**Comparison of casual, ambulatory and self-measured blood pressure in a study of nitrendipine vs bisoprolol**


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**Summary.** In a double-blind, placebo-controlled study the antihypertensive efficacy and tolerability of a single morning dose of either 10 mg bisoprolol (n = 26) or 20 mg nitrendipine (n = 27) were investigated. Blood pressure was measured by three techniques: (1) Casual blood pressure 24 h after the dose; (2) ambulatory 24-h whole-day monitoring; and (3) self-recorded blood pressure in the morning (6–8 a.m.) and in the evening (6–8 p.m.). After 4 weeks of therapy bisoprolol had produced a highly significant reduction in blood pressure as assessed by casual, ambulatory day- and night-time monitoring, and self-measured morning and evening readings. Bisoprolol was significantly more effective than nitrendipine, which did not induce a significant reduction in the ambulatory night-time recordings. Whole-day ambulatory blood pressure profiles showed an antihypertensive effect of bisoprolol throughout the entire 24-h period. 24-h blood pressure curves after nitrendipine demonstrated a markedly shorter duration of action, with no reduction in early morning blood pressure. Adverse effects and tolerability of the two drugs were comparable. The average changes in systolic and diastolic blood pressure after bisoprolol and nitrendipine in 2-h periods of ambulatory monitoring (6–8 a.m. and 6–8 p.m.) and self-measured blood pressure (6–8 a.m. and 6–8 p.m.) showed a good agreement between ambulatory and self-measured blood pressure determinations with no significant difference between the methods.

With the increasing use of once-daily dosing for the treatment of mild to moderate hypertension it is crucial to assess whether the action is sustained over 24 h, including the period of the rapid, early morning rise in blood pressure. As this period corresponds to an increased incidence of strokes and coronary events, it may be particularly important to maintain therapeutic blood pressure control during the early hours of the day [1–4]. The value of casual blood pressure determinations in accurately establishing the duration of antihypertensive action appears to be limited, even if the blood pressure is measured in the morning before administration of the drug [5–6]. Therefore, non-invasive automatic ambulatory blood pressure monitoring has gained increasing importance in pharmacological studies. In clinical studies ambulatory monitoring provides a convenient means of assessing 24-h efficacy and has been proven to be superior to clinical readings [5–8].

The use of self-measurement at home as a further useful means of blood pressure measurement is also increasing and may improve the precision of blood pressure estimations in pharmacological studies [9, 10]. It remains unclear, however, whether self-measurement provides information on the degree of blood pressure reduction that is different from that provided by clinical readings [11]. Up to now, there have only been limited data available on the use of casual, non-invasive ambulatory and self-measured blood pressure determinations in a single pharmacological study.

Given the increasing array of once-daily antihypertensive drugs available, physicians are faced with many conflicting choices in selecting medicines that are both effective and well tolerated; calcium-channel antagonists and β-adrenoceptor blockers have been recommended as initial therapy for hypertension and comparative studies that assess blood pressure control and tolerability are needed to provide needed data for the prescribing physician [12].

The new dihydropyridine calcium channel antagonist nitrendipine was supposed to carry the potential for single daily administration because of its longer half-life [13, 14]. Therefore, its efficacy and tolerability were compared biso-
prolol, a highly selective β1-adrenoreceptor-blocker with a long elimination half-life [15, 16].

At the same time the utility was studied of self-measured blood pressure values, determined 12 and 24 hours after the dose, in assessing the duration of the antihypertensive action of the two drugs.

Patients and methods

Patients

Patients with mild to moderate essential hypertension were included in the study. Subjects were considered for inclusion, if they were between 18 and 70 y, and were not females of childbearing potential. Hypertension was defined as diastolic blood pressure > 95 mm Hg on three occasions during the placebo run-in period.

There were no significant differences between the groups in age, body-mass-index, smoking history or alcohol consumption at entry into the trial.

Sixteen of the 25 patients in the bisoprolol group and 15 of the 26 patients in the nitrendipine group had previously been on antihypertensive therapy.

Study design

The study design was double-blind with two parallel, randomised groups. If the patients still fulfilled the entry criteria at the end of the two week placebo run-in period, they proceeded to the active treatment phase, taking either 10 mg bisoprolol or 20 mg nitrendipine each day in a single morning dose for four weeks. The study was approved by the Ethical Committee of the University of Zürich.

Blood pressure measurement

All visits were scheduled between 08.00–10.00 h and patients were asked not to take their morning medication prior to measurement of the blood pressure in the clinic on the consultation days. The casual blood pressure was measured after 5 min rest in the sitting position, with a mercury sphygmomanometer, always in the same arm and at the same time of the day, by the same observer, using the same instrument. According to the recommendations of the American Heart Association Phase V Korotkoff sounds were taken as the diastolic blood pressure [17]. Three readings were taken, on Days 1, 7, and 14 of the placebo period, and on Days 1, 14 and 28 of the active treatment phase; the mean value of the last placebo day and the last two weeks of treatment and the means were used for the group comparisons.

Compliance

Compliance with the treatment was measured by pill-counting and was regarded as adequate if more than 80% of the prescribed pills had been taken. Patients with inadequate compliance were excluded from the study.

Tolerability

Side effects were recorded at each visit in response to the question "How do you feel today?". The sense of well-being was assessed with a self-rating questionnaire, constructed as an adjective check-list of 28 items, administered at the end of the placebo period and after 4 weeks active treatment. This test has a high internal reliability and validity, and has proved particularly useful for identifying mental changes in longitudinal studies. The total index, consisting of the sum of subscales, is 12.5 (9.62) in a healthy population, with a lower score indicating greater well-being [20].

Statistical analysis

Results are expressed as means with (SD/SEM). Student’s paired t-test was used for intraindividual and the unpaired t-test for interindividual comparison of blood pressure values. The scores for the evaluation of subjective well-being and changes during therapy were compared using Wilcoxon’s signed rank test and the Mann-Whitney U test.

Two sided tests were used and a P < 0.05 was considered statistically significant.

Results

53 patients entered the study, of whom 1 in each group had to be withdrawn because of intolerable side-effects. The remaining 51 patients completed the study, 25 taking bisoprolol (10 f, 15 m; mean age 50 y, range 29–65 y) and 26 taking nitrendipine (9 females and 17 males; mean age 48 y, range 22–70 y).

Antihypertensive efficacy and heart rate

On admission to the study, there was no difference in blood pressure between the two groups, as assessed by casual, ambulatory and self-recorded values (Table 1). Casual blood pressure values after 4 weeks of therapy were significantly reduced by bisoprolol (P < 0.001) and

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