24 Hour blood pressure monitoring in healthy and hypertensive children

György S Reusz, Miklós Hóbor, Tivadar Tulassay, Péter Sallay, Miklós Miltényi

Abstract

24 Hour ambulatory blood pressure monitoring (ABPM) was performed to provide data on the normal daily blood pressure of healthy schoolchildren and on patients with hypertension. The subjects studied were 123 healthy schoolchildren with a mean (SD) age of 12.5 (1.6) years (range 9.5-14.5 years), 24 children with borderline or mild hypertension, 17 with renal hypertension and normal renal function, 10 with chronic renal failure, and six with a renal allograft. In eight children with definite renal disease a second measurement was performed after treatment modification.

The monitor used for ABPM was validated with a mercury column manometer. The mean (SD) of the signed differences of the blood pressure measured by the two methods was -0.19 (1.75) mm Hg for the systolic and -0.21 (2.11) mm Hg for the diastolic blood pressure (n=60). Normal values for daytime and night time blood pressure were determined for those aged 10-14 years. The mean (SD) blood pressure of the 123 children was 109 (7)/66 (8) mm Hg (systolic/diastolic) for the daytime and 96 (8)/52 (7) mm Hg at night time. Of the 24 children with borderline or mild hypertension 14 had a raised blood pressure on ABPM. The circadian rhythm was disturbed in three children of this group. Even children with normal daytime blood pressure had significantly higher systolic blood pressure in the night when compared with the controls. The incidence of disturbed circadian rhythm was higher in the groups with renal hypertension (4/17 in the subgroup with normal renal function, 5/16 in the group with renal failure and/or transplantation). All children undergoing a second ABPM measurement had a lower average blood pressure after treatment adjustment.

ABPM measurements were reproducible and accurate. The method provided new data on the physiological circadian variation of blood pressure in healthy children. It proved to be a helpful tool in the diagnosis of hypertension, particularly in the detection of cases of disturbance of the circadian rhythm of blood pressure pattern and individual adjustment of treatment.

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of blood pressure. The disturbing effects of the medical environment are excluded ('white coat hypertension'). Measurements taken in the clinic may not be representative of fluctuations of blood pressure during the day. In adults ABPM is widely used in the diagnosis of hypertension and the subsequent evaluation of antihypertensive treatment.¹⁻³ Raised mean ABPM values and the failure of significant blood pressure reduction during the night are reported to correlate with cardiovascular structural changes.⁴ On the other hand, mortality from coronary heart disease may be increased if pressures are dropped too low.⁵ Although the efficacy of ABPM is established in children, the experience of its use in pathological states is limited.⁶⁻¹⁰

The aim of the present study was (1) to establish normal values for the preadolescent/adolescent age group of children (9-15 years) and (2) to collect and evaluate blood pressure data from (a) children with borderline hypertension, and (b) children with established renal hypertension.

Patients and methods

Blood pressure monitoring was performed in the following patient groups:

(1) One hundred and twenty five healthy schoolchildren, aged from 9.5 to 15 years (mean (SD) 12.5 (1.6) years, median 13 years) with a male to female ratio of 57:68.

(2) Twenty four children with a presumptive diagnosis of hypertension, based on at least three clinic blood pressure measurements exceeding the 95th centile for chronological age. The age specific centiles for blood pressure values proposed by the Second Task Force on Blood Pressure Control in Children were used.¹¹ Their mean age was 12.8 (2.9) years (median 12 years) with a male to female ratio of 11:13.

(3) Seventeen children with established hypertension and underlying renal disease. Mean age in this group was 13.4 (3.7) years (median 14 years) with a male to female ratio of 9:8. The renal disease was chronic glomerulonephritis (n=6), chronic pyelonephritis with renal scarring (n=2), idiopathic nephrotic syndrome (minimal change nephrotic syndrome (MCNS), n=5), focal segmental glomerulosclerosis (FSGS, n=2), and lupus nephritis (n=2). The five children with MCNS had a frequently relapsing course; at the time of the study all were treated with steroids (0.5-1 mg/kg/day) on alternate days. The nephrotic syndrome of the patients with FSGS was steroid resistant; at

1st Department of Paediatrics, Semmelweis University Medical School, H-1083 Budapest, Bokay u 53, Hungary
György S Reusz
Miklós Hóbor
Tivadar Tulassay
Péter Sallay
Miklós Miltényi

Correspondence to:
Dr Reusz.

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The use of ambulatory blood pressure monitoring (ABPM) allows an improved assessment

the time of the study they were not receiving medication.

The basic antihypertensive treatment consisted of a diuretic (frusemide) and a β blocking agent (propranolol) or a calcium antagonist (nifedipine). An angiotensin converting enzyme inhibitor (captopril) and/or a vasodilator (dihydralazine) were added when blood pressure was inadequately controlled.

(4) Ten children with chronic renal failure and six after renal transplantation. Two grafts had lost their function at the time of the study and the children were on dialysis treatment. Mean age of the group was 14.6 (4.0) years (median 16 years). The underlying renal disease was renal hypoplasia (n=4), FSGS (n=1), interstitial nephritis (n=1), nephrocalcinosis of unknown origin (n=1), autosomal recessive polycystic kidney disease (n=1), unknown (n=2) in the chronic renal failure group; renal hypoplasia (n=2), chronic glomerulonephritis (n=1), nephronophthisis (n=1), unknown (n=2) in the transplanted group. The antihypertensive treatment was the same as in group 3.

(5) In eight patients with renal disease or chronic renal failure there was a second 24 hour blood pressure monitoring period to evaluate the efficacy of the treatment.

All patients from groups 2–4 were under regular medical supervision in our department. Before the ABPM measurement, concentrations of serum creatinine, sodium, potassium, calcium and phosphorus, and urinary creatinine were measured by a Technicon RA1000 autoanalyser using routine laboratory methods.

Blood pressure was monitored by the Meditech-ABPM monitor (Hungary) weighing 380 g with batteries. It measures blood pressure by oscillometry. Monitor programming, such as frequency of measurements, enables individual assessment of blood pressure for day and night periods. In addition the monitor can be activated at any time for blood pressure measurement. All values obtained are stored in memory for later analysis. The monitor was programmed to measure blood pressure every 20 minutes during the day (8 am to 9 pm) and every 50 minutes during the night. The measured value was not stored but repeated if the pulse pressure was less than 50% of that measured previously, if the absolute value of the pulse pressure was less than 20 mm Hg, if the diastolic pressure was 130% higher than previously, or the pulse rate was less than 35 beats min. The averages of day and night readings for each child were calculated and stored.

The device was validated by using a conventional mercury column manometer connected by a Y connector tube. Sixty measurements were analysed (10 consecutive measurements in six children). All validation measurements were performed by the same staff member (MH). The values measured by the mercury column manometer were noted without knowledge of the corresponding data reported by the ABPM, and compared only at the end of the validation process.

Table 1 Blood pressures measured simultaneously by conventional mercury column manometer and ABPM (mean (SD) of 10 measurements/patient; systolic/diastolic)

Patient No	Conventional	ABPM
1	132.8 (3.4)/71.0 (9.9)	132.2 (3.4)/72.3 (9.1)
2	122.3 (6.6)/60.5 (2.1)	121.8 (5.8)/60.2 (1.6)
3	156.6 (1.7)/91.2 (2.5)	157.6 (2.9)/91.0 (1.9)
4	140.2 (6.0)/85.8 (6.4)	140.2 (5.8)/85.6 (6.3)
5	111.2 (3.7)/64.0 (4.5)	111.8 (3.2)/65.3 (3.4)
6	90.8 (2.5)/57.4 (4.3)	91.3 (3.5)/57.0 (4.4)

The recommendations on blood pressure measurement of the British Hypertension Society and those of the Second Task Force were used to determine the cuff size.^{11 12} Two cuff sizes were used: paediatric (bladder width $\times$ length=9 $\times$ 18 cm) and standard adult (bladder 12 $\times$ 24 cm). The measurements were performed according to Daniels *et al.*⁶ The children were instructed to remain motionless with their arm hanging limply at their side each time a reading was taken. They were further instructed to avoid excessive physical activity during the study period. Informed consent was obtained conforming to the Helsinki declaration.

Student's *t* test for paired data, unpaired data, and analysis of variance were used for statistical analysis where appropriate.

Results

VALIDATION OF THE EQUIPMENT

The average difference of 10 consecutive measurements obtained by ABPM and conventional mercury column manometer was determined in six children. The mean (SD) of the signed differences was -0.19 (1.75) mm Hg for the systolic and -0.21 (2.11) mm Hg for the diastolic blood pressure. The blood pressure averages obtained for each child are shown in table 1.

DATA ON HEALTHY SCHOOLCHILDREN

The data obtained from 123 children were used in the study. Two children disconnected the equipment during the night so their data were excluded from further analysis. No subjects were identified with a history of hypertension, cardiac or renal disease, or who were taking any medication at the time of the study. Data were evaluated from 6579 blood pressure measurements. The data of 167 blood pressure determinations (2.5% of the total) were deleted because of spurious readings. There was no significant difference between the blood pressure of boys and girls, therefore the data were pooled and processed together.

The averages of the mean values of blood pressures measured during day and night periods are shown in fig 1. There was a significant decrease of the systolic and diastolic blood pressure in all age groups during the night period ($p<0.001$ in all groups). There was no significant difference between the blood pressure values of those aged 11 to 14 years, although there was a constant tendency to increase. A slight but statistically significant difference could be observed between those

Figure 1 Mean (SD represented by error bars) diurnal and nocturnal blood pressures of 123 healthy children. Number of patients/age group: 10 years (range 9.6–10.5), $n=13$; 11 years (10.6–11.5), $n=29$; 12 years (11.6–12.5), $n=29$; 13 years (12.6–13.5), $n=26$; 14 years (13.6–14.5*), $n=26$; total number=123. *One child in this group was 15 years old.

aged 10 and those of 14 years for the following blood pressure indices: daytime systolic ($p<0.01$), night time systolic ($p<0.01$), and night time diastolic ($p<0.05$); for daytime diastolic the difference was not significant.

CHILDREN WITH BORDERLINE OR MILD HYPERTENSION

Children were originally allocated to this group on the basis of three consecutive blood pressure values from the clinic that exceeded the 95th centile for their age.¹¹ All children had normal renal function (creatinine clearance between 88 and 121 ml/min/1.73 m²) and normal serum electrolyte values.

According to the results obtained by ABPM, eight of the 24 children assessed had an average daytime systolic blood pressure above the 90th centile for their age but below the 95th centile (borderline hypertension), six had an average daytime blood pressure over the 95th centile. Ten children had normal daytime blood pressure. The data of the 14 hypertensive children and the 10 with normal daytime blood pressure are shown in table 2.

Table 2 Blood pressures measured in the borderline and mild hypertension group. A=14 children with verified hypertension; B=10 children with normal daytime blood pressure; C=123 healthy children (controls). Data shown as mean (SD) for the blood pressure averages and mean (SEM) for the blood pressure differences (systolic/diastolic)

Patients	Daytime	Night time	Daytime–night time difference
A	127.4* (8.9)/73.0** (9.8)	116.5* (9.6)/61.0* (8.5)	10.9 (2.5)/12.0 (1.9)
B	112.7 (3.8)/64.4 (6.7)	104.9** (5.7)/56.1 (6.9)	7.8† (2.1)/8.3† (1.4)
C	109.4 (6.8)/65.6 (7.5)	95.9 (7.9)/51.6 (7.1)	13.5 (0.71)/14.0 (0.71)

* $p<0.0001$ v controls; ** $p<0.002$ v controls; † $p<0.03$ v controls.

Table 3 Blood pressure values of 17 children with established renal hypertension and normal renal function and 16 children with chronic renal insufficiency and/or renal transplantation. Data shown as mean (SD) for blood pressure averages and mean (SEM) for the blood pressure differences (systolic/diastolic)

	Daytime	Night time	Daytime–night time difference
Renal hypertension/normal renal function	133.4 (10.7)/84.3 (12.0)	124.3 (14.2)/74.7 (12.5)	9.1 (2.8)/9.6 (1.6)
Chronic renal failure and/or renal transplantation	130.7 (14.4)/82.2 (13.3)	123.4 (11.5)/73.6 (10.6)	7.3* (3.3)/8.6† (4.5)

For all blood pressure averages $p<0.0001$ v controls; * $p<0.01$ v controls; † $p<0.04$ v controls (control group: see table 2, group C).

There was a significant difference between the average daytime and night time blood pressure values in both groups. It is notable that all hypertensive children had raised daytime and night time systolic and diastolic pressures when compared with the control group. One child in the hypertensive group had higher systolic and diastolic blood pressure at night than during the day; in another case the difference between daytime and night time blood pressure disappeared.

The 10 children with normal daytime blood pressure had significantly higher mean night time systolic blood pressure compared with the control group ($p<0.002$). The average diastolic blood pressure at night was also raised (although the difference was not significant, $p=0.056$). The mean difference between the daytime and night time averages was significantly lower when compared with the control group ($p<0.03$). The difference between night time and daytime blood pressure values disappeared in one child in this group.

CHILDREN WITH RENAL HYPERTENSION

All children had normal creatinine clearance (78–136 ml/min/1.73 m²) and serum electrolyte values. The average blood pressure data of the 17 children are shown in table 3.

All blood pressure data differed significantly from the control values. Although a daytime–night time blood pressure variation was present in the majority of patients, two had an inverse pattern; in two further children the diurnal difference disappeared. The mean difference between daytime and night time blood pressure was somewhat lower than in the controls, but statistically not significant.

CHILDREN WITH CHRONIC RENAL INSUFFICIENCY AND/OR RENAL TRANSPLANTATION

Twelve children from this group were on regular dialysis (nine haemodialysis, three continuous ambulatory peritoneal dialysis). The creatinine clearance of the four children with a functioning renal graft was between 34 and 68 ml/min/1.73 m². The blood pressure data of this group are shown in table 3. All children received combined antihypertensive treatment.

The night time decrease of the mean systolic and diastolic blood pressure was statistically significant, although the differences were significantly below those observed in the control group. Three children had an inverse pattern, and in two of them the daytime

Figure 2 Effect of treatment modification on blood pressure ($n=8$). The data include the individual values (mean day and night reading for each subject), before and after treatment; the error bars represent the mean SD; * $p<0.01$ v before treatment.

and night time blood pressure difference disappeared.

INFLUENCE OF TREATMENT ON THE BLOOD PRESSURE PATTERN

Eight children with renal disease or chronic renal failure had a second period of blood pressure monitoring to assess the effect of changes in treatment. The blood pressure data are shown in fig 2.

Antihypertensive treatment was given according to the steps described above.

A significant decrease of daytime systolic and diastolic blood pressure was noted. In contrast

there was no significant change in the systolic and diastolic night time blood pressure. The individual 24 hour blood pressure profile of a patient with systemic lupus erythematosus nephropathy before and after modification of treatment is shown in fig 3.

Discussion

Non-invasive blood pressure monitoring has been useful in adults to define average blood pressure in patients with borderline hypertension, assess the effects of antihypertensive treatment, and predict clinical outcome.^{3,4,13-18} The Second Task Force on Blood Pressure in Children has published standards for blood pressure measurement in children and normal adolescents.¹¹ At present no standards exist for normal ambulatory blood pressure values in children. Daniels *et al* pointed out some difficulties of ABPM.⁶ In his group of patients, blood pressure measurements were obtained with a monitor using auscultatory technology. A large proportion of spurious readings was attributed to extraneous room noise. The monitor used was bulky and awkward for use in younger children. Portman *et al* used an oscillometric ambulatory monitor. It was well tolerated and measurements were reproducible and accurate. The level of physical and emotional activity was recorded and correlated to the blood pressure results.⁷

In our study, blood pressure measurements taken by ABPM and mercury manometer were virtually identical. The device largely fulfilled the criteria proposed for validation of the accuracy of ABPM.¹⁹ The percentage of spurious readings (2.5%) was lower than in other reports (9–25%)^{6,8,13,20} and similar to that of Portman *et al*.⁷ The reasons could include the automated editing criteria, the oscillometric blood pressure measurement, and the instructions to avoid physical overactivity during the measurements. The monitor was well tolerated with only two failures due to disconnection of the device during the night.

A clear circadian blood pressure pattern was noted in the control group of 123 healthy schoolchildren; mean systolic and diastolic blood pressures were higher during the day than at night. The difference between boys and girls was not significant in these age groups, therefore the data were pooled. Larger numbers would perhaps lead to statistical differences between the sexes, although the biological significance of such small dissimilarities could be questionable. The pooled data were used as reference for blood pressure values and patterns of children with pathological blood pressure.

In their study on 99 schoolchildren, Portman *et al* could not find the white coat phenomenon reported in adult studies.⁷ Instead their subjects had higher blood pressure during the study, due perhaps to the unlimited physical activity of their patients during the ABPM period. The issue of physical activity during ABPM raises further

Figure 3 Twenty four hour blood pressure profile of a patient with systemic lupus erythematosus nephropathy (aged 14 years) (A) before and (B) after treatment modification. The horizontal dotted lines are supplied by the computer program to help orientation on the figure (they are not centile lines)

questions. First, unlimited physical activity, when recorded at the time, makes standardisation difficult or even impossible. Furthermore, the reliability of the oscillometric blood pressure measurement decreases during dynamic exercise, as reported by Jacoby and coworkers.¹⁰ In their study ABPM provided a reasonably accurate assessment of blood pressure in mildly active and inactive children only. In our study the children were instructed to avoid excessive physical exercise during the study period, and especially to remain motionless during the insufflation-deflation periods. This technique could explain the small proportion of spurious readings and the good accordance between the diurnal blood pressure of our healthy children and that measured by conventional methods.¹¹

On the basis of ABPM results, the group of children with a diagnosis of hypertension based on clinic blood pressure readings was heterogeneous. Ten children had normal daytime average blood pressure pattern when measured with ABPM, the remaining 14 children had raised daytime systolic and diastolic blood pressures compared with the controls. The circadian blood pressure pattern was conserved in both groups as a whole; however, there was one child with an inverse pattern in the hypertensive group and the circadian rhythm disappeared in one patient in both groups. Although 10 children had normal daytime blood pressure, the higher blood pressure measured during the night needs further investigation.

The circadian rhythm of the blood pressure readings was also conserved in the majority of children with renal hypertension and normal renal function and in those with chronic renal failure, although more pathological patterns were observed. These results are in accord with recent data,⁹ and point to the need for careful follow up of patients in order to adjust antihypertensive treatment and prevent late cardiovascular sequelae.^{13-15 17}

Our data show that ABPM is well tolerated by children of school age and has provided new information regarding physiological blood pressure regulation and the circadian variation of blood pressure. Moreover, based on these data, ABPM is a useful tool in the diagnosis of borderline hypertension. It can be used not only to establish the diagnosis of definite hypertension, but also to detect patients showing an altered circadian rhythm of their blood

pressure pattern, which could be a first sign of modified vascular reactivity.^{14 16}

The use of ABPM was particularly useful in children with established secondary hypertension, helpful in detecting blood pressure fluctuations especially during the night and early morning hours and in adjusting antihypertensive medication corresponding to the blood pressure pattern observed.

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