University of Szeged
Albert Szent-Györgyi Medical School
Doctoral School of Clinical Medicine

Investigation of neonatal blood pressure

PhD Thesis Booklet

Dr. Judit Klára Kiss

Supervisor

Dr. Csaba Bereczki, PhD

Szeged

2024

1. Publications

I. Kiss, J. K., Gajda, A., Mari, J., Nemeth, J., & Bereczki, C. (2023)
Oscillometric arterial blood pressure in haemodynamically stable neonates in the first 2 weeks of life, Pediatric Nephrology, 38:3369–3378., https://doi.org/10.1007/s00467-023-05979-x

II. Kiss, J. K., Gajda, A., Mari, J., & Bereczki, C. (2024)
Blood pressure in preterm infants with bronchopulmonary dysplasia in the first three months of life, Pediatric Nephrology, accepted, ahead of print.

2. Introduction

Blood pressure measurements are essential to evaluate the cardiovascular stability of preterm and term infants. Diagnosing and treating hypotension and hypertension are important to reduce the lifelong consequences of prematurity. Over the last 40 years, several studies have provided data on the blood pressure values of preterm and term neonatal patients. However, defining normal blood pressure remains very challenging in this population. The difficulties arise from the different measurement methods, patient population and wide variety of prenatal and postnatal influencing factors examined by different studies. Studies conducted to determine normal blood pressure differ fundamentally regarding patient inclusion criteria. Some early studies examined all patients without exclusion criteria and tried to identify the influencing factors statistically. The other approach to conducting studies was to select a haemodynamically stable patient group to determine normal blood pressure. Several studies examined maternal health and therapy's influence on neonatal blood pressure, but the results are still controversial.

Particular diseases of premature infants can affect blood pressure development and cardiovascular outcome of the infant. Bronchopulmonary dysplasia (BPD) is one among these conditions, and several working groups have investigated its effect on blood pressure. Previous research has shown that preterm infants with BPD have a significantly higher risk of developing systemic hypertension. According to the literature, the incidence of hypertension varies widely, with rates between 12% and 43% in preterm infants with BPD. Despite improved neonatal care, BPD remains one of the most common complications of preterm birth, affecting 17-75% of preterm infants born before the 28th week of gestation worldwide. BPD and the consequent hypertension can significantly affect premature infants' short- and long-term life outcomes.

3. Aims and questions

The main scientific questions of our research and the aims formulated based on the questions are as follows:

1. What is the normal blood pressure of a haemodynamically stable neonate? How do neonatal characteristics (birth weight, postnatal age, gestational age) affect neonatal blood pressure?

- We aimed to determine the normal average blood pressure in haemodynamically stable neonates according to different gestational ages and birth weights.
- We aimed to create a percentile table for the first five days of life for different gestational ages and birth weights.

2. Does antenatal steroid administration increase neonatal blood pressure after birth?

- We aimed to prove the antenatal steroid neonatal blood pressure stabilising effect.

3. Does the patient group with moderate and severe BPD have a different blood pressure than the control group?

- We aimed to compare the blood pressure of moderate and severe BPD patient group to the reference data.

4. Can we detect hypertension by performing individual examinations of BPD patients' blood pressure data?

- We aimed to examine the blood pressure variation of moderate to severe BPD patients in the first three months of life. We compared the individual patient's blood pressure to the 95th percentile.

4. Materials and methods

We conducted two retrospective single-centre studies at the Neonatal Intensive Care Unit (NICU) of the University of Szeged, Hungary, to determine normal average neonatal blood pressure, the corresponding percentiles and the effect of BPD on neonatal blood pressure changes. Over a three-year period (from 01. January 2019 to 31. December 2021), relevant clinical data and all the blood pressure readings were collected from the entire patient group admitted to the unit.

Our first study determined the normal average blood pressure and percentiles in haemodynamically stable neonates. In order to select the corresponding group of patients, we excluded all infants with a substantial risk of hypotension or hypertension from the study. The exclusion criteria were the following: (1) need for inotropic support, (2) postnatal steroid administration, (3) patients who required invasive ventilation for more than 24 hours, (4) renal parenchymal disease, renovascular abnormality and acute kidney injury, (5) major congenital

heart defect, (6) chromosomal anomaly, (7) intracranial hypertension, (8) diagnosed hypertension of the newborn, (9) maternal substance abuse and withdrawal syndrome of the newborn, (10) use of an umbilical arterial catheter, (11) severe and moderate BPD, (12) endocrine disorder with a risk of hypertension and (13) death. As there have been changes in neonatal medicine since the earlier research, we have not excluded interventions that are part of routine care today. We also collected maternal medical data. However, we did not exclude patients based on the investigated maternal medical problems, as the results are still controversial on their effect on neonatal blood pressure.

All preterm infants born before 30 weeks gestation with moderate or severe BPD admitted to our NICU over three years were included in our second investigation. We excluded the patients from the study who were transferred out or died before 36 weeks of postmenstrual age.

Definitions

The gestational age determination was based on the last menstrual period and early ultrasound scans done by the obstetrics team. A complete steroid course was defined as four times 6 mg doses of dexamethasone administered intramuscularly every 12 hours. We used the National Institute of Child Health and Human Development (NICHD) 2001 definition to diagnose moderate and severe BPD. All patients in the studied population also met the criteria for grade 1-3 BPD based on the NICHD 2019 study. Neonatal hypertension was defined as persistent systolic and/or diastolic measurements above the 95th percentile for postmenstrual age (PMA). The definition of a persistent blood pressure increase was a high blood pressure above the 95th percentile for three or more days. We used the modified Kidney Disease: Improving Global Outcomes (KDIGO) definition to diagnose neonatal acute kidney injury (AKI).

Blood pressure measurement

Blood pressure was measured using an oscillometric device (GE Dash 3000 multiparameter monitor system with the GE DINAMAP blood pressure algorithm) with an appropriately sized cuff (cuff-width-to-arm-circumference ratio closest to 0.50). The blood pressure measurements were taken according to the unit's guideline in a quiet, awake state or during sleep. We preferably used the right upper arm to measure the blood pressure. Left arm or calf blood pressure measurements were used only in case of contraindications (e.g., right arm tissue injury, peripheral cannula or PICC-line).

Data collection and handling

The blood pressure values and patient and maternal demographic and medical data were retrieved from the IntelliSpace Critical Care and Anesthesia (ICCA) electronic medical records by Phillips and the hospital information system Medsol. The ICCA hospital administration system automatically stores the monitoring data in databases. All noninvasive blood pressure values in the records of the ICCA's database were retrieved using relevant SQL queries and were output as CSV text files. We developed a standalone software program, PDAnalyzer, to perform all the main calculations based on the measured numeric blood pressure values and relevant additional raw data in our database. This data management method prevented data quality problems and maintained data reliability and accuracy. Altogether, 360507 systolic, diastolic, and mean blood pressure data were analysed. The PDAnalyzer program calculated the daily average blood pressure values, the corresponding deviations, and the daily percentile values.

In our first investigation, the collected data included all the blood pressure records, antenatal steroid administration, Apgar scores at 1 and 5 minutes of life, birth weight, number of ventilated days, information on certain neonatal medications, maternal medical history and neonatal diagnoses. We calculated the normal average blood pressure for preterms less than 30 weeks gestation without moderate or severe BPD or other risk factors for hypertension. By linear regression analysis, we created the reference 95th-percentile trendlines at both weekly and daily resolutions. In our second study, these results served as a reference.

In our second investigation, we examined the blood pressure data of the entire patient group with moderate and severe BPD. We compared the results of the BPD patient group to the previously defined normal daily average from a preterm patient group born under 30 weeks gestation. Since we found a difference between the daily average blood pressure curves of the two groups, we examined the development of the patient's blood pressure individually on a daily and weekly basis.

Statistical analysis

In most cases, statistical analysis was carried out using the IBM SPSS Statistics program (version 29) and Microsoft Excel Data Analysis module. One Sample Kolmogorov-Smirnov test was performed to prove the normal distribution of the blood pressure data. We used paired samples t-test to compare paired samples with continuous variables, and in the case of discrete variables, we used a simple binomial test. For the verification, the significance level was usually set at $p < 0.05$. Linear regression analyses were used to determine trend lines to

approximate the arithmetic means calculated from the raw blood pressure values. The graphs were created using Microsoft Excel version 2209.

Ethical approval

Ethical approval was granted by the local Ethics Committee of the University of Szeged and the Hungarian Medical Research Council Scientific and Research Ethics Committee. The number of ethical approvals: 78/2021-SZTE RKEB, BM/15221-1/2023.

5. Results

We admitted 839 patients in our neonatal intensive care unit over three years (2019-2021). After applying the exclusion criteria, we included data from 629 infants in the study, of whom 378 (60%) were preterm and 251 (40%) were full-term patients. The electronic patient records over the three years consisted of 119714 systolic, 119700 diastolic, and 121093 mean blood pressure data (i.e., 360507 data altogether). After applying the exclusion criteria, the remaining 629 patients had 44990 systolic, 44977 diastolic, and 44971 mean blood pressure values.

Average blood pressure values of the different gestational age groups in the first 14 days of life

The arithmetical average blood pressure values were determined in different gestational age groups in the first two weeks of life. All the blood pressure curves representative of a certain gestational age were created. We calculated the daily arithmetical average blood pressure and the standard deviation for each gestational age from the daily blood pressure measurements. Due to the low patient number in the very preterm group and the low measurement number in the term group, we investigated gestational weeks between 25-28 and 40-42 together, respectively. As a representative example, we presented the daily average systolic blood pressure curve as the function of time for different gestational age groups in the first two weeks of life (see Fig. 1). We found a statistically significant difference among the average blood pressure values of the different gestational age groups using the SPSS program paired samples t-test. We found that blood pressure increases with an increasing number of postnatal days and gestational age (see Fig. 1). According to our findings, the systolic blood pressure rise over the first three days of life is steeper in preterm infants (25-36 weeks gestation) than in the term infant group. The systolic blood pressure increased by 3.75 mmHg/day in preterm infants and 1.60 mmHg/day in term infants in the first three days. After the first five days, the average systolic blood pressure values might show a mild decrease (see Fig. 1), but the trend remains increasing within the first two weeks of life.

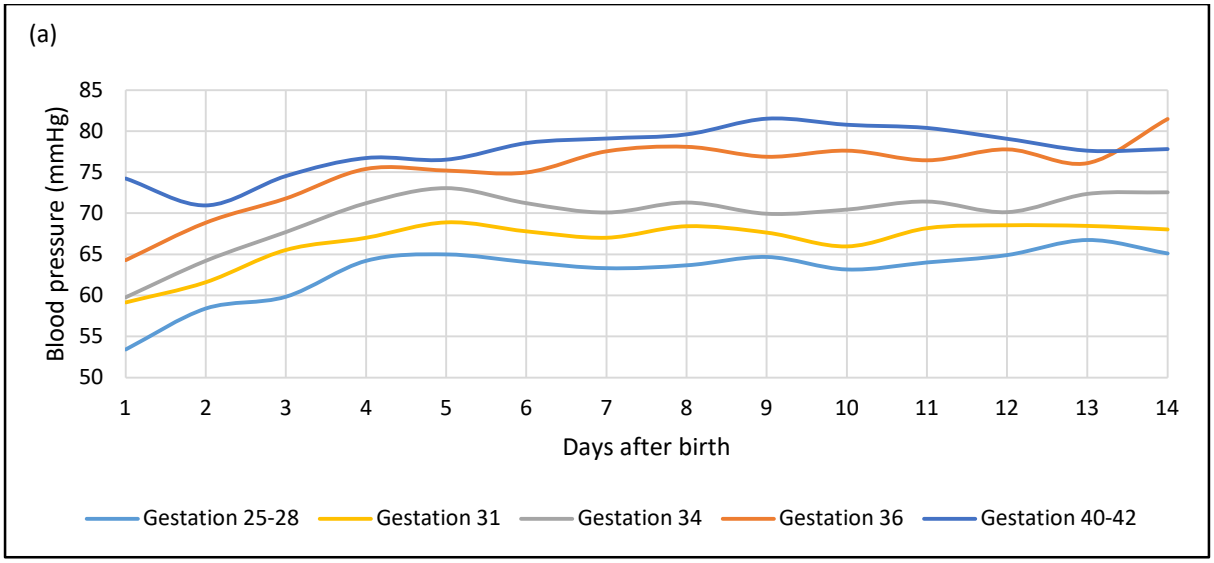

Fig. 1 Systolic blood pressure curves for different gestational ages

We experienced a similar pattern examining the diastolic and mean blood pressure data. In the first three days, the daily diastolic blood pressure increase was 3.57 mmHg in preterm infants and 1.95 mmHg in term newborns, and the mean blood pressure elevation per day was 3.73 mmHg in the preterm and 1.93 mmHg in the term group.

Blood pressure in the first five days of life by gestational age

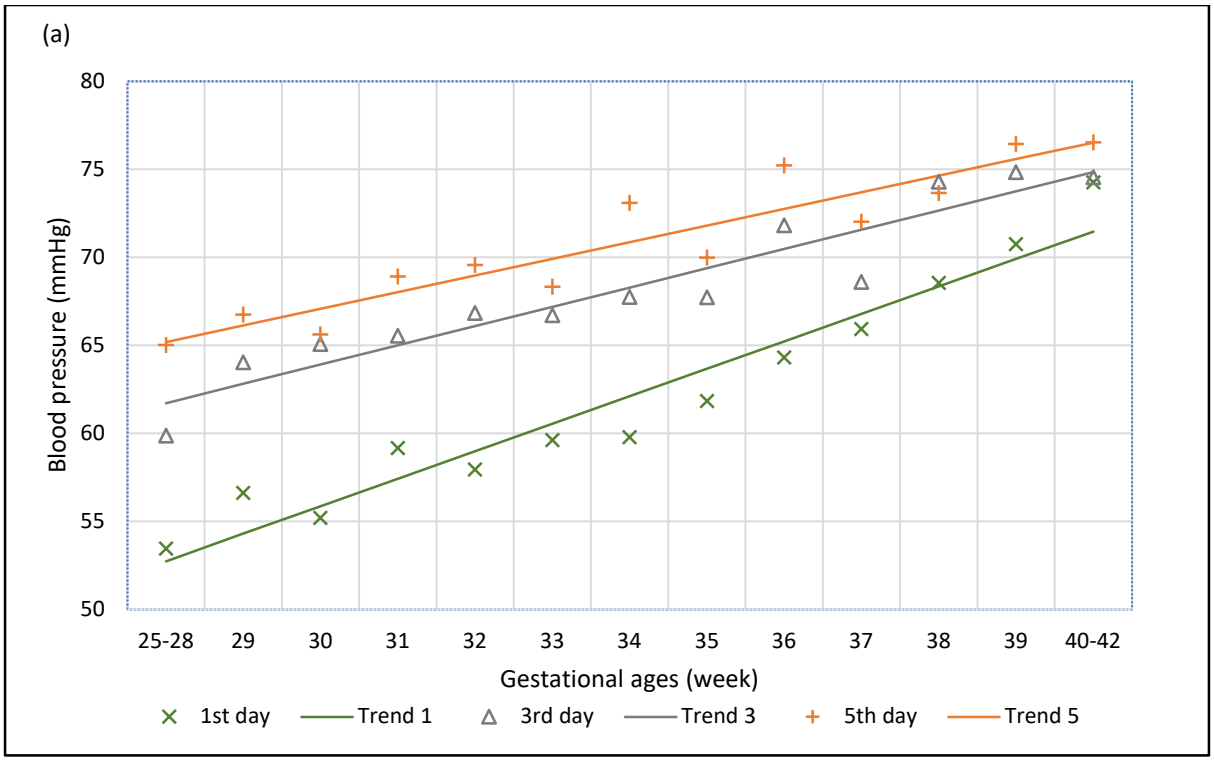

Fig. 2 Systolic blood pressure by gestational ages on the first, third and fifth day of life

As the blood pressure changes are most pronounced in the first week of life, the average daily blood pressure has been calculated on the first, third and fifth days, and the results are

graphically presented (see Fig. 2). Figure 2 shows the systolic blood pressure values and linear regression lines in different gestational ages on the first (Trend 1), third (Trend 3) and fifth (Trend 5) day of life. According to our analysis, the linear regression lines strongly correlate with the daily average blood pressure data. As shown in Figure 2, the trendlines increase steeper in the first than in the third or fifth day of life. It means that the blood pressure difference between the first, third, and fifth days of life decreases as the gestational age increases. We created a table that provides data on the daily average blood pressure values and percentiles in different gestational age groups on the first, third, and fifth days of life. The table is presented in the supplements of the published article.

Blood pressure by birth weight

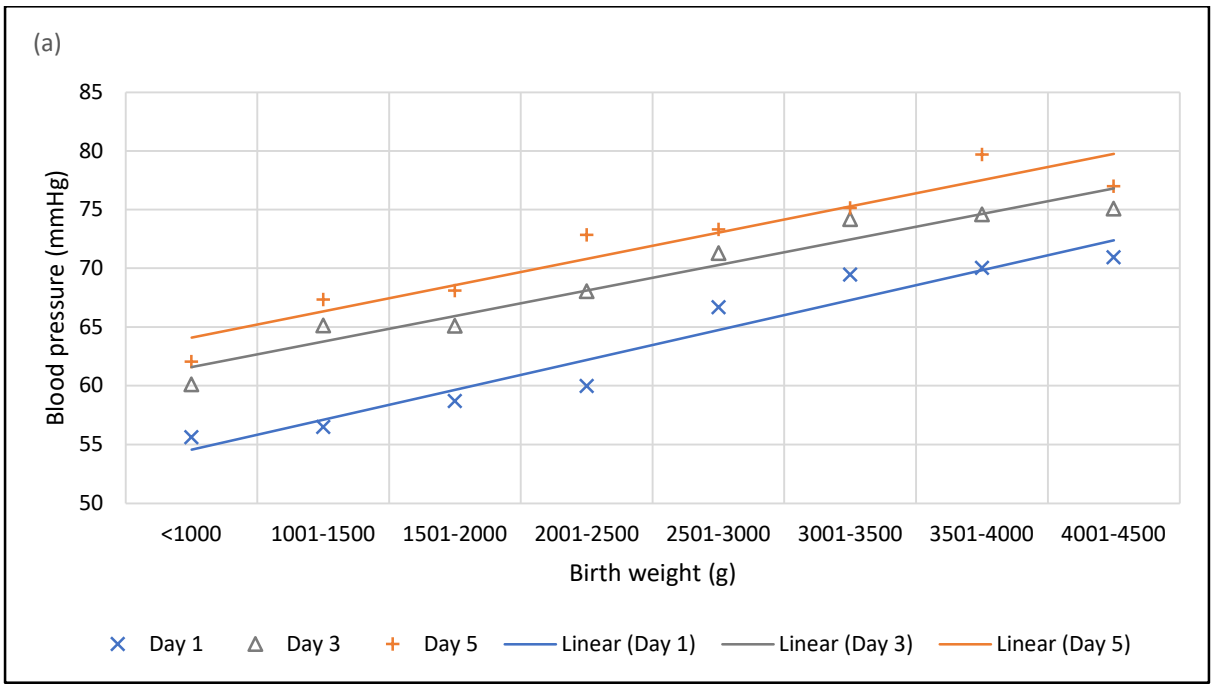

Fig. 3 Systolic blood pressure by birth weight

We investigated the change in neonatal blood pressure by increasing birth weight and generated eight patient groups; every patient group had a 500g difference in birth weight. The blood pressure data of 613 patients were included in the analysis. The data of 16 patients with a weight higher than 4500g was not used for calculation due to the low number of measurements and short hospital stay. The systolic blood pressure values and linear regression lines are shown in Fig. 3. The following table (see Table 1) contains the average blood pressure values and percentiles of the different birth weight groups on the first, third and fifth days of life.

Table 8 Average blood pressure values and 10th, 50th and 90th percentile by birth weight on the first, third and fifth day of life

Birth weight (g)		Day 1 BP				Day 3 BP				Day 5 BP			
		Average	10th Pc	50th Pc	90th Pc	Average	10th Pc	50th Pc	90th Pc	Average	10th Pc	50th Pc	90th Pc
≤1000	SBP	56	40	55	72	60	46	59	77	62	49	62	77
	DBP	35	21	36	48	40	27	38	56	39	29	38	51
	MBP	43	27	41	56	48	35	46	64	47	36	47	59
1001-1500	SBP	56	43	55	71	65	53	65	78	67	54	68	79
	DBP	35	24	36	45	42	32	42	53	43	33	43	54
	MBP	43	31	43	56	51	40	51	61	52	41	52	62
1501-2000	SBP	59	48	58	70	65	54	65	77	68	57	68	81
	DBP	35	26	35	44	42	33	41	52	42	32	42	53
	MBP	44	34	44	54	51	42	51	60	52	42	52	64
2001-2500	SBP	60	50	59	72	68	58	68	79	73	60	73	86
	DBP	37	27	36	46	44	35	44	53	45	35	44	57
	MBP	46	36	45	55	53	44	53	62	56	45	55	69
2501-3000	SBP	67	54	64	82	71	59	71	84	73	63	74	83
	DBP	43	30	41	58	45	34	44	56	43	35	42	54
	MBP	52	40	50	68	55	44	54	67	55	45	54	66
3001-3500	SBP	69	56	69	82	74	62	73	87	75	63	75	88
	DBP	42	32	42	52	47	37	46	58	46	37	45	56
	MBP	52	42	52	63	58	46	57	70	57	48	57	68
3501-4000	SBP	70	59	70	81	75	62	74	86	80	69	80	91
	DBP	42	32	41	52	48	37	47	59	48	39	48	59
	MBP	53	43	52	64	58	46	58	70	60	50	60	71
4001-4500	SBP	71	58	70	88	75	62	75	88	77	61	78	90
	DBP	43	35	42	54	47	36	45	59	46	36	44	58
	MBP	53	43	52	66	58	45	58	71	58	45	58	69

SBP: systolic blood pressure, DBP: diastolic blood pressure, MBP: mean blood pressure, BP: blood pressure, Pc: percentile

Investigation of antenatal steroid administration effect on neonatal blood pressure

Based on the blood pressures of the first two weeks of life, we compared the average blood pressure values of the preterm patients (gestational age: 25-34 weeks, patient number: 306) who received a complete course of antenatal steroids (n=170, 55%) to the patient group who had an incomplete antenatal steroid course (n=82, 27%) or did not receive steroid prophylaxis (n=54, 18%). There was no significant difference between the two groups.

Investigation of blood pressure changes in moderate and severe BPD patients

Our study aimed to investigate the changes in blood pressure in the premature BPD patient group during the first three months of life. Over three years, our unit admitted 126 patients born

at less than 30 weeks gestation, of whom 26 had moderate to severe BPD. Our database comprised 19481 measured blood pressure data separately for systolic, diastolic, and mean blood pressure in the first 90 days of life. Therefore, the average number of raw data points per patient was 749.3 for each blood pressure category. This amounted to an average of 8.3 daily blood pressure measurements per patient.

The evolution of the average systolic, diastolic and mean blood pressures in the BPD patient group compared to the reference blood pressure data

We calculated the daily average systolic, diastolic and mean blood pressure values of the BPD patient group. Based on the daily average blood pressure data, we generated two trendlines: one for the BPD group and the other for the reference data. We compared the blood pressure curve and the corresponding trendline to the reference group's average daily blood pressure.

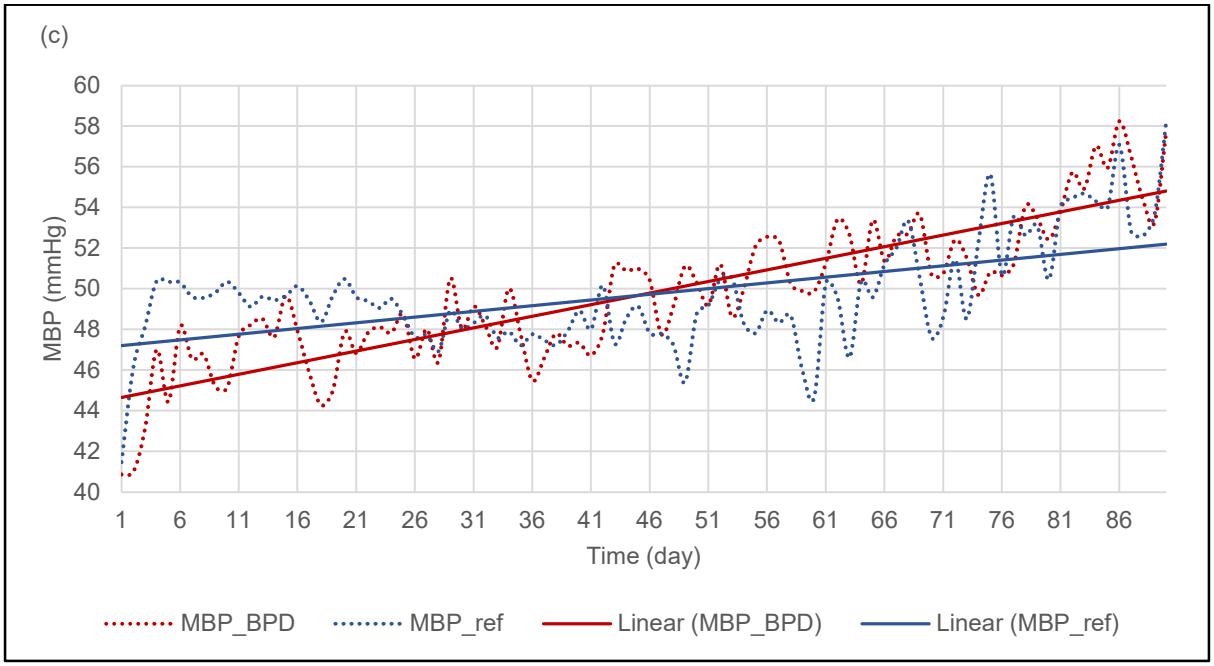

Fig. 4 Mean blood pressure curves and linear trendlines of the BPD group and the reference group as a function of time. MBP: mean blood pressure, BPD: bronchopulmonary dysplasia, ref: reference group

The BPD patients' SBP trendline initially had lower values and rose gradually until around the 70th day of life, when it crossed the reference trendline. The DBP and the MBP (see Fig.4) showed similar trends to that of the SBP, but they reached the reference trendline around the 30th and the 45th days of life, respectively.

Comparison of the daily average blood pressure to the 95th percentile blood pressure trendline

We calculated and compared each patient's daily average blood pressure to the 95th percentile trendline. Considering the 2340 patient days, we found 38 systolic (1.6%) and 50 diastolic

(2.1%) daily average measurements above the 95th percentile. In our whole sample, only nine patients had no daily average blood pressure spikes (i.e., a systolic or diastolic daily average blood pressure above the 95th percentile), and 65% (n=17) had at least one day with a hypertensive average daily blood pressure in the first three months of life. We found 13 patients (50%) who had average daily SBP and 16 patients (61.5%) who had average daily DBP values that exceeded the 95th percentile. Most of them had occasional daily blood pressure spikes. Eleven patients (42%) had three or more days with an average blood pressure above the 95th percentile. We compared the patients with elevated blood pressure values for three or more days to the remaining patients. Our statistical analysis showed that patients with three or more hypertensive days had a 25% chance of having AKI. AKI episodes (91.6%) mainly occurred within the first two weeks of life. All the investigated BPD patients had normal renal function (i.e. age-appropriate serum creatinine levels and urine output) after the fifth week of life.

We also examined the onset of the blood pressure increase. Most daily average hypertensive blood pressure measurements occurred at the 2nd, 9th, 12th, and 13th weeks of life, corresponding to the 28th, 35th, 38th, and 39th weeks of corrected gestational age, respectively (see Fig. 5).

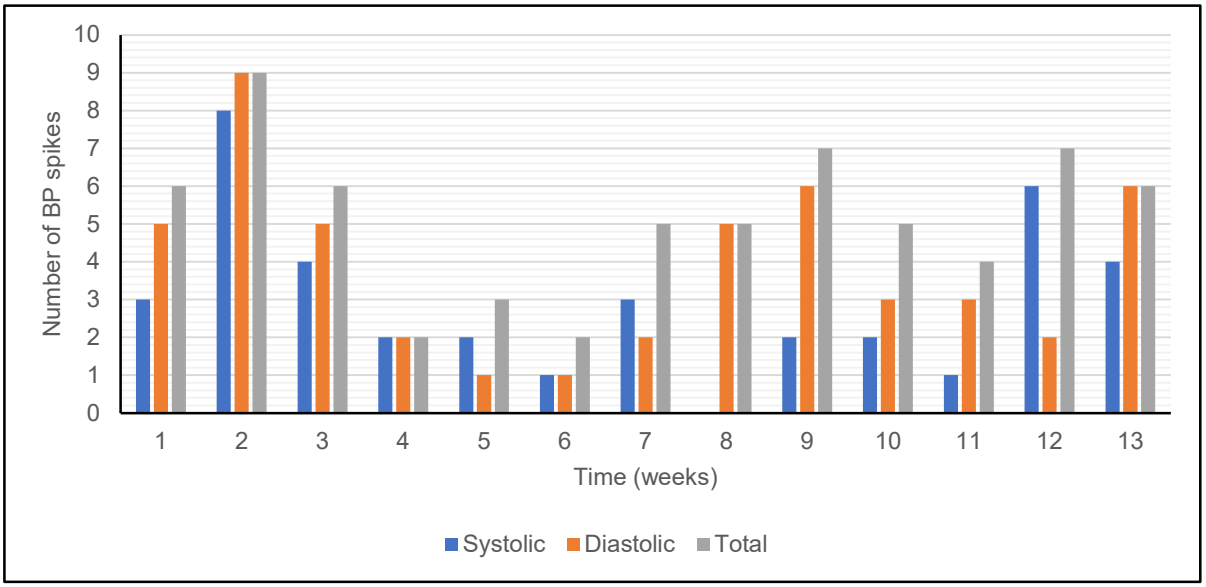

Fig. 6 Number of systolic, diastolic, and total blood pressure spikes over 13 weeks
BP: blood pressure, total: systolic and/or diastolic BP spikes

We investigated the data on fluid boluses, blood transfusions and inotropic support in the database and found that the duration of administration did not coincide with periods of high blood pressure. These therapies were given mainly within the first three weeks of life: 44% of blood transfusions, 88% of fluid boluses and 62% of inotropes. The use of these particular

therapies was limited compared to the entire investigated time interval. Therefore, these factors should not influence the results of our blood pressure analysis.

6. Discussion

We conducted two single-centre retrospective studies to provide oscillometric blood pressure measurement data on normal neonatal blood pressure and its influencing factors with particular reference to BPD as one of the most common complications of extreme prematurity.

In our first investigation, both our patient number and the volume of our measured data were comparable to the largest previous investigations done in this field of research. As a novel method, a large number of blood pressure data was retrieved from electronic hospital records and analysed further with the help of a standalone software. This retrospective approach enabled the use of large data sets and significantly reduced the possibility of errors due to data inaccuracies. Most of the other clinical studies investigated healthy patient populations by excluding cardiovascularly compromised patients, but infants with a risk of hypertension were just partly excluded. Since earlier research, several improvements have arisen in neonatal therapy, and the patient's survival has improved. These changes also increased the importance of performing new studies and investigating a patient population without severe morbidities and major therapeutic interventions.

We compared our results to studies carried out previously by using oscillometric blood pressure measurement methods. Kent and colleagues investigated a homogenous preterm patient group without ventilated patients or patients needing inotropic support. Their published blood pressure values by gestational age are close to our results on the second day of life. Another study led by Pejovic also published data to estimate normal blood pressure values in neonates. As a comparison, our patient group's blood pressure values were consequently higher than Pejovic's findings. We assumed that the different patient populations and oscillometric devices might cause the difference.

The importance and actuality of the topic are shown by the fact that since our first publication, two more original research studies have been published, which have aimed to determine normal blood pressure values. A Canadian research group determined the normal neonatal arterial blood pressure in a preterm group (less than 29 weeks of gestation) within the first three days of life when significant haemodynamic changes occur. Another recent study with a similar aim, led by Zadelhoff, developed normal blood pressure curves for different gestational age groups and percentiles. Our study analysed extensive oscillometric data and calculated the normal average values and percentiles for different gestational age and birth

weight groups. An educational article about common hypertensive scenarios recommended using the percentile table for different birth weight groups generated in our first study.

The blood pressure stabilising effect of antenatal steroids is still controversial, although most of the studies show that antenatal steroid increases neonatal blood pressure. Our study shows no essential difference between the complete antenatal steroid group and the group of patients with incomplete or no steroid administration. In our study, we could not examine the effect of partial steroid administration separately due to patient and measurement numbers.

In our second article, we presented the blood pressure changes of BPD patients in the first three months of life. The length of the investigated period, the frequency of data collection, and the high number of blood pressure measurements make our second study different from other related studies. Several clinical studies have confirmed the increased risk of hypertension in BPD patients, while other studies have not shown a risk of high blood pressure in premature infants with BPD. In addition to the different diagnostic criteria used for BPD and hypertension, this difference may arise from the various and short periods during which blood pressure measurements were taken.

Based on the literature, the most likely onset time of hypertension varies widely, from 0.5 to 15 months of life. Jenkins and colleagues reported that hypertension began at a mean age of 11.3 ± 3.2 chronological weeks, corresponding to 39.6 ± 3.6 weeks PMA. In our patient group, the likelihood of a blood pressure increase was high in the 2nd, 9th, and 12th to 13th weeks of life. The latter corresponds to 38-39 weeks of corrected gestational age. In our investigation, an early increase in blood pressure might be related to other pathologies, such as AKI. However, a blood pressure increase beginning in the third month of life can be associated with BPD.

The aetiology of hypertension in BPD patients is still unknown, but several conditions likely contribute to its development. As pulmonary hypertension is frequently present in BPD patients, consequent hypertension of the infant to maintain adequate pulmonary perfusion and oxygenation could be one of the possible explanations. Another investigated explanation is the impaired elastogenesis in preterm infants, which leads to arterial rigidity and impaired vasodilatation. One of the most studied explanations is that the systemic effects of kidney failure negatively affect the developing lungs. The secondary analyses of the AWAKEN (Assessment of Worldwide Acute Kidney Injury Epidemiology in Neonates) and the PENUT (Preterm Erythropoietin Neuroprotection Trial) trials confirmed that preterm infants with AKI have a higher risk of developing BPD. AKI contributes to the development of chronic lung disease through different mechanisms. A discrepancy in fluid and electrolyte homeostasis,

extravascular fluid retention and increased capillary alveolar permeability can lead to impaired gas exchange and worsening lung disease. The systemic inflammatory insult caused by AKI can contribute to pulmonary injury and fibrosis. Animal studies also have shown that AKI affects angiogenesis and alveolarisation, leading to a BPD phenotype in experimental animals. Neonates with AKI also have a nearly two times higher risk of developing neonatal hypertension. In our study, the incidence of AKI was significantly greater among patients with three or more hypertensive days, which confirms the role of AKI in the development of BPD and hypertension.

A recent study by Farnbach et al. investigated the changing spectrum of neonatal hypertension. Their research showed that most hypertensive neonates with pulmonary and miscellaneous causes had low plasma renin activity and potentially high Di-2-ethylhexyl phthalate (DEHP) exposure. DHEP is used to increase softness and flexibility in plastics. During the treatment of a preterm infant, DEHP can leach out from intravenous bags, infusion and respiratory tubing. The metabolite of DEHP inhibits the 11βHSD2 enzyme, resulting in mineralocorticoid receptor activation and leading to fluid retention and sodium reabsorption, potentially playing a role in the development of hypertension in BPD patients.

Limitations

The investigation of normal neonatal blood pressure has some limitations, coming from its retrospective nature. The infants' wakefulness state and the measurement's place are not documented in our electronic records. However, data are collected in natural life circumstances, where the schedule and the quality of the measurements are ensured by following the NICU's corresponding protocols. In our second study, we could only draw limited conclusions on the effect of medications and therapy on blood pressure. There are several general therapies (e.g., postnatal steroids, diuretics, blood transfusions, fluid boluses, inotropic support) used during the treatment of preterm infants with BPD, which might cause changes in blood pressure. An extensive and prospective study would be useful to clarify the effect of these influencing factors further.

Suggestions for future research

Although several studies investigated normal blood pressure data on newborns, further research is still needed on how maternal and neonatal therapeutic factors and diagnoses affect blood pressure. The partial steroid administration and its effect on neonatal haemodynamic stability also needs further research. One of the most exciting questions in investigating neonatal hypertension is the role of environmental factors, such as phthalate. A prospective multicenter study with a large case number would be of great importance in newborn care to be able to

eliminate substances causing potentially serious side effects. A larger, prospective study is needed to investigate the relationship between AKI, BPD, hypertension, and pulmonary hypertension. Collecting blood pressure follow-up data from the BPD patient group and investigating daily blood pressure changes in AKI could also improve our understanding of blood pressure changes in preterm infants with different underlying disorders.

7. Conclusions

Based on the results of our two studies, the summary of our key findings is the following:

1. What is the normal blood pressure of a haemodynamically stable neonate? How do neonatal characteristics (birth weight, postnatal age, gestational age) affect neonatal blood pressure?

- We have calculated the normal average blood pressure by gestational age and birth weight for haemodynamically stable preterm and term infants for their first two weeks of life. We found a significant difference between the blood pressure of each gestational age group. Our study provides additional data on how blood pressure varies with birth weight. A positive linear correlation exists between birth weight and blood pressure on the first, third and fifth day of life. The blood pressure differences are significant in the different birth weight groups.
- We generated percentile tables for different gestational ages and birth weights to show 10th, 50th and 90th blood pressure percentiles on the first five days of life. The percentile tables bring new information, as the tables previously calculated by Dionne used the blood pressure measurements only after the second week of life.

2. Does antenatal steroid administration increase neonatal blood pressure after birth?

- No significant blood pressure differences were found between the group with a complete antenatal steroid course and those who received incomplete steroid prophylaxis or did not receive antenatal steroids. We could not prove the antenatal steroid neonatal blood pressure stabilising effect.

3. Does the patient group with moderate and severe BPD have a different blood pressure than the reference data?

- We found a statistically significant correlation between the blood pressure values of the BPD patient group and the reference data. The difference between the blood pressure curve of the group with BPD and the reference group was also statistically significant.

4. Can we detect hypertension by performing individual examinations of BPD patients' blood pressure data?

- We compared the individual BPD patients' average daily blood pressure to the 95th percentile and found that 11 patients (42%) had hypertensive blood pressure values for three or more days within the first 90 days of life. Our statistical analysis showed a 25% chance of acute kidney injury within this group.

8. Acknowledgements

I would like to thank my supervisor, Dr. Csaba Bereczki, for providing the opportunity to work on this research project. I am grateful for his comments and scientific guidance while preparing the publications and the thesis.

I am grateful to Professor Márta Katona for convincing me to become a neonatologist and for setting an example as a neonatologist.

I also thank the help of my medical and nursing colleagues working at the NICU, especially Dr. Anna Gajda and Dr. Judit Mari, for their support.

I am indebted to my brother, György Kiss, for his help with software programming and his excellent data management advice.

Last but not least, I am tremendously grateful to my father, Dr. Lajos Kiss, for his opinion and advice on my research work and its scientific publications and his tireless proofreading of my works.