COMBINED THERAPY OF HYPERTENSION IN PRIMARY PREVENTION OF STROKE

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ABSTRACT

Cardiovascular disease is the leading cause of morbidity and mortality globally, due to the high prevalence of cardiovascular risk factors difficult to correct

Hypertension remains the most important modifiable risk factor for classic and stroke and antihypertensive treatment is the most effective strategy for the prevention of stroke and other organ damage secondary hypertension.

***Key words**: cardiovascular risk factors, stroke, hypertension.*

INTRODUTION

Hypertension is considered the most important cardiovascular risk factor because of its high prevalence of at least 1 billion adults worldwide and direct linear relationship between blood pressure and cardiovascular events (Pearson TA et al, 2002, Strong JP et al, 1999, Libby P, 1996)5).

Hypertension is associated with an estimated 9.4 million deaths each year; it is responsible for at least 45% of deaths due to heart disease, and 51% of deaths from stroke worldwide (Vogel RA., 1999, Gibbons GH and Dzau VJ., 1994).

In fact, pharmacological rationale of combination therapy is to combine different drugs acting on physiological systems involved in the regulation of blood pressure in a state in which fenotipulul that determines their response to antihypertensive drugs is not known.

It is assumed therefore that pharmacological acting on two (or more) systems, the impact will be greater blood pressure reduction than

monotherapy (Zwaka TP et al, 2001, Verma S et al, 2002, Pasceri V et al, 2001).
In really, for every 20 mm Hg increase in systolic blood pressure, there is an approximate doubling of the risk of future cardiovascular event. Therefore, the objective of antihypertensive therapy must always be so improve blood pressure control and reduction of cardiovascular events (Engstrom G et al, 2002).
In this regard, the combination therapy produced a significantly greater reduction of cardiovascular risk and cerebrovascular events versus monotherapy, independent of blood pressure control (Glagov S et al, 1987, Hackett D et al, 1998, Engstrom G et al, 2002, Lalouschek W et al, 2003, Carroll CA et al, 2003, Chapman N et al, 2004). Therefore, there is convincing evidence that combination therapy offers significant advantages over alone

MATERIAL AND METHOD

The inclusion criteria were: age over 65 years, diagnosis of hypertension at the time of selection, antihypertensive therapy, other risk factors for cerebrovascular disease.
Were excluded from the study patients with atrial fibrillation, patients with significant stenosis of the carotid arteries, those with anemia and those with neoplastic disease, and patients with associated pathologies that could reduce the life expectancy of patients.
After signing informed consent for participation in the study, patients were noted initials, demographics and were measured vital signs (weight, height, systolic and diastolic blood pressure, heart rate). These were measured at rest and were performed 3 consecutive BP measurements at intervals of 5 minutes.
All patients were included in the study was performed carotid Doppler cross following which a number were excluded 19 patients that were recorded significant stenosis of the carotid arteries

RESULTS AND DISCUSSION

Depending on the therapy prescribed, patients were divided into 2 groups: group M which included 89 patients with a Sungur antihypertensive agent and group C included 94 patients receiving prescribed combination therapy (2 or 3 antihypertensive). Characteristics of the study group are shown in Table. 1

Table. 1 Characteristics of the study group

Parameter	Mediate	Min	Max	Standard deviation
age	69,540	65,00	78,00	3,54
sex	Masculin N=63			0,53
TAS	164,66	149,00	190,0	8,96
TAD	98,13	94,00	115,0	3,04
Risk factors	3,5137	2,00	6,00	1,29
	Number of patients	**%**		
Diabetes	N=65	35,51%		
Smok	N=56	30,60%		
Dyslipidemia	N=70	38,25%		
Controlled hypertension	N=117	63,93%		

It was noted that in the hypertensive group are receiving a single antihypertensive number of smokers was significantly higher ($p = 0.004$) and the number of patients with controlled blood pressure values were also statistically significantly higher in the group of patients with combined antihypertensive therapy.

Among female subjects, it was observed that the higher percentage of patients followed combination therapy, compared with male gender prevailed at that antihypertensive treatment with monotherapy, but the differences were not statistically significant.

The optimal control of blood pressure, blood glucose and dyslipidemia correction lower the risk of stroke in hypertensive patients regardless of the number used hypotensives.

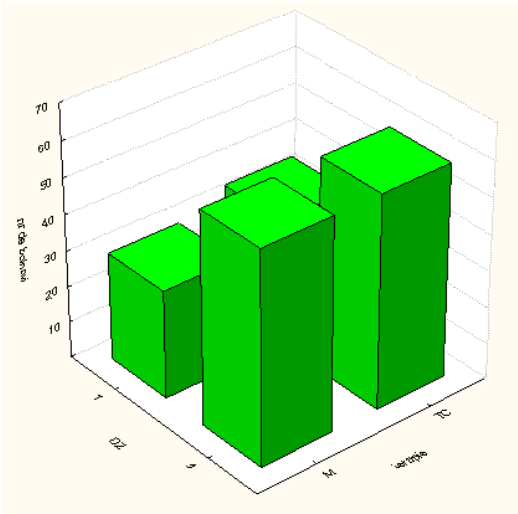

Fig. 1. Results obtained with use monotherapy and combination antihypertensive therapy

CONCLUSIONS

Our study showed that initial combination antihypertensive therapy is an effective as monotherapy in preventing a first stroke within the first 6 months of treatment. This finding is inconsistent with previous observational evidence from some studies that have shown a significantly greater reduction of occurrence of cardiovascular events, including stroke by antihypertensive initial combination therapy over monotherapy.

The incidence of stroke is similar in hypertensive patients treated with monotherapy or combination therapy as long as the blood pressure values are control.

REFERENCES

1.Vogel RA., 1999, Cholesterol lowering and endothelial function. Am J Med ;107:479-87.

2.Forgione MA, Leopold JA, Loscalzo J., 2000, Roles ofendothelial dysfunction in coronary artery disease. Curr Opin Cardiol 2000; 15:409-15.

3.Gibbons GH, Dzau VJ., 1994, The emerging concept of vascular remodeling. N Engl J Med;330:1431-8.

4.Pearson TA, Blair SN, Daniels SR, Eckel RH, Fair JM, Fortmann SP, Franklin BA, Goldstein LB, Greenland P, Grundy SM, Hong Y, Miller NH, Lauer RM, Ockene IS, Sacco RL, Sallis JF Jr, Smith SC Jr, Stone NJ, Taubert KA., 2002, AHA Guidelines for Primary Prevention of Cardiovascular Disease and Stroke: 2002 Update: Consensus Panel Guide to

Comprehensive Risk Reduction for Adult Patients Without Coronary or Other Atherosclerotic Vascular Diseases. American Heart Association Science Advisory and Coordinating Committee. Circulation;106:388-91.
5. Strong JP, Malcom GT, McMahan CA, Tracy RE, Newman WP, 1999, 3rd, Herderick EE, Cornhill JF. Prevalence and extent of atherosclerosis in adolescents and young adults: implications for prevention from the Pathobiological Determinants of Atherosclerosis in Youth Study. JAMA;281:727-35.
6. Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ., 1987 Compensatory enlargement of human atherosclerotic coronary arteries. Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med ;316:1371-5.
7.Libby P. Atheroma: more than mush. Lancet 1996;348 Suppl 1:S4-7.
8.Hackett D, Davies G, Maseri A., 1988, Pre-existing coronary stenoses in patients with first myocardial infarction are not necessarily severe. Eur Heart J, 9: 1317-23.
9.Engstrom G, Lind P, Hedblad B, Stavenow L, Janzon L, Lindgarde F., 2002, Long-term effects of inflammation-sensitive plasma proteins and systolic blood pressure on incidence of stroke. Stroke; 33:2744-9.
10. Zwaka TP, Hombach V, Torzewski J., 2001, C-reactive protein-mediated low density lipoprotein uptake by macrophages: implications for atherosclerosis. Circulation;103:1194-7.
11. Verma S, Li SH, Badiwala MV, Weisel RD, Fedak PW, Li RK, Dhillon B, Mickle DA., 2002, Endothelin antagonism and interleukin-6 inhibition attenuate the proatherogenic effects of C-reactive protein. Circulation; 105:1890-6.
12. Pasceri V, Cheng JS, Willerson JT, Yeh ET, Chang J., 2001, Modulation of C-reactive protein-mediated monocyte chemoattractant protein-1 induction in human endothelial cells by anti-atherosclerosis drugs. Circulation;103:2531-4.
13. Tiu C, Antochi F, Bajenaru O., 2003, Studiul reactivităţii cerebro-vasculare prin examen Doppler transcranian la pacienţii cu HTA cronică. Comunicare la Conferinţa Naţională de Stroke (AVC). Bucureşti, 12-16.
14. Kubler W., 2003, Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesteroal concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOL-LLA): a multicentre randomised controlled trial Peter Ssever, Bjorn Dahlof, Neil R. Poulter, Hans Wedel, Gareth Beevers, Mark Caulfield, Rory Collins, Sverre Kjeldsen, Arni Kristinsson, Gordon T. McInnes, Jesper Mehlsen, Makku

Nieminen, Eoin O'Brian, Jan Ostergren for the ASCOT. Lancet;361:1149-58.
15. * * * Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344:1383-9.
16. Doggrell S.A. 2001, Statins in the 21st century: end of the simple story? Expert Opin Investig Drugs; 10:1755-66.
17. Schwartz GG, Olsson AG, Ezekowitz MD, Ganz P, Oliver MF, Waters D, Zeiher A, Chaitman BR, Leslie S, Stern T., 2001, Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL) Study Investigators. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. JAMA; 285:1711-8.
18. Collins R, Armitage J, Parish S, Sleigh P, Peto R; 2003, Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. Lancet; 361:2005-16.
19. Jacobs DR., 1994, The relationship between cholesterol and stroke. Health Rep;6:87-93.
20. Vaughan CJ.,2003, Prevention of stroke and dementia with statins: Effects beyond lipid lowering. Am J Cardiol ;91:23B-29B.
21. Lalouschek W, Lang W, Greisenegger S, Mullner M., 2003, Vienna Stroke Study Group. Determination of lipid profiles and use of statins in patients with ischemic stroke or transient ischemic attack. Stroke ; 34:105-10.
22. Carroll CA, Coen MM, Rymer MM., 2003, Assessment of the effect of ramipril therapy on direct health care costs for first and recurrent strokes in high-risk cardiovascular patients using data from the Heart Outcomes Prevention Evaluation (HOPE) study. Clin Ther; 25:1248-61.
23. Devereux RB, Dahlof B, Kjeldsen SE, Julius S, Aurup P, Beevers G, Edelman JM, de Faire U, Fyhrquist F, Helle Berg S, Ibsen H, Kristianson K, Lederballe-Pedersen O, Lindholm LH, Nieminen MS, Omvik P, Oparil S, Snapinn S, Wedel H; LIFE Study Group. 2003, Effects of losartan oratenolol in hypertensive patients without clinically evident vascular disease: a substudy of the LIFE randomized trial. Ann Intern Med; 139:169-77.
24. Chapman N, Huxley R, Anderson C, Bousser MG, Chalmers J, Colman S, Davis S, Donnan G, MacMahon S, Neal B, Warlow C, Woodward M; 2004 Writing Committee for the PROGRESS Collaborative Group.Effects of a perindopril-based blood pressure-lowering regimen on the risk of recurrent stroke according to stroke subtype and medical history: the PROGRESS Trial. Stroke; 35:116-21.