J. Perinat. Med.
15 (1987) 307

Fetal kidney volume and urine production in cases of fetal growth retardation

Josef Deutinger, Wolfgang Bartl, Christian Pfersmann, Julius Neumark¹, and Gerhard Bernaschek

Second Department of Obstetrics and Gynecology and ¹Department of Anesthesia, University of Vienna, Austria

1 Introduction

Studies regarding the function of the fetal renal system could be performed only by employment of radiologic methods or radioactive substances prior to the introduction of ultrasound investigations into obstetrics. VAN GEUNS [8] instilled labeled creatinine into the amniotic fluid. From the decrease of the known creatinine level in the amniotic fluid, he determined the glomerular filtration rate. Sonographic measurement of the fetal urine production was first described by CAMPBELL et al. [4]. This method represented the first non-invasive method to observe the physiological filling and emptying of the fetal urinary bladder as well as to investigate the amount of fetal urine production.

The amount of amniotic fluid is determined by a dynamical balance of membrane production and resorption and by fetal excreting and swallowing. A reduction of the amount of amniotic fluid can be obtained not only in cases of malformations of the fetal urogenital system but also in cases of growth retardation.

The aim of our study was to investigate the hourly fetal urine production rate (HFUPR) and the growth of the fetal kidneys in cases of fetal growth retardation and to evaluate its meaning for the origin of oligohydramnios in those cases.

Curriculum vitae

JOSEF DEUTINGER was born in 1954 in Salzburg, Austria. He studied medicine at the University of Vienna and was graduated from there in 1980. From 1980 to 1982 he worked at several hospitals in Salzburg. Since 1982 he has been working at the 2nd Department of Obstetrics and Gynecology, University of Vienna. His main fields of interest are ultrasound and sterility.

2 Patients and methods

Our investigations were performed on 79 pregnant women between the 28th and 40th week of pregnancy (table I). The study group consisted of 27 patients with fetal growth retardation. Criteria for acceptance into this study group were: confirmed gestational age by ultrasound in early pregnancy, E-3 and/or HPL levels less than the 10th percentile in maternal serum and sonographically estimated retardation (figure 1). Standard values of HFUPR and growth of the fetal kidneys were also evaluated in a control group consisting of 52 patients with an uncomplicated pregnancy. For our control

Table I. Maternal data of patients, reference, control and study group.

	Reference group	Control group	Study group
Number (n)	768	52	27
Primiparae	273	18	11
Multiparae	495	34	16
Age at delivery (years)	25.4 ± 5.5	26.3 ± 4.1	23.4 ± 4.6
Weight before pregn. (kilogram)	49.8 ± 1.8	48.6 ± 2.4	50.2 ± 2.1
Weight at delivery (kilogram)	59.5 ± 6.2	58.7 ± 5.3	57.8 ± 4.9
Delivery (week)	40.0 ± 1.2	39.6 ± 1.4	36.0 ± 2.8

Figure 1. Birthweights of the study group in relation to gestational age and to the Hohenauer diagram indicating normal fetal birthweights.

group we selected the two patients with consecutive numbers and uncomplicated course of pregnancy after each patient with fetal growth retardation who was accepted into the study group. Pregnancy was defined to be uncomplicated, if blood pressure remained below 140/90 torr, no proteinuria, infectious diseases or diabetes mellitus occurred during pregnancy. Patients with multiple pregnancy, blood pressure > 140/90 torr on one investigation during pregnancy or dilatation of the fetal renal pelvis were excluded from the control group [6]. If patients did not agree to participate or if the pregnancy was complicated, the next consecutive patient was chosen.

As a reference group for the control group, the 768 pregnancies which were delivered during the study interval were studied. All patients with blood pressure > 140/90 torr on one investigation, proteinuria, diabetes mellitus, multiple pregnancy, infectious disease, delivery before 37th week of gestation and a newborn weight > 2500 g were excluded from the reference group. The data of all patients were stored in a data base (WAMIS), and evaluation of those data were performed employing BMDP. In regard to maternal age, weight before pregnancy and at delivery, week of pregnancy at delivery and newborn weight, no differences were noted between the control group and the

clinical parameters of 768 uncomplicated pregnancies of the reference group (table I). Fetal weights did not demonstrate a difference between the control and reference groups ($3367.5 \pm 389.8 : 3351.9 \pm 363.4$) (mean values $\pm$ SD). By this means it could be proved that our control group is representative for uncomplicated pregnancies.

The ultrasound investigations were performed with a sector probe with 4.0 MHz (Combison

320, Kretztechnik, Zipf, Austria). The criterion used to diagnose oligohydramnios ultrasonographically was the apparent near absence of amniotic fluid with only small pockets of fluid present around the fetal extremities. A longitudinal scan of the maternal abdomen was made, so that a sagittal section of the fetus was obtained. Scanning over the lower part of the fetal body revealed the bladder outline and the largest diameter was determined (figure 2).

Fig. 2 a

Fig. 2 b

Figure 2. Fetal bladder before and after miction, longitudinal section.

Then several transverse scans over the fetal bladder at right angles to the axis of the fetal spine were performed until the largest transverse and anterior-posterior section of the fetal bladder was obtained. Because of the ovoid shape of the fetal bladder calculations of the volume could be performed by means of the formula $\frac{4}{3} \times \Pi \times a/2 \times b/2 \times c/2$. Measure-

ment of the three diameters of the fetal bladder took about one minute. Calculation of its volume was done between four and eight consecutive times in 15 minutes intervals. Intervals occupied by emptying of the bladder were excluded. In order to standardize the investigation, all sonographical explorations were done between 10 and 12 o'clock a. m.

Fig. 3 a

Fig. 3 b

Figure 3. Sonographic imaging and measurement of fetal kidneys; a: longitudinal section. b: cross section.

The average increase of the fetal bladder volume from the minimum value to the maximum value converted to one hour yields the hourly fetal urine production rate (HFUPR). Then the maximum values of the three diameters of the fetal kidneys were measured (figure 3) and the volumes were calculated by means of the above mentioned formula. In order to compare the results of HFUPR and fetal kidney volume obtained at different gestational ages of normal and growth retarded fetuses, we calculated regression gradients. Regression lines and their 90% confidence limits were calculated for both groups. Data were also tested by employing analysis of variance in order to prove coincidence as well as parallelism of the regression lines.

3 Results

In 66 cases, all three diameters of both kidneys of the 79 fetuses could be measured, in 13 cases the volume of only one kidney could be calculated. The volumes of the kidneys did not show a significant difference between right and

left. In the control group the volume increased from 5.1 cm³ (mean value) in the 28th week of gestation to 17.6 cm³ in the 40th week nearly linearly. In instances of fetal growth retardation, the reduction of the increase of renal volume was statistically evident (from 4.2 cm³ in the 28th week to 16.1 cm³ in the 40th week), while the increase of volume with advancing age was comparable with the control group (figure 4). The test for hypothetical coincidence of the two regression lines yielded a significant difference with $p = 0.004$ ($F = 5.7$; 2 and $DF2 = 141$), but the hypothesis of parallelism was not rejected ($p = 0.85$; $F = 0.27$; $DF1 = 3$ and $DF2 = 140$). That indicates, that between 28th and 40th gestational week, the fetal kidneys were significantly smaller in the study group than in the control group, but the volume increased during advancing age at the same rate in both groups.

The HFUPR of the 52 normal pregnancies increased from 5.9 ml (mean value) in the 28th week of gestation to 26.8 ml in the 40th week. The increase was nearly linear. The increase of the HFUPR in the 27 patients with growth

Figure 4. volumes of fetal kidneys in uncomplicated pregnancies and in cases with placental insufficiency, both with their 90% prediction bands (a = control group, b = study group).

retardation was reduced significantly (from 4.7 ml to 15.4 ml) between the 28th and the 40th week of gestation (figure 5). The test for hypothetical coincidence of the two regression lines yielded a highly significant difference with $p =$

0.0000000007 ($F = 28.1$; $DF1 = 2$ and $DF2 = 77$). The hypothesis of parallelism of the two regression lines also had to be rejected with high significance ($p = 0.000004$; $F = 11.2$; $DF1 = 3$ and $DF2 = 76$) (figure 6). The latter

Figure 5. Hourly fetal urine production rate (HFUPR) in uncomplicated pregnancies and in cases with placental insufficiency, both with their prediction bands (a = control group, b = study group).

Figure 6. HFUPR — regression lines and 90% confidence limits of the control group (dotted) and the study group, proving the lack of parallelism.

demonstrates that with advancing gestational age HFUPR increases significantly less in patients with growth retardation.

In two third of the patients with fetal growth retardation, we found an obviously reduced volume of amniotic fluid. Unfortunately only in 6 cases were the results of placental histological investigation available. In all cases trophoplastic hypertrophy, intervillous fibrin deposits, hemorrhagic necrosis and extended fibrosis was demonstrated.

4 Discussion

The effect of placental insufficiency in the last trimester is an asymmetrical growth retardation. The fetal abdomen is affected earlier and more pronounced than the head [10]. This kind of retardation was designated "late flattening" by CAMPBELL [5], which indicates that a reduced increase of the fetal biparietal diameter occurs in the last weeks of pregnancy. Abdominal diameters as well as biparietal diameters are commonly used as a screening method for retardation. Many sonographically detectable signs exist in pregnancies with fetal growth retardation such as reduced fatty layers including the subcutaneous layer of the abdomen, in the perirenal area, lack of detectable Wharton's jelly in the area of the umbilical cord, alternations of the structure of the placenta, and reduction of the amount of amniotic fluid. In case of late retardation a reduced increase of the cell volume is evident histologically, while the number of cells is not affected [13]. Internal organs of abdomen and thorax are affected primarily; whereas, the fetal brain shows a significantly higher weight in comparison to the body. The favored nutrition of head and brain is caused by special features of fetal blood circulation. The reduced increase of the cell numbers was proven in pathological-anatomical studies on thymus, lung, liver, spleen, kidney and suprarenal gland [9].

Because retardation is evident especially in the area of the abdomen and the kidney can be measured best in this region sonographically, it

is suggested to investigate the kidney in cases of growth retardation. The volume of the fetal kidney increases constantly in the second half of pregnancy [1] and opens even the possibility to estimate the fetal weight [2]. In our study we found a significant difference between normal pregnancies and those with fetal growth retardation.

In cases of placental insufficiency, the reduced perfusion of the whole fetus is the reason for growth retardation. Also evident is a reduced perfusion rate of the fetal kidney. In cases of growth retardation the glomerular filtration rate is responsible for the reduction of the HFUPR, which is influenced by the perfusion rate of the fetal kidneys. The tubular function does not seem to be affected [11, 14]. Recently pulsed doppler equipments have been employed for the non-invasive determination of the fetal blood flow. This method allows only measurement of flow velocity with sufficient accuracy; whereas, the measurement of blood flow volume is affected too much by the diameter of the blood vessel. Even a small error in measurement may lead to altered results [7]. Determination of the HFUPR refers not only to already existing fetal malnutrition, but also may be possibly helpful to detect early fetal hypoxia. Our results exhibited significantly lower values in cases of fetal growth retardation in comparison to the control group. A significant difference between the study group and control group occurs after the 31st week of gestation when the confidence limits of both groups are separated (figure 6). Confidence limits were calculated for illustrating our results.

The origin of amniotic fluid has been investigated in several studies. A relation to the perfusion rate of the fetal kidney and to the fetal urine output is obvious [3, 15]. In cases with renal agenesis, no anhydramnis is evident occasionally. In such cases with distinct malformations, other mechanisms may become more important for the production of amniotic fluid at least, including perhaps an altered exchange rate of fluid at the chorio-amnion [12]. It can not yet be answered, if in addition to fetal urine

output and chorionic exchange, other structures may be responsible for the origin of amniotic fluid [16]. The fact, that in two-thirds of our patients a diminution of amniotic fluid was evident, emphasizes the role of fetal urine output for the origin of amniotic fluid.

Sonographically determined reduced biometrical dates of the fetus in case of growth retardation refer to a longer existing malnutrition. They do not include diagnosis of the actual

fetal condition. Sonographic investigation does not allow the determination of subacute or acute potential of hypoxia. Cases with acute fetal distress may be easily diagnosed by employing cardiotocography. Due to the fact that HFUPR is a dynamical parameter and has a positive correlation to the perfusion of fetal kidneys, determination of this parameter may help to detect subacute distress and emerge as a warning of a fetal distress condition in case of biometrical proven fetal malnutrition.

Summary

The amount of amniotic fluid has a close correlation to the function of the fetal renal system. In many cases of fetal growth retardation oligohydramnios is obvious. The aim of this study is the investigation of the hourly fetal urine production rate (HFUPR) and the growth of fetal kidneys during pregnancy in cases of fetal growth retardation and to evaluate the renal participation in the origin of oligohydramnios in cases of growth retardation.

In 52 healthy pregnancies and 27 cases with known fetal growth retardation, the volume of the fetal kidneys was measured sonographically and the hourly rate of fetal urine production was determined. Two third of the

patients with fetal growth retardation had obvious oligohydramnios. In cases of fetal growth retardation the volume of the fetal kidneys was significantly smaller when compared to the control group, and the volume of fetal urine production was significantly lower. The reduced perfusion of the fetal kidneys in those cases with fetal growth retardation may be the reason for the reduction of the HFUPR. Due to the fact that HFUPR is a dynamical parameter and in close relationship to the perfusion of the fetal kidneys, the identification and measurement of this parameter may help to detect subacute and imminent fetal distress in cases of sonographically proven fetal growth retardation.

Keywords: Amniotic fluid, fetal kidney volume, fetal urine production, growth retardation, ultrasound.

Zusammenfassung

Fetale Nierenvolumina und Harnproduktion in Fällen von fetaler Wachstumsretardation

Die Fruchtwassermenge steht in engem Zusammenhang mit der Funktion des fetalen uropoetischen Systems. Fälle mit fetaler Wachstumsretardierung gehen häufig mit einer Verminderung der Fruchtwassermenge einher, in zwei Drittel unserer Patientinnen mit Plazentainsuffizienz konnte eine Oligohydramnie nachgewiesen werden. Ziel unserer Untersuchung war es, den Faktor der fetalen Harnproduktion und den des Wachstums der fetalen Nieren in Fällen von Plazentainsuffizienz näher einzugrenzen und seine Rolle in der Genese des Oligohydramnios bei Wachstumsretardation zu ermitteln.

Bei 52 klinisch unauffälligen Schwangerschaften und 27 Schwangerschaften mit Plazentainsuffizienz wurde sowohl das Volumen der fetalen Nieren sonographisch vermessen als auch die Änderung des fetalen Harnblasenvolumens registriert und dadurch die stündlich produzierte fetale Harnmenge ermittelt. Die Volumensbestimmung der fetalen Harnblase erfolgte bei Ausschuß

einer zwischenzeitlichen Harnblasenentleerung bis zu 8 mal in Abständen von 15 Minuten. Die durchschnittliche Zunahme des fetalen Harnblasenvolumens vom Minimalwert zum Maximalwert bezogen auf die volle Stunde ergab die stündlich produzierte Harnmenge. Das Volumen der fetalen Nieren lag in Fällen von Plazentainsuffizienz unter dem von unauffälligen Schwangerschaften. Signifikant geringer war ebenfalls, verglichen mit dem Normalkollektiv, die stündlich produzierte fetale Harnmenge bezogen auf die Schwangerschaftswoche. Der Grund für die bei Wachstumsretardierung auftretende verminderte fetale Harnproduktion ist in der Minderperfusion der Nieren zu sehen. Die Bestimmung der fetalen Harnproduktion als dynamischen Parameter, welcher in Korrelation zur Perfusion der fetalen Nieren steht, könnte geeignet sein, bei biometrisch nachgewiesener Plazentainsuffizienz auch subakute bzw. sich abzeichnende akute Gefahren der fetalen Versorgung zu erfassen.

Schlüsselwörter: Fetale Harnproduktion, fetales Nierenvolumen, Fruchtwasser, Plazentainsuffizienz, Ultraschall.

Résumé

Volume du rein fœtal et production d'urine au cours du retard de croissance intra-utérin

Il existe une relation étroite entre la quantité de liquide amniotique et la fonction du système uropoïétique du fœtus. En cas de retard somatique intra-utérin on constate souvent une diminution du liquide amniotique. Chez deux tiers des patientes présentant une insuffisance placentaire, on a pu constater un oligoamnios. Nos recherches ont pour but de définir le facteur de production d'urine et de la croissance des reins fœtaux dans les cas d'insuffisance placentaire, et de déterminer son rôle dans la genèse de l'oligoamnios dans les cas de retard de croissance.

Au cours de 52 grossesses normales et de 27 avec insuffisance placentaire nous avons, à l'aide de l'échographie, mesuré le volume rénal fœtal ainsi que les modifications de volume de sa vessie et nous en avons déduit la quantité d'urine produite par heure par le fœtus. Pour

obtenir ce résultat nous avons répété l'examen jusqu'à huit fois en 15 minutes tout en excluant une évacuation vésicale intermédiaire. La quantité d'urine produite en une heure résulte de la moyenne entre le minimum et le maximum de croissance du volume de la vessie, rapporté sur la durée d'une heure.

Le volume des reins fœtaux est plus réduit dans les cas d'insuffisance placentaire qu'au cours des grossesses normales: de même, on constate une diminution de la quantité d'urine produite par heure en rapport avec le terme. La réduction de la production d'urine fœtale dans les cas de retard somatique a pour cause une diminution de perfusion rénale. En définissant la production d'urine du fœtus comme paramètre dynamique, mis en corrélation avec la perfusion rénale, on pourrait parer aux dangers subaigus ou potentiels qui menacent l'alimentation du fœtus dans les cas d'insuffisance placentaire déterminés de façon biométrique.

Mots-clés: Echographie, insuffisance placentaire, liquide amniotique, production d'urine, volume des reins fœtaux.

References

- [1] BERNASCHEK G, A KRATOCHWIL: Echographische Studie über das Wachstum der fetalen Niere in der zweiten Schwangerschaftshälfte. *Geburtshilfe Frauenheilkd* 40 (1980) 1059
- [2] BERNASCHEK G, A KRATOCHWIL: Die Möglichkeit der intrauterinen Gewichtsschätzung aus dem fetalen Nierenvolumen. *Ultraschall* 1 (1980) 223
- [3] BIGGS JS, RO DUNCAN: Production rates and sources of amniotic fluid at term. *J Obstet Gynaecol Br Commonw* 77 (1970) 326
- [4] CAMPBELL S, JW WLADIMIROFF, CJ DEWHURST: The antenatal measurement of fetal urine production. *Br J Obstet Gynaecol* 8 (1973) 680
- [5] CAMPBELL S: The assessment of fetal development by diagnostic ultrasound. In: MILUNSKI A (ed): *The pregnancy at risk*. *Clin Perinatol* 1/2 (1974) 507
- [6] DEUTINGER J, R SPERNOL, G BERNASCHEK: Können fetale Nierenbeckenerweiterungen physiologisch sein? *Geburtshilfe Frauenheilkd* 44 (1984) 441
- [7] FENDEL H, M FENDEL, R WARNKING: Fehlermöglichkeiten der gepulsten Dopplermethode zur Blutflußmessung am Feten. *Z Geburtshilfe Perinatol* 187 (1983) 83
- [8] GEUNS HJ VAN: *Cretnine en Vruchtwater*. Thesis, p 68. Vrije Universiteit Amsterdam 1973.
- [9] GRUENWALD P: Chronic fetal distress and placental insufficiency. *Biol Neonate* 5 (1963) 215
- [10] HANSMANN M, H BÄKER, S FABULA, H MÜLLER-SCHOLTES, HJ NELLEN, U VOIGT: Biometrische Daten des Feten. Ergebnisse einer modifizierten Methodik der Ultraschalldiagnostik. In: SALING E, JW DUDENHAUSEN (eds): *Perinatale Medizin*, vol III, p 136. Thieme Verlag, Stuttgart 1972
- [11] KURJAK A, P KIRKINEN, V LATIN, D IVANKOVIC: Ultrasonic assessment of fetal kidney function in normal and complicated pregnancies. *Am J Obstet Gynecol* 141 (1981) 266
- [12] OTTERO LC VAN, JW WLADIMIROFF, HCS WALLENBURG: Relationship between fetal urine production and amniotic fluid volume in normal pregnancy and pregnancy complicated by diabetes. *Br J Obstet Gynaecol* 84 (1977) 205
- [13] WINICK M: Cellular growth in intrauterine malnutrition. *Pediatr Clin North Am* 17 (1970) 69
- [14] WLADIMIROFF JW, S CAMPBELL: Fetal urine production rates in normal and complicated pregnancy. *Lancet* I (1974) 151
- [15] WLADIMIROFF JW, LC VAN OTTERLO, HCS WALLENBURG, AC DROGENDIJK: A combined ultrasonic and biochemical study of fetal renal function in the term fetus. *Eur J Gynecol Reprod Biol* 6 (1976) 103
- [16] WLADIMIROFF JW: Studies of fetal physiology by sonography. *Handbook of Clinical Ultrasound*, p 203. Wiley & Sons, New York 1978

Received February 21, 1986. Revised June 6, 1986. Accepted June 18, 1986.

Dr. Josef Deutinger
2nd Department of Obstetrics and Gynecology
Spitalgasse 23
A-1090 Wien, Austria