – Clear cell renal carcinoma (HE stain, ob. ×10) (M.I., 21-year-old, with paroxysmal HBP=200/110 mmHg).

Figure 6 – Clear cell renal carcinoma (HE stain, ob. ×10) (P.R., 28-year-old, with severe form of HBP=210/110 mmHg).
Discussion

The aim of this study was to measure the level of plasma renin of hypertensive young patients with ages between 18 and 35 years to determine its role in the pathogenesis of secondary hypertension in young adults, and also, the conditions in which plasma renin level is increased in the context of secondary hypertension in the young patients.

Renovascular hypertension was one of the important causes of secondary hypertension in the young, its frequency in the group of patients studied being of 49 cases with renal artery stenosis representing 40.50% \( (p<0.001) \), in all these cases the renin plasma level being increased above 4.3 ng/mL.

Safian RD and Textor SC [1] found the frequency of renal artery stenosis in a group of young hypertensive patients with increased plasma renin activity, as being 42.36%, which is slightly higher than in our study; this difference could be explained by a better paraclinical investigation of the young patients with hypertension.

In the group of young hypertensive patients included in the study, we found eight cases of unilateral congenital small kidney, representing 6.61% \( (p<0.001) \).

Goddard C et al. [2] found that the incidence of hypertension in young people with kidney hypoplasia was 25%. They suggested that the renin–angiotensin–aldosterone system plays an important role in the pathogenesis of hypertension in the situation of renal hypoplasia. This difference could be explained by the fact that young patients in other countries had an increased teratogenic risk compared with the young in our country.

Renal cell carcinoma (Grawitz tumor) was responsible for the younger group of four patients studied, representing 3.30% \( (p<0.001) \) of all the young hypertensive patients. Two cases were clear cell renal carcinoma, histopathology analyzed after a renal biopsy. The data obtained are slightly lower than those in the literature (5%) – Sukarochana K and Kiesewetter WB [3], and 4% – Gangurly A et al. [4]. This difference could be explained by the fact that in our country carcinogenic risk factors are lower.

Rose HJ and Pruitt AW [5] reported the case of a young patient with severe hypertension of 190/110 mmHg, after further investigations finding increased plasma renin levels and, after paraclinical investigations, a solitary simple kidney cyst.

Robertson PW et al. [6] reported the case of a young man who had elevated blood pressure (HBP=180/120 mmHg) and, after investigations, an increased plasma renin level was found and a left renal tumor (primary reninoma); blood pressure values were normalized after tumor resection.

Pheochromocytoma was found in 60 of the cases representing 49.59% of all young hypertensive adults.

Abrams HL et al. [7] found that the incidence of pheochromocytoma in the young hypertensive cases was 21.03%, Bravo EL [8] found a percentage of 42.38% for the cases of pheochromocytoma, and Bravo EL and Gifford RW Jr [9] 46.03% of young hypertensive patients with pheochromocytoma. These results are lower than those obtained in our study are. This could be explained by the risk factors in this geographical area and by the dominant genetic factor, which has an important role in the etiology of pheochromocytoma.
Conclusions

Plasmatic renin level is an important marker of hypertension in young adults. The highest plasmatic renin levels, up to 320 ng/mL, were found in the cases of renal cell carcinoma, because the kidney tumor cells secrete increased amounts of renin.

This situation suggests that hypertension in young adults is a hyperreninemia hypertension in most cases dominated by a vasoconstriction and increased peripheral vascular resistance due to the hyperactivity of the sympathetic nervous system, being a rapidly evolving form of hypertension with vascular complications.

The results of plasma renin dosing shows its important role in the pathogenesis of secondary hypertension of young adults, these conditions being not quite as rare as one might think, but not enough investigated.

This marker should be routinely performed in young patients with hypertension, especially those with medium and severe forms of blood pressure (>170/100 mmHg), having a role in establishing the etiology of hypertension in the young. However, it is still not performed often enough.

References


Corresponding author
Manuela Stoicescu, MD, Department of Internal Medicine, County Hospital of Oradea, 35 Louis Pasteur Avenue, Faculty of Medicine and Pharmacy, University of Oradea, 410154 Oradea, Romania; Phone +40723–019 951, e-mail: manuela_stoicescu@yahoo.com

Received: November 15th, 2010
Accepted: December 21st, 2010