THE EFFECTS OF DIOVAN AND NEBILET TREATMENT ON SOME AMBULATORY BLOOD PRESSURE INDICES IN HYPERTENSIVE PATIENTS

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Abstract: *Objective: The aim of this study is to evaluate the effects of the treatment with the angiotensin receptor blocker - Diovan and of the cardioselective beta-blocker – Nebilet, on some ambulatory blood pressure indices in patients with hypertension, grade II-III. Materials and Methods: a prospective, clinical study was conducted on a six month follow–up period. The hypertensive patients were randomly assigned to either Diovan (80-160mg/day) or Nebilet (5-10mg/day). Results: 80 patients were enrolled in the study, 42 of them in the Diovan group and 38 in the Nebilet group. Pulse pressure significantly decreased from baseline values in both groups, but without significant differences between groups. Smoothness index for both systolic and diastolic blood pressure significantly increased in both groups but without significant differences between treatment groups. Conclusions: After 6 months of treatment, both Diovan and Nebilet were efficient antihypertensive therapies by improving pulse pressure and the smoothness index in the hypertensive patients.*

Keywords: *arterial hypertension, pulse pressure, smoothness index, Diovan, Nebilet*

Rezumat: *Obiective: Scopul acestui studiu a fost evaluarea efectelor tratamentului cu blocant al receptorilor de angiotensină (Diovan) şi ale tratamentului cu beta blocant cardioselective (Nebilet) asupra unor indici ai monitorizării automate ambulatorii (MATA) la pacienţi cu grad II-III de hipertensiune. Material şi metode: S-a realizat un studiu clinic, prospectiv, pe o perioadă de 6 luni. Pacienţii hipertensivi au fost trataţi aleator fie cu Diovan (80-160mg/zi) sau cu Nebilet (5-10mg/zi). Rezultate: 80 de pacienţi au fost înrolaţi în studiu, 42 în grupul tratat cu Diovan şi 38 în grupul tratat cu Nebilet. Presiunea pulsului a scăzut semnificativ comparativ cu valorile iniţiale(P<0,05) în ambele grupuri dar diferenţa nu a fost semnificativă între cele două grupuri de pacienţi (p=0.152) când acestea au fost comparate. Indexul de omogenitate pentru TAS şi TAD a crescut semnificativ, în ambele grupuri de pacienţi, dar fără diferenţe semnificative când cele două grupuri au fost comparate (p=0,223). Concluzii: După 6 luni de tratament, atât Diovanul, cât şi Nebiletul au reprezentat terapii antihipertensive eficiente, prin îmbunătăţirea presiunii pulsului şi prin oferirea unui efect antihipertensi omogen.*

Cuvinte cheie: *hipertensiune arterială, presiunea pulsului, index de omogenitate, Diovan, Nebilet*

INTRODUCTION

Hypertension is a major risk factor for both cardiovascular morbidity and mortality. It is also well known that hypertension has important variability during the same day, between different months and seasons.(1)

This is why the diagnosis for hypertension and the efficacy of the treatment is based on multiple measurements during different moments. By ambulatory blood pressure monitoring (ABPM) can be obtained different information about 24 hours, day or night blood pressure and a lot of other indices like pulse pressure or smoothness index.(2)

The optimal antihypertensive treatment for reducing and preventing the target organ damage is to:

- provide an efficient control during the 24 hour period of blood pressure
- a reduced variability and a smooth effect on the blood pressure curve
- maintain a normal circadian profile (3)

The aim of the study is to evaluate the effects of the treatment with the angiotensin receptor blocker (Diovan) and of the cardioselective beta-blocker (Nebilet) on *some ambulatory blood pressure indices in pacients with grade II-III of Hypertension* after 6 months of treatment.

MATERIAL AND METHODS

A prospective, clinical study was conducted and the consecutive eligible adult outpatients of either sex with grade II and III hypertension (office sitting SBP of ≥160mmHg and/or office DBP≥100mmHg), defined according to the international guidelines [5] were included into the study. The patients were prospectively followed-up for a period of 6 months.

The patients were not included into the study if they met any of the following criteria: malignant and known or suspected secondary hypertension; clinically significant heart disease (coronary heart disease, major arrhythmias, cardiac valvular defects, heart failure with decreased ejection fraction); concomitant cerebrovascular, renal, hepatic diseases, diabetes, haematological and malignant diseases, psychiatric disorders, pregnant

women and known or suspected hypersensitivity to ARB or β blockers.

The patients who met the inclusion criteria were randomly assigned to one of the two treatment groups: Diovan (valsartan) or Nebilet (Nebivolol). We used the original drugs of Novartis - Diovan® and Berlin Chemie/Menarini- Nebilet®

The starting dose was 80 mg for Valsartan and 5 mg for Nebivolol, once daily as recommended in the international guidelines.(5) The doses were doubled (160 mg for Valsartan and 10 mg for Nebivolol) in the patients with inadequate BP control (office SBP ≥ 140 mmHg or office DBP ≥ 90mmHg).

In all patients, the medical history was recorded, while the physical examination, the office BP measurement and the 12-lead electrocardiograms were performed at the screening visit. Upon the study initiation and at the 6 month visit, echocardiography and ABPM were performed. The office BP was measured using a standard sphygmomanometer, with the patient seating for at least 10 minutes. For the office BP reference value, the mean of 3 measurements at rest, in sitting position, was used. Ambulatory blood pressure monitoring (ABPM) was performed using ABPM-04, 99/BP411 – Medibase.

The following ABPM indices were measured for each patient: pulse pressure and smoothness index.

Statistical Analyses

The values of the quantitative variables were expressed as means ± SD (standard deviation); Changes from baseline in ABPM indices (PP and SI) were analyzed using the Student t test after the investigation of the normality distribution. Whenever p-value < 0.05, the parameter was considered statistically significant. Statistical analyses were performed, by using SPSS 12.0.

RESULTS

Eighty hypertensive patients were randomized to either Diovan (n=42) or Nebilet (n=38) once daily. The demographic and clinical characteristics of the two study groups are presented in Table 1. There were no statistically significant differences in demographic and clinical baseline characteristics. All patients included into the study completed the 6-month follow-up.

After 6 months of treatment, PP significantly reduced (p<0.001) from baseline values with:

- 8,66±10,31 mmHg in group A
- 6,84±13,75 mmHg in group B
- When the two groups were compared, after 6 moths of treatment with either Diovan or Nebilet the PP decrease was similar, without statistically significant differences between groups (p=0,107).

After 6 months of treatment, the smoothness index for SBP/24 hours increased at:

- 1.27±1.22 in group A
- 1.09±1.07 in group B
- When the two groups were compared, after 6 moths of treatment with either Diovan or Nebilet the smoothness index was similar, without statistically significant differences between groups (p=0,152).

After 6 months of treatment, the smoothness index for DBP/24 hours increased at:

- 1.15±0.86 in group A
- 0.98±0.75 in group B
- When the two groups were compared, after 6 moths of treatment with either Diovan or Nebilet the smoothness index was similar, without statistically significant differences between groups (p=0,223).

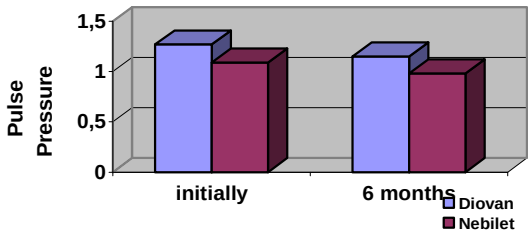
The evolution of ABPM indices after 6 months of treatment with Diovan and Nebilet is presented in pictures no. 1, 2 .

Table no. 1. Demographic and clinical baseline characteristics

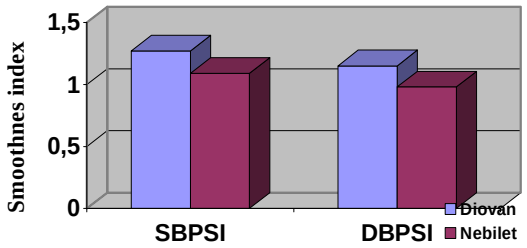
	LOT A(Diovan)	LOT B (Nebilet)	p
Patients number	42	38	ns.
Men/women ratio (%)	47,6%/52,4%	47,4%/52,6%	ns.
Mean age (years) ±SD	56,76 ±14,2	56,65±13,45	ns
BMI (kg/m²)	31,5±4,6	30,3±3,6	ns
Glycaemia (mg/dl)	114±35,2	113±15,11	ns
Total cholesterol (mg/dl)	195±34	198±37	ns
Triglycerides (mg/dl)	184±85	179±66	ns
Clinical SBP(mmHg)±SD	172,76 ±12,7	173,58±14,23	ns
Clinical DBP (mmHg)±SD	106,86±13,92	107,37±16,63	ns
BP grade à grade II(%,)	88,1%	81,6%	ns
à grade III(%,)	11,9%	18,4%	ns

SD= standard deviation, SBP= systolic blood pressure, DBP= diastolic blood pressure

Picture no. 1. Evolution of PP by treatment group



Picture no. 2. SBPSI and DBPSI at 6 months by treatment group



SBPSI=smoothness index for sistolic blood pressure
DBPSI=smoothness index for diastolic blood pressure

DISCUSSIONS

In this study, after 6 months of treatment, pulse pressure and smoothness index for systolic blood pressure

and diastolic blood pressure parameters significantly improved with Diovan and Nebilet, in comparison with the baseline values. These results are in accordance with those from other previous studies.(6,7)

Pulse pressure (PP) defined as the difference between systolic blood pressure and diastolic blood pressure proved to be a predictor for cardiovascular and cerebrovascular events. The predictive value of PP, for total cardiovascular risk, in hypertensive patients was proved in PIUMA study (8) Syst Eur trial (9)

There are evidences that an increased PP is associated with an increased arterial stiffness,(10-12) anticipates the coronary stenosis,(3) the carotids lesions (14) diabetes nephropathy (15) and left ventricular hypertrophy.(16)

The predictive value of pulse pressure, during the ABPM measurements, was proved to be superior to the value from clinical measurement.(17)

This prognostic value brought the interest for this parameter, that was seen as a therapeutic target. This is why some authors consider a PP decrease below 50mmHg as necessary in all hypertensive patients.(18)
In this study were studied the effects of the two therapies on 24hours PP. PP was significantly decreased with both therapies after 6 months treatment compared to baseline values. The decrease was similar in both groups when the groups were compared.

Mathematic indices like smoothness index, represents an efficient measure of the homogeneous antihypertensive effect during the 24 hours. The optimal antihypertensive treatment is by using drugs with a smoothness index >1 (19). Smoothness index measures the antihypertensive distribution during the day and night.(20) The preferred antihypertensive drugs are those that offer a smooth blood pressure profile on the 24 hours.

In this study, after 6 months of antihypertensive therapy both drugs determined an increase in the smoothness index without statistically significant differences between therapies.

In conclusion, after 6 months of treatment, Diovan and Nebilet improve ambulatory blood pressure monitoring PP during the 24 hour and also offer a smooth antihypertensive effect in the patients with grade II and III of hypertension.

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