Blood pressure circadian rhythm in essential hypertension

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Summary

1. Both systolic and diastolic blood pressure show a well defined circadian variation in ambulatory hypertensive subjects.

2. Blood pressure is highest in the mid-morning (10.00 hours) and lowest during sleep at 03.00 hours.

3. Treatment with oxprenolol (taken during the day) reduces daytime blood pressure but is less effective during the night and early morning.

Key words: ambulatory monitoring, blood pressure, circadian rhythm, oxprenolol.

Introduction

It was first appreciated at the end of the last century (Hill, 1898) that sleep was associated with a fall in arterial blood pressure and that there was a daily cyclical variation of blood pressure. Attempts to study blood pressure changes have in the past been limited to repeated indirect blood pressure measurement by nursing staff, the patient himself or by semiautomated measuring devices. Observations have been largely restricted to inactive patients in hospital with somewhat conflicting results (Brooks & Carroll, 1912; Mueller & Brown, 1930; Zulch & Hossmann, 1967; Irving, Kerr, Ewing & Kirby, 1974). Using similar indirect measurement in hospitalized patients Bock & Kreuzenbeck (1966) showed that treatment with methyl dopa and a diuretic reduced both daytime and night-time blood pressure with no apparent effect on diurnal variation. However, the relevance of these findings in patients exposed to normal environmental stress, both at home and at work, is largely unknown.

The development of a method for continuous recording of intra-arterial blood pressure in ambulant subjects (Bevan, Honour & Stott, 1969; Littler, Honour, Sleight & Stott, 1972) has permitted detailed accurate observations of blood pressure changes over long periods.

We have used this method to make detailed analysis of long-term recordings in hypertensive patients who are free to return to their normal work in the day, and to their own home at night.

Methods

Twenty untreated patients were selected from those referred to the Harrow hypertension clinic. They were all male with an age range of 36–72 years (mean 49 years). In each case clinic diastolic blood pressure was greater than 95 mmHg and secondary hypertension was excluded by routine screening.

We used a perfused transducer unit recently developed at Northwick Park (Millar Craig, Hawes & Whittington, 1978) and the blood pressure signal, together with the electrocardiograph, was recorded on magnetic tape using a miniature cassette recorder (Oxford Instruments Ltd.). Blood pressure was recorded from a Teflon cannula inserted percutaneously into the left brachial artery under local anaesthesia. An initial 24 h recording, starting in either the morning or afternoon, was carried out in each patient. Treatment was then started with conventional oxprenolol three times daily, the dosage being adjusted as necessary according to the clinic blood pressure (mean daily dose 344 mg; range 160–480 mg/day). In five patients a diuretic (cyclothiazide or amlodipine/hydrochlorothiazide) was used in addition to the oxprenolol. After approx. 6 weeks chronic therapy a second 24 h recording was performed in each patient.

Data analysis was carried out using a hybrid computer system which enabled mean systolic
pressure, mean diastolic pressure and mean heart rate to be calculated for each hour of the 24 h cycle in each patient.

Results
Blood pressure and heart rate in untreated hypertension

When the hourly data for systolic blood pressure were combined for the 20 patients for each hour of the 24 h cycle (Fig. 1), it was found that blood pressure was highest in the morning and then fell throughout the rest of the waking day. Systolic blood pressure reached a nadir at 03.00 hours and then began to increase again. There was a progressive increase in blood pressure from 03.00 hours until the time of rising when the increase became more rapid. The initial rise in blood pressure occurred before waking and was not associated with any physical activity. Variation of diastolic blood pressure was very similar to that observed with systolic pressure. Heart rate, however, was maximal at 12.00 hours and then fell progressively throughout the rest of the waking day. During sleep heart rate was maintained at a low level and did not begin to rise until waking (07.00 hours) when it began to increase rapidly.

Effects of chronic antihypertensive treatment on blood pressure and heart rate

Hourly data for blood pressure and heart rate was available for a full 24 h period on each of the 20 patients while on chronic treatment with oxprenolol. Statistical analysis was carried out using a paired Student's t-test for systolic blood pressure, diastolic blood pressure and heart rate for each hour of the 24 h cycle in the 20 paired studies. The statistical significance of blood pressure reduction observed was expressed by calculation of P for each hour and displaying the data graphically.

Treatment with oxprenolol taken during the waking day at 09.00, 12.00 and 18.00 hours was associated with a highly significant fall in daytime systolic blood pressure (Fig. 1). During the evening, night and following morning (22.00–12.00 hours) blood pressure reduction was less pronounced. The anti-hypertensive action was least effective between 05.00 and 08.00 hours, when the pretreatment and chronic treatment curves were in close proximity. The effects of treatment on diastolic blood pressure and heart rate throughout the 24 h was very similar to the effect on systolic blood pressure.

Discussion

These studies have shown a marked circadian variation in blood pressure and heart rate in hypertensive subjects with highest readings during the morning and lowest readings during the middle of the night. We have found a very similar pattern in normotensive subjects (Millar Craig, Bishop & Raftery, 1978).

Continuous blood pressure recordings in our patients have shown that throughout each 24 h
period substantial changes in blood pressure may occur which could be important in the routine assessment of hypertensive patients. In general, blood pressure measurements are likely to be lower in the late afternoon and evening than in the morning. During sleep hourly mean systolic blood pressure may fall below 100 mmHg even in apparently hypertensive individuals.

Myocardial infarction and stroke are important complications of hypertension, and it is of interest that several studies suggest that these may occur most commonly between 06.00 and 10.00 hours (Agnoli, Manfredi, Mossuto & Piccinelli, 1975; Marshall, 1977; Bock and Kreuzenbeck, 1966; Myers and Dewar, 1975; Tunstall Pedoe, Clayton, Morris, Brigden, McDonald, 1975). Stewart (1965) demonstrated a rapid rise in blood pressure at the time of waking in hypertensive subjects which in some cases was associated with headache and giddiness. We believe that the rise in blood pressure that we have observed in the early morning may be associated with the higher incidence of both stroke and myocardial infarction occurring at that time. Moreover our blood-pressure recordings have shown that this is the time when conventional antihypertensive therapy is least effective.

It would seem likely that circadian blood pressure variation is dependent on an underlying neurohormonal mechanism in addition to the effects of physical activity. The exact nature of this controlling mechanism is at present unknown. However, it would seem logical to consider the circadian blood pressure variation in the design of a pharmacological antihypertensive regimen for use in the long-term management of hypertension.

References


