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Hyperuricemia and Associated Factors during Arterial Hypertension in Brazzaville (Congo)

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Abstract

A longitudinal analytical and comparative study including outpatients was carried between June 1st and December 31st 2017. The objectives were to determine the hyperuricemia frequency during arterial hypertension, to identify associated factors, and to evaluate its impact on the blood pressure control. We have included, hypertensive patients having a minimum blood test including at least an uricemia. They were divided into two groups according to whether they have presented a hyperuricemia (HU) or a normouricemia (NU). Among these 202 patients included, 61 (30.2%) presented a hyperuricemia. The mean age in HU group was 54.6 ± 11.6 years vs 53.6 ± 11 years for NU group (p = 0.573). Following cardiovascular risk factors were more found in the HU group than NU group: overweight/obesity (68.8% vs 46.1%; p = 0.003), metabolic syndrome (42.6% vs 39%; p = 0.021). Diuretics were used in 72.1% of patients in HU group vs 47.5% in NU group (p = 0.002). Bitherapy was used in 56% of the patients of HU group vs 69% in the NU group (p = 0.295), and the quadritherapy in 8% and 1% of the patients respectively (p = 0.049). Blood pressure was not controlled in 68.8% of HU group vs 48.9% in the NU group (p = 0.014). In multivariate analysis after logistic regression, factors associated with hyperuricemia were: glucose intolerance or diabetes (p = 0.004; OR = 1.35) and uncontrolled blood pressure (p = 0.006; OR = 2.51). This preliminary study showed that hyperuricemia is commonly found in hypertensive patients and has negative impact on blood pressure control.

Keywords

Hypertension, Hyperuricemia, Frequency, Blood Pressure Control, Congo

1. Introduction

Arterial hypertension (HTN) is a major public health problem worldwide [1]

[2]. Hyperuricemia is increasingly pointed out in the occurrence of cardiovascular complications [3] [4] [5]. The relation between hyperuricemia and HTN has been known for several years [6] [7] [8] [9]. However, the question of the responsibility for the one on the other remains unsolved. Blood pressure control and the reduction of the global cardiovascular risk are the main objectives of the HTN management. Studies carried out in Congo showed a poor blood pressure control due to a precarious socio-economic condition and an insufficient therapeutic education [10] [11]. Also, the accountability of the hyperuricemia was not studied. It is in this context that we conducted this study. The objectives are to determine the hyperuricemia prevalence during the HTN, to identify associated factors, and to evaluate its impact on blood pressure control.

2. Patients and Methods

A longitudinal study with a prospective data collection, analytical and comparative was carried in cardiology department of outpatient at the Brazzaville University Hospital Center, from June 1 to December 31st 2017. Were included, hypertensive patients recently diagnosed or known hypertensive patients on treatment, having blood tests done including uricemia, complete blood count, fasting blood sugar, renal function test (creatinine and glomerular filtration rate were estimated by using the MDRD equation; considered to be lowered if GFR < 60 ml/min), cholesterol and its fractions, triglycerides, and a morphological assessment including electrocardiogram, echocardiography, and an ambulatory blood pressure monitoring (ABPM) if necessary. Hyperuricemia was defined by an uric acid rate >70 mg/l (420 µmol/l) for man and > 60 mg/l (385 µmol/l) for woman. Patients were thus subdivided into two groups according to whether they presented an hyperuricemia (HU) or a normouricemia (NU).The dosage of the uricemia was made at the laboratory of biochemistry of the Brazzaville UniversityHospital, using spectrophotometric method on device brand name KENZA MAX Bio ChemisTry, manufactured by BIOLABO.The sociodemographic, clinical and paraclinical data of 202 patients were collected and analyzed.Thus, several variables have been studied, such as:

- sociodemographic data: age, gender, socio-economic level defined according to ECOM investigation [12] into low, medium and high;
- associated cardiovascular risk factors: diabetes, overweight/obesity, tobacco use, dyslipidemia, sedentariness, metabolic syndrome;
- predisposing factors to hyperuricemia (neoplasia, chemotherapy, alcohol intake), and its complications (gout, tophus);
- data related to the HTN: levels of blood pressure, drug classes and therapeutic protocols used, the threshold of blood pressure control was defined by a blood pressure < 140/90 mmHg during a clinical measurement and/or < 130/80 mmHg during an ambulatory blood pressure monitoring (ABPM).

2.1. Definition of the Concepts

- Hypertension was defined by a blood pressure >140/90 mmHg on the average of three measurements in a medical office or a normal blood pressure for patients on antihypertensive treatment, or blood pressure greater than 135/85 mmHg during daytime of the ABPM.
- Diabetes was defined by a fasting blood sugar > 1.26 g/l twice or a non-fasting blood sugar > 2 g/l or diabetic patient on treatment.
- Glucose intolerance was defined as a fasting blood sugar between 1.10 and 1.26 g/l.
- The dyslipidemia was defined as a hypoHDLemia< 0.50 g/l and/or a hypertriglyceridemia > 1.65 g/l and/or a hyperLDLemia > 1.40 g/l.
- Obesity corresponded to a body mass index (BMI) >30 kg/m^2 and/or overweight with a BMI between 25 and 29.9 kg/m^2.
- Abdominal obesity was defined by a waist circumference> 80 cm for woman and > 94 cm for man.
- Metabolic syndrome was defined according to the criteria of the International Diabetes Federation (IDF) [13] by the association of at least three of the five following items: HTN, glucose intolerance, abdominal obesity, a hypoHDLemia, hypertriglyceridemia.
- Renal failure was defined as a glomerular filtration rate (GFR) less than 60 mL/min using MDRD formula.

2.2. Statistical Analysis

The software SPSS 16.0 and Stata 12.0 were used to make the statistical analysis. The test of Wald was used to make the multivariate analysis by logistic regression.The significance level was $p < 0.05$.

3. Results

Among these 202 hypertensive patients included in the study, 61 (30.2%) presenting hyperuricemia, with an average uric acid rate of 84.9 ± 23.0 mg/l in HU group versus 52.3 ± 32.9 mg/l in the NU group ($p < 0.001$). In the group, there were 104 men (51.5%) and 98 women (48.5%), average age of 53.9 ± 11.2 years old (range: 32 - 89 years), without statistical difference between both groups (HU:54.6 ± 11.6 years old vs NU: 53.6 ± 11 years old; $p = 0.573$). Thirty four patients (16.8%) had a low socio-economic status, 131 patients (64.8%) had a medium socio-economic status, and 37 patients (18.3%) had a high socio-economic status, without statistical difference between the both groups. The HTN, known in 147 patients (72.7%), had an average duration of 8.3 ± 6.9 years in HU group versus 6.9 ± 6.5 years in the NU group ($p = 0.246$).Associated cardiovascular risk factors such as overweight/obesity and the metabolic syndrome were more frequently found in HU group than in the NU group (68.8% vs 46.1%; $p = 0.003$ and 42.6% vs 39%; $p = 0.021$ respectively).We did not found any case of arthritis or tophus.Main characteristics of the population studied are represented in **Table 1**, and the biological parameters of the patients in **Table 2**.

Table 1. Characteristics of the studied population.

	HU group (n = 61)	NU group (n = 141)	p
Known hypertension, n (%)	47 (77.0)	100 (70.9)	0.467
Associated cardiovascular risk factors, n (%)			
- diabetes	8 (13.1)	13 (9.2)	0.219
- glucose intolerance	7 (11.5)	8 (5.7)	0.071
- dyslipidemia	28 (45.9)	60 (44.7)	0.873
- overweight/obesity	42 (68.8)	65 (46.1)	**0.003**
- abdominal obesity	38 (62.3)	96 (68.1)	0.424
- metabolic syndrome	26 (42.6)	55 (39.0)	**0.021**
- tobacco use	4 (6.5)	9 (6.4)	1
Factors predisposing with the hyperuricemia, n (%)			
- neoplasia	2 (3.3)	0 (0)	**0.031**
- chemotherapy	1 (0.7)	0 (0)	0.127
- alcohol consumption	17 (27.8)	51 (36.2)	0.325
Complications of hypertension, n (%)			
- left ventricular hypertrophy	12 (19.7)	16 (11.3)	0.181
- heart failure	19 (31.0)	35 (25.0)	0.131
- stroke	5 (8.0)	44 (31.0)	0.071
- renal insufficiency	33 (54.0)	62 (44.0)	0.098
Therapeutic classes used, n (%)			
- thiazides	44 (72.1)	67 (47.5)	**0.002**
- calcium antagonists	42 (68.8)	96 (68.1)	1
- ACEi/ARBs	40 (65.6)	89 (63.1)	0.862
- betablockers	16 (26.2)	21 (14.9)	0.086
- spironolactone	4 (6.6)	3 (2.1)	0.092
***Controlled hypertension, n* (%)**	19 (31.2)	72 (51.1)	**0.01**

ACEi: angiotensin-converting enzyme inhibitors; ARBs: angiotensin receptor blockers.

The average blood pressure of the patients at inclusion was of 164.8 ± 23.1 vs 164.3 ± 22.7 mmHg for the systolic (p = 0.886), and 96.1 ± 13.4 vs 98.0 ± 12.5 mmHg for the diastolic (p = 0.334), respectively in HU and NU groups.Table 3 gives the evolution of the blood pressure levels at the medical office and ABPM.

The main drug classes used are shown in Table 1.

The antihypertensive protocol used were monotherapy (8% vs 12%; p = 0.8), biotherapy (56% vs 69%; p = 0.3), tritherapy (28% vs 23%; p = 0.5), quadritherapy and more (8% vs 1%; p = 0.04) respectively in HU and NU groups.Five patients have received allopurinolas treatment.

HTN was controlled among 19 patients of HU group (31.2%) versus 72 patients of the NU group (51.1%), with a significant statistical difference (p = 0.01).

Table 2. Biological parameters of the patients.

	HU group mean ± SD	NU group mean ± SD	p
Uricemia (mg/l)	84.9 ± 23.0	52.3 ± 32.9	<0.001
Creatininemia (mg/l)	11.6 ± 12.6	11.3 ± 4.2	0.777
GFR (ml/min)	84.7 ± 25.3	89.0 ± 20.2	0.715
Glycemia (g/l)	1.0 ± 0.3	1.1±0.8	0.459
Total cholesterol (g/l)	2.0± 0.4	2 ± 0.6	0.859
HDL cholesterol (g/l)	0.7 ± 0.4	0.6± 0.2	0.332
LDL cholesterol (g/l)	1.2 ± 0.5	1.2 ± 0.5	0.691
Triglycerides (g/l)	1.0± 0.4	0.91 ± 0.42	0.183
Haemoglobin (g/dl)	12.4 ± 1.2	13.0± 6.4	0.282

GFR: glomerular filtration rate; SD: standard deviation.

Table 3. Evolution of the blood pressure level (mmHg) in private clinic and ABPM.

	HU group mean ± SD	NU group mean ± SD	p
SBP M0	164.8 ± 23.1	164.3 ± 22.7	0.886
DBP M0	96.1 ± 13.4	98.0± 12.5	0.334
SBP M3	150.2 ± 22.8	147.9 ± 16.9	0.496
DBP M3	89.1 ± 13.4	89.6 ± 10.3	0.773
SBP M6	140.4 ± 15.1	138.4 ± 14.4	0.374
DBP M6	85.2 ± 12.1	84.1 ± 11.2	0.538
SBP in 24 h ABPMM6	138.6 ± 13.2	134.9 ± 15.6	0.321
DBP in 24 h ABPMM6	86.8 ± 8.7	84.8 ± 10.6	0.411

ABPM: ambulatory blood pressure monitoring; DBP: diastolic blood pressure; M0: in inclusion; M3: in the third month; M6: in the sixth month; SBP: systolic blood pressure; SD: standard deviation.

The multivariate analysis after logistic regression found out that among the various analyzed factors, only glucose intolerance/diabetes and uncontrolled blood pressure were associated with the hyperuricemia. The results of this logistic regression are presented in Table 4.

4. Discussion

The prevalence of the hyperuricemia was 30.2% in our study, comparable with those noted in Cameroun [14] and Nepal [15], respectively of 31.8% and 28.8%, thus raising strong relationship between the HTN and the hyperuricemia.This fact is so obvious that the uricemia is listed among the WHO minimum assessment for the HTN. In the general population, this prevalence is much lower, lies between 14% - 25% according to series' [16] [17] [18]. In the hypertensive population, the considerable use of diuretic in the management of the HTN contributes to maintain this reality [7] [19] [20]. This fact was pointed out in our series where thiazides diuretics were used in 72% of patients with hyperuricemia against 67% of patients with normal uric acid rate. Although certain factors such

Table 4. Logistic regression of the hyperuricemia associated factors.

	Coefficient	OR	CI (95%)	p
Overweight/obesity	0.013	1.13	0.34 - 1.93	0.799
Glucose intolerance/diabetes	1.40	1.35	1.30 - 1.39	**0.043**
Metabolic syndrome	0.87	0.42	0.22 - 0.61	0.194
Renalin sufficiency	0.90	2.24	1.05 - 3.44	0.198
Neoplasy	2.10	1.35	0.35 - 2.35	0.999
Thiazides	0.99	2.56	2.46 - 2.64	0.090
Quadritherapy and more	2.13	8.43	8.34 - 8.50	0.082
Uncontrolled hypertension	0.88	2.51	2.50 - 2.51	**0.006**

as the existence of a neoplasia, chemotherapy, and the regular alcohol intake were identified as predisposing factors to the occurrence of a hyperuricemia, some studies pointed out a link between the hyperuricemia and some factors of cardiovascular risk. Such is the case of overweight/obesity [21] [22] [23] [24], glucose intolerance/diabetes [24] [26], and metabolic syndrome [16] [20] [23] [25] [27]. This association would be the fact of a food rich in purins, an insulin-resistance and an hyperinsulinism in obese subject [23]. These various factors of cardiovascular risk were found in our study in variable proportions, and only glucose intolerance/diabetes was strongly associated to the hyperuricemia in multivariate analysis.

Blood pressure control remains a real problem in medical practice, because approximately 50% of the hypertensive patients do not achieve the therapeutic goal according to a great cohort study involving twelve European countries [28]. In sub-Saharan Africa, the report is even more alarming, with less than 10% of the hypertensive patients achieving the blood pressure goal [29]. The factors in question are classically related to a noncompliance to treatment [10] [11]. However, in subjects with hyperuricemia, the achievement of this objective is much more difficult because this metabolic disorder is known to be a powerful factor of uncontrolled blood pressure [9]. As pointed out by Zhu *et al.* in China [27], the intensification of antihypertensive treatment was more significant in the group of the patients having an hyperuricemia. In the same way, the reduction of the blood pressure level under antihypertensive treatment was marked in this group. This fact was reported in an European multicentric study [30] and in Asia [27] [31] [32] [33]. Indeed, the arterial rigidity more marked in subjects of HU group could be the most plausible explanation in spite of an adequate treatment [30]. Thus, the majority of the patients of HU group of our series was not controlled.Hyperuricemia can make the bed of a resistant HTN, as reported by Alberto Mazza in Italy [9] where a rate of 63.6% of resistant HTN was noted among patients with hyperuricemia.

5. Conclusion

This preliminary study showed that the hyperuricemia is a frequent comorbidity

during arterial hypertension and occurs in a pluri-metabolic context.The overweight/obesity, the metabolic syndrome, the use of diuretics, the regulation of the quadritherapy and uncontrolled blood pressure were more frequently found among patients presenting a hyperuricemia in comparison to the normouricemic group. If hyperuricemia has an obvious negative impact on the blood pressure control, however, studies on a large scale seem necessary to determine the benefit of a significant reduction of uric acid rate during the management of arterial hypertension.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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