EUROPEAN WORKING PARTY ON HIGH BLOOD PRESSURE IN ELDERLY (EWPHE): ORGANIZATION OF A DOUBLE-BLIND MULTICENTRE TRIAL ON ANTIHYPERTENSIVE THERAPY IN ELDERLY PATIENTS

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SUMMARY

The protocol of a double-blind multicentre trial on the influence of antihypertensive therapy on the morbidity and mortality in elderly patients with high blood pressure is described.

It has been clearly shown in repeated epidemiological studies that both increased systolic and increased diastolic blood pressures are related to increased mortality. The same tendency has been found in elderly subjects although the difference could be smaller.

Well-controlled clinical trials have also demonstrated that antihypertensive therapy can decrease the morbidity and mortality of the disease in certain well-defined groups of hypertensive subjects. However, the value of antihypertensive therapy in elderly subjects is still debated. Certain centres feel that in elderly patients increased blood pressure causes increased mortality and that therefore the high blood pressure should be treated. Other centres feel that both increased blood pressure and increased mortality depend upon one or more other factors (X) and that increased blood pressure can be necessary for an adequate tissue perfusion in elderly patients, especially with major artery obstruction.

Since large-scale double-blind control trials on this subject are lacking we decided to embark on a multicentre trial. We felt indeed that sufficient evidence was available suggesting that antihypertensive therapy in elderly subjects was probably not dangerous (Veterans Administration Study, 1972).

A common study protocol was elaborated by a European working party (EWPHE) (Table 1) on high blood pressure in elderly patients.

Elderly patients with high blood pressure can become candidates for the study only if they fulfill all positive criteria and none of the negative criteria. Before final admission of a candidate to the study, his initial record form is sent to the co-ordinating office in Leuven, Belgium, and the patient is followed during a run-in period on placebo capsules.

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The positive (selection) criteria are as follows.
1. Age of 60 years or more on admission into the study.
2. Blood pressure under placebo during the run-in period within certain limits.
3. Patients should be willing to co-operate and regular follow-up should be possible.

The negative (exclusion) criteria are as follows.
1. Certain specific causes of blood pressure elevation.
2. Certain complications of hypertension.
3. Certain other diseases.
4. Lack of co-operation.

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<th>Country</th>
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<td>Norway</td>
<td>Oslo</td>
<td>Lund-Johansen and Humerfelt</td>
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<td>Holland</td>
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<td>Gerbrandy and Birkenhager</td>
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<td>Belgium</td>
<td>Gent, Liège, Leuven</td>
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<td>France</td>
<td>Ivry, Lille, Grenoble</td>
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Near the end of the run-in period initial record forms are sent to the co-ordinating office and the patients are stratified for each collaborating centre into one of eight categories combining age, sex and the presence or absence of cardiovascular complications of their high blood pressure.

The patient's stratification and treatment randomization is designed in such a fashion that in each of the participating centres the same number of patients will receive active or placebo treatment (stratification per centre).

After stratification they are at random located in an active or placebo-treated group. The corresponding drugs are sent to the different centres where the patient can be admitted into the study if he continues to fulfil the admission criteria.

During the first phase of the study period all patients receive one capsule containing either 25 mg of hydrochlorothiazide and 50 mg of triamterene or a matching placebo. The dosage may be increased after not less than 2 weeks to two capsules per day.

If after not less than 1 month the blood pressure remains high with this therapeutic regimen, the second phase will be started with the addition of alpha methyldopa; first half a tablet of 500 mg and later one tablet, increasing eventually to four 500 mg tablets daily according to defined criteria. Tablets and matching placebos are identical in shape, taste and colour.

During this study different end points will be looked for. All patients will end the study for one of the following reasons:
1. By completion of the 5 years’ observation.
2. By being lost to the follow-up.
3. By interruption of all study treatment during more than 3 months.
Hypotensive therapy in the elderly

4. By a study terminating event:

   (a) Death.
   (b) Cerebral or subarachnoid haemorrhage.
   (c) Papilloedema, retinal haemorrhage or retinal exudates.
   (d) Evolutive or dissecting aneurism.
   (e) Congestive heart failure not controllable without diuretics or antihypertensive drugs.
   (f) Hypertensive encephalopathy.
   (g) Increase of signs of left ventricular hypertrophy.
   (h) Serum creatinine increase.
   (i) Rise in diastolic BP exceeding certain defined limits.

Also specific non-terminating events will be recorded and side-projects on catecholamines and renin are part of the study.

During this study period, which can last up to 5 years per patient, the data will be recorded and sent to the co-ordinating office every 4 months by using the quarterly record form, yearly by using the annual record form and, when a patient terminates the study, by using the study terminating record form. These forms were elaborated in collaboration with the cardiovascular diseases unit of the World Health Organization.

Where do we stand now?

The pilot study was started in September 1972 in the pilot centres indicated above. While the study continues a first computer analysis is planned for June 1973 and the study should start definitely in 1974; other centres could possibly join.

ACKNOWLEDGMENTS

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REFERENCE