Changing patterns of antihypertensive drug use in a German population between 1984 and 1987

Results of a population based cohort study in the Federal Republic of Germany

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Summary. In the MONICA Augsburg project, a cohort of 3324 men and women randomly selected from the population (aged 30 to 64 y) was surveyed in 1984/85 and in 1987/88. Their antihypertensive medication as well as their demographic characteristics, blood pressure values, and awareness of hypertension were assessed at each visit in an identical manner. In 1984/85 the prevalence of antihypertensive drug use in the cohort was 7.8\% (n = 260). In 1987/88, 204 of the hypertensives were still being treated (continuously treated hypertensives) and there were 167 newly treated hypertensives, thus increasing the prevalence of antihypertensive drug use to 11.2\%.

Of the 204 continuously treated hypertensives, 45.6\% had changed their antihypertensive medication over the three-year follow-up period. Combinations with diuretics (except those containing calcium antagonists or ACE-inhibitors) had largely been discontinued, and the prevalence of calcium antagonist mono- and combination therapy had markedly increased from 84/85 to 87/88. Men were treated more frequently with recently introduced antihypertensive agents than women.

Newly treated hypertensives (n = 167) showed antihypertensive treatment patterns reflecting the changes observed in continuously treated hypertensives. Triple drug combinations, mostly in fixed ratios, were being taken by approximately 25\% of all hypertensives at each visit. Prospective analysis revealed an underlying discontinuation rate of 49\%.

It is concluded that the epidemiology of antihypertensive therapy in individuals and in the community is subjected to rapid changes and various influences. Cohort studies of treated antihypertensive individuals offer a more comprehensive understanding of its determinants.

Key words: Antihypertensive drugs, pharmacoepidemiology, population based study, cohort analysis, demographic characteristics, hypertension

In 1967 and 1970, the Veterans Administration Study Group demonstrated for the first time in a randomized, controlled clinical trial the benefits of antihypertensive drug treatment [1, 2]. Subsequently, antihypertensive therapy became a routine part of medical care for one of the most common medical conditions in the community. The initiation of antihypertensive drug therapy often implies the commencement of potentially life-long treatment and drug exposure for a substantial proportion of the population.

In general, it is not very well understood what makes people stay on a specific drug therapy, how often they change the treatment, or what is the duration of exposure to specific drug combinations. The epidemiology of antihypertensive drug therapy in individuals is largely unknown. Rapid changes have occurred in treatment guidelines [3, 4], the drug market and in recommended antihypertensive therapies [5] over recent years. Thus, in addition to individually variable efficacy and side effects of specific drugs, it is expected that changes in treatment within individual hypertensives, as well as in the population as a whole, might be quite substantial, even over short observation periods.

The objective of the present study was to describe prevalence, persistence and changes in antihypertensive drug treatment between 1984/85 and 1987/88 in a cohort of randomly sampled subjects from a community in the southern Federal Republic of Germany, and to relate those data to demographic characteristics, blood pressure levels and drug types.

Materials and methods

Augsburg, the site of the international WHO-MONICA project [6], is located in the south of the Federal Republic of Germany. The 1984/85 cross-sectional survey was designed to measure the prevalence of cardiovascular risk factors in the 25 to 64 years old population of Augsburg city and in the nearby rural areas of Landkreis
Augsburg and Landkreis Aichach-Friedberg [7]. The participants in that survey formed the core of a cohort study and were invited to participate in the first follow-up in 1987/88.

In the 84/85 survey, two-stage cluster sampling was employed (for details see [8]). The overall participation was 79.3% (n = 4022). In 1987/88, the first follow-up examination was attended by 3755 subjects (93.3% participation).

For survey and follow-up, each subject was interviewed and asked about medical history and life style. In addition, each subject was asked to bring to the interview all the prescription and nonprescription medications taken in the preceding 7 days. Anti-hypertensive drug treatment was assessed from the labels of these medications brought to the interview. Drugs were categorized using the “Rote Liste”, a German listing of drugs, organized into 86 categories. Antihypertensive agents were defined as any preparation from the “Rote Liste” categories ‘antihypertensives’, ‘diuretics’, ‘beta-blockers’, and ‘calcium antagonists’. Each drug brand from those categories used by any study participant was characterized with regard to its active antihypertensive component.

The types of antihypertensive drug treatment were subsequently grouped into the following categories:

**Monosubstances.** beta-blockers (BBL), diuretics (DIU), calcium channel blockers (CCB), angiotensin converting enzyme (ACE) inhibitors.

**Combinations of two substances.** CCB in combination with one other antihypertensive (CCB + 1), ACE plus one antihypertensive other than CCB (ACE + 1), diuretic plus one antihypertensive other than CCB/ACE (DIU + 1), any other double combination (OTHER).

**Triple combinations.** Any combination of three or more antihypertensive drugs.

After interview, i.e. at least 20 minutes at rest, three blood pressure measurements were taken from each subject in the sitting position, and the first and fifth phase Korotkov sounds were recorded. The diastolic and systolic blood pressures reported here are the average of the second and third measurements.

Treated hypertensives were defined as participants who were aware of their hypertension, and who were taking antihypertensive drugs irrespective of their blood pressure. They were divided into two groups: 1) continuously treated hypertensives who had been receiving antihypertensive medication both at the initial survey (1984/85) and at follow-up (1987/88); 2) newly treated hypertensives were treated only in 1987/88. The prevalences of drug use was stratified by sex and year of examination. Age adjustment did not alter any prevalence by more than 1%, so the values reported are unadjusted.

For continuously treated hypertensives the persistence of treatment was defined as the percentage on identical antihypertensive medication both at survey and follow-up. The complementary proportion was defined as therapy changers. Continuously treated hypertensives, who stayed within the same category of antihypertensives but changed brands or components, e.g. changed from one triple combination to another between survey and follow-up, were rated as changers.

The present analysis is restricted to the age group 30–64 y in order to make the results comparable to previously published work involving the same study population [9]. Pearson’s Chi-Square test was employed for statistical analysis.

**Results**

In 1984, 289 ( = 8.1% ) of the 3564 participants aged 30–64 years took antihypertensive drugs. The follow-up examination was not attended by 240 subjects, including 29 treated hypertensives. Of the latter, 12 had died and 17 were lost to follow-up for other reasons. The attrition rates were greater for treated hypertensives than for the rest of the sample (10.0% vs 6.3%).

Of the 3324 men and women aged 30–64 years in 1984 who participated in the survey of 1984/85 and in the follow-up in 1987/88, 260 (7.8%) were on antihypertensive treatment at the time of the 84/85 survey examination. The prevalence of antihypertensive drug use in women (8.9%) was higher than in men (6.7%), despite the lower prevalence of hypertension in women. This reflects the substantially higher degree of antihypertensive treatment observed during the survey in female hypertensives [7].

The number of treated hypertensives within the cohort increased over the observation period, so that in 1987/88 a total of 371 individuals (11.2%) was on antihypertensive medication. The rise occurred even though 56 formerly treated hypertensives were lost from the category in 87/88, and it was attributable to 167 newly treated cases of hypertension (Table 1). The male: female ratio remained essentially constant.

Of the 56 subjects who were treated hypertensives at survey but not at follow-up, 52 had discontinued antihypertensive treatment for an unknown time span prior to the follow-up examination. This included 36 individuals, who, despite drug withdrawal, showed blood pressure levels below 160/95 mm Hg, and 20 who were still hypertensive but were no longer on treatment. For 4 people information on their awareness of their hyper-

**Table 1.** Numbers and sex composition of all treated hypertensives in the survey (1984/85) and at follow-up (1987/88). All were aged 30–64 y in 1984. MONICA Augsburg cohort (1639 men and 1685 women)

<table>
<thead>
<tr>
<th>Treated Hypertensives</th>
<th>Total</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initially treated:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(treated at survey, untreated at follow-up)</td>
<td>56</td>
<td>22</td>
<td>34</td>
</tr>
<tr>
<td>Continuously treated:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(treated at survey, treated at follow-up)</td>
<td>204</td>
<td>88</td>
<td>116</td>
</tr>
<tr>
<td>Newly treated:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(untreated at survey, treated at follow-up)</td>
<td>167</td>
<td>74</td>
<td>93</td>
</tr>
</tbody>
</table>

**Table 2.** Sex and age composition, place of residence (rural or city), and prevalence of uncontrolled hypertension (BP ≥ 160/95 mm Hg) in treated hypertensives in the 1984/85 survey. Comparison by treatment status at follow-up in 1987/88: untreated (i.e. treatment discontinued or withdrawn) and treated (i.e. continuously treated). P-values for Chi²-test of homogeneity of the two groups

<table>
<thead>
<tr>
<th>Prevalence (in %) of:</th>
<th>n</th>
<th>Men</th>
<th>Women</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>60.7</td>
<td>56.8</td>
<td>&gt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Rural Residence in 1984/85</td>
<td>53.6</td>
<td>54.4</td>
<td>&gt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Age 30-49 in 1984/85</td>
<td>39.3</td>
<td>23.5</td>
<td>&lt; 0.025</td>
<td></td>
</tr>
<tr>
<td>BP ≥ 160/95 mm Hg in 1984/85</td>
<td>28.6</td>
<td>47.1</td>
<td>&lt; 0.025</td>
<td></td>
</tr>
</tbody>
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