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ORIGINAL ARTICLE

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Arterial hypertension after surgical closure of omphalocele and gastroschisis

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Abstract Arterial hypertension has been reported as a complication of surgical closure of an abdominal wall defect. No report studying the incidence, the characteristics and the clinical significance of hypertension after surgical correction of an omphalocele or gastroschisis has been published so far. The medical records of all newborns with surgically corrected gastroschisis or omphalocele identified in two centers were retrospectively evaluated. Arterial hypertension was defined as a mean daily systolic and/or diastolic blood pressure value higher than the 95 percentile for age and/or weight, according to literature data. The timing of surgery, weight gain, plasma creatinine and the use of diuretics or vasoactive drugs were compared between the groups with and without hypertension. Seventy-two patients were identified and included in the study, 29 with omphalocele and 43 with gastroschisis. Those with omphalocele were born at a mean age of 37.3±2.6 weeks with a mean birth weight of 2,971±715 g, and those with gastroschisis were born at 36.1±2.0 weeks with a mean birth weight of 2,527±498 g. Blood pressure values of 66 patients were available for analysis. Of the omphalocele patients, 46.2% (12/26) developed systolic hypertension, compared to 17.5% (7/40) of the patients with gastroschisis (P=0.024). Hypertension was always transient, lasting an average of 4 and 1 day in the omphalocele and gastroschisis groups, respectively. Two patients with omphalocele were given anti-hypertensive therapy. There was no difference between patients with or without hypertension regarding weight gain, use of vasoactive drugs or diuretics, mean weekly creatinine values or the timing of surgery. Newborns with an abdominal wall defect frequently present with transient arterial hypertension. Hypertension occurs significantly more often, is more severe and lasts longer in patients with omphalocele than in patients with gastroschisis. In both groups, hypertension is transient and rarely requires therapy. The cause of hypertension remains unclear.

Keywords Arterial hypertension · Newborn · Gastroschisis · Omphalocele

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Introduction

In 1980, Adelman et al. reported four patients developing arterial hypertension (HTN) after surgical closure of gastroschisis (G) or omphalocele (O) [1]. HTN was thought to be secondary to an increased intra-abdominal pressure following replacement of the eviscerated gut into the abdominal cavity and closure of the abdominal wall defect (AWD). Compression of the renal vascular pedicle, increased release of renin, renal ischemia, increased cathecolamine production or transient hydronephrosis from ureteral compression have all been suggested as a cause of HTN after closure of the AWD. Since the first report, surgical closure of an AWD has been reported as a

Table 1 Mean birth weight (in g) and gestational age (in weeks) by abdominal wall defect

		<32 weeks	32–36 weeks	>36 weeks	Total
Omphalocele	*n*	2 (6.9%)	9 (31.0%)	18 (62.1%)	29 (100%)
	Mean BW ± SD	2,188±1375	2,515±546	3,287±551*	2,972±716
Gastroschisis	*n*	3 (7.0%)	24 (55.8%)	16 (37.2%)	43 (100%)
	Mean BW ± SD	1,927±316	2,432±432	2,783±488	2,527±498
Total	*n*	5 (6.9%)	33 (45.8%)	34 (47.2%)	72 (100%)
	Mean BW ± SD	2,031±737	2,454±459	3,050±574	2,706±630

* P=0.0134 between O and G patients for mean birth weight in term patients

classical cause of HTN in the newborn in major textbooks of pediatric nephrology [2], although studies looking specifically at this problem are still lacking. Numerous studies looking at the short- and long-term outcome of infants with AWD exist, but none of them looked specifically at the development of HTN [3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13]. The only other study mentioning HTN was published by DeLuca et al. [14], in which the authors described a newborn with giant O and intermittent HTN following closure of the defect. In our study, we analyzed the incidence and severity of HTN in patients with O or G after surgical closure of their AWD.

Materials and methods

Information about patients with O or G was retrieved using computer-based searches of the medical archives of the children's hospitals of the University of Virginia in Charlottesville, VA, USA, and Lausanne, Switzerland, and using personal records from the pediatric surgeons. We searched the database from 1 January 1980 to 30 June 2002. Charts were reviewed, and every blood pressure value charted during the neonatal stay was recorded, with no exception. BP values were evaluated without determination of the time of day or state of arousal of the infant (sleep or awake). Similarly, no attempt was made to distinguish between invasive and non-invasive BP records. Infants with no BP records or BP recorded for 24 h or less were not included. Infants without gestational age and weight were also not included in the study.

Newborns were considered hypertensive if they presented at least 1 day with a mean daily systolic and/or diastolic blood pressure value greater than or equal to the 95th percentile, as defined below (in mmHg systolic/diastolic), according to the gestational and post-natal ages:

	Days 1–7	Days 8–30	>Day 30
>36 weeks	93/70	95/70	105/70
32–36 weeks	90/60	95/70	105/70
<32 weeks	82/50	90/65	105/70

These values were compiled from different sources regarding the normal values of blood pressure in premature and term newborn babies [15, 16, 17, 18, 19, 20]. Also, because blood pressure not only varies according to gestational age but also according to birth weight, we defined the following limits:

	Days 1–7	Days 8–30	>Day 30
BW >3,000 g	93/70	95/70	105/70
BW 2,000–3,000 g	90/60	95/70	105/70
BW <2,000 g	82/50	90/65	105/70

Secondary closure was defined as the need of a Silo or a mesh for reduction of the omphalocele or gastroschisis. We defined use of diuretics and vasoactive drugs (dopamine, dobutamine or norepinephrine) if the child received such drugs for greater than 24 h. Any associated congenital cardiac, urogenital or other anomalies were recorded.

Results are expressed as the mean ± standard deviation. Anova and Fisher's exact test were used when indicated. One-way Fisher's exact test was used when the outcome could be predicted from available literature data. Significance was considered when P was less than 0.05. Ethics committees at both institutions approved the study.

Table 2 Associated congenital anomalies

Defects	Cardiac	Uro-genital	Other anomalies
Omphalocele	61.3%*	22.6%	38.7%
Gastroschisis	11.6%	14.0%	20.9%
Total	32.4%	17.6%	28.4%

* P<0.0001 between O and G patients for congenital cardiac anoma- lies

Results

Patient characteristics

A total of 74 patients were identified in the two centers. Two patients with giant O were operated upon at the age of 3 years: because of their age at surgical repair and lack of neonatal data, they were not included in the study. Neither child developed HTN or digestive complications after surgical correction.

The distribution of the remaining 72 patients with AWD, listed by gestational age, is shown in Table 1. O patients were born at a mean gestational age of 37.3±2.6 weeks and the G patients at 36.1±2.0 weeks (Fisher's exact test = 0.087). Of all patients, 53% were born earlier than 37 weeks. Gender distribution was equal in both groups, with male patients comprising 17 out of 29 patients with O (59%) and 22 out of 43 (51%) in the G group. There was a significant difference in birth weight between the O and the G group in term babies (P=0.013), but not in infants born prematurely, i.e., <37 weeks (Table 1).

Patients with O presented significantly more cardiac defects than patients with G (61.3 vs. 11.6%, one-sided Fisher's exact test <0.0001) (Table 2). Cardiac anomalies included: atrial septal defects/foramen ovale (ten cases), ventricular septal defects (seven cases), patent ductus arteriosus (six cases), Cantrell's pentalogy (four cases), pulmonary valve stenosis (two cases), Fallot tetralogy (one case) and dextrocardia (one case). Urogenital

Table 3 Incidence of systolic hypertension

	% of patients with systolic HTN lasting at least 1 day	% patients with systolic HTN lasting ≥2 days	Number of days with systolic HTN	Duration of systolic HTN (in days)
Omphalocele	12/26 (46.2%)	11/26 (42.3%)	108/782 (13.8%)	4.2
Gastroschisis	7/40 (17.5%)*	4/40 (10.0%)**	40/1,174 (3.4%)***	1.0****
Total	19/66 (28.8%)	15/66 (22.7%)	148/1,956 (7.6%)	

*P=0.024 when compared with the O group; **P=0.016 when compared with the O group; ***P<0.0001 when compared with the O group; ****P=0.009 when compared with the O group

Table 4 Incidence of diastolic hypertension

	% of patients with diastolic HTN lasting at least 1 day	% of patients with diastolic HTN lasting ≥2 days	Number of days with diastolic HTN	Duration of diastolic HTN (in days)
Omphalocele	4/26 (15.4%)	2/26 (7.7%)	27/782(2.8%)	0.8
Gastroschisis	3/40 (7.5%)#	2/40 (5.0%)##	6/1174 (0.5%)###	0.2####
Total	7/66 (10.6%)	4/66 (6.1%)	33/1956 (1.7%)	

P=0.564 when compared with the O group; ## P=0.773 when compared with the O group; ### P<0.001 when compared with the O group; #### P=0.30 when compared with the O group

anomalies included: uretero-pelvic junction obstruction (three cases), vesico-ureteral reflux (two cases), kidney dysplasia (two cases), bilateral crytorchidism (two cases), posterior uretral valves (one case) and hypospadias (one case). Other malformations included: intestinal malrotation (seven cases), Beckwith-Wiedemann syndrome/ macrosomy/hemihypertrophy (three cases), microcolon (two cases), congenital atresia of the small gut (two cases), congenital pseudarthrosis of the right clavicle, Miller-Diecker syndrome, clinodactyly, mesenteric defect of the terminal ileum and multiple café-au-lait spots (one case each). Urogenital and other malformations were evenly distributed in both groups. Five patients (16.1%) in the O group died in the postoperative period (one Beckwith-Wiedemann syndrome, one Miller-Diecker syndrome, one trisomy 18 and two Cantrell's pentalogy). Only one (2.3%) died in the G group, secondary to digestive complications (small gut volvulus and extensive necrosis; one-sided Fisher's exact test =0.043).

Surgical procedure

Of the patients, 79.3% with O underwent primary surgical closure of the defect at a mean age of 3.4±7.2 days post-natal vs. 72.1% in the G group, at a mean age of 1.0±0.0 days post-natal (Fisher's exact test = 0.011). The other patients underwent secondary closure of their defect, with procedures such as external compression and the use of a silo or a mesh.

Blood pressure

Six children (three O and three G patients) could not be evaluated for HTN because of insufficient data (no BP recordings or BP recordings lasting less than 24 h). For the other 66 children (26 O and 40 G patients), 11,141 BP values were recorded (mean 168±103/patient, range: 1–38/patient/day) during a follow-up of 29.6±24.2 days (range: 1–141 days).

Overall, G patients had an averaged systolic BP of 70.6±8.4 mmHg and 91.8±11.4 mmHg before and after surgery, respectively. O patients had an averaged systolic BP of 72.8±10.7 mmHg and 86.7±9.7 mmHg before and after surgery, respectively (no significant difference between the two groups). There was also no difference in the BP values among groups with renal, cardiac anomalies or no anomalies.

The characteristics of HTN in patients with AWD are depicted in Table 3 and Table 4. Except for one child (with G) who developed HTN on day 3 of life, before closure of his AWD, every child developed HTN after closure of the AWD. G and O patients who developed HTN had a mean systolic BP of 80.2±13.9 mmHg before surgery and 103.2±7.2 mmHg after surgery (one sided Fisher's test 0.001). The occurrence of HTN in patients with primary or secondary closure of the AWD did not differ.

Of the O patients, 46.2% (12/26) had a least 1 day with HTN, and 42.3% had at least 2 days or more with HTN. Of the G patients, 17.5% (7/40) had hypertension lasting at least 1 day (P=0.024, when compared with the O group). Four G patients (10.0%) developed HTN lasting more than 2 days. Seven patients (five O and two G) had systolic HTN lasting more than a week, including two patients in the O group treated for HTN. None of the G patients received anti-hypertensive therapy. Systolic HTN lasted an average number of 4.2 and 1.0 days in the O and G patients, respectively (P=0.009) (Table 3). Systolic HTN started at a mean age of 18.6±16.4 days in the O group (13.1±15.7 days after surgery) and at a mean age of 13.1±8.2 days in the G group (9.6±8.5 days after surgery; no significant differences between the O and G groups). Table 4 depicts the incidence of diastolic hypertension. Overall, four O patients (15.38%) and three G patients (7.50%) (P=0.564) developed diastolic HTN. Two patients in each group (7.69% of O patients and 5.00% of G

patients) had diastolic HTN lasting more than 2 days. Diastolic HTN lasted a mean duration of 0.8 days and 0.2 days in the O and G patients with HTN, respectively (P=0.30). Diastolic HTN occurred at the same time as systolic HTN. When HTN was defined according to birth weight and not gestational age, we found exactly the same results except for one newborn (O patient, birth weight 1,940 g; gestational age 36 weeks). That particular patient was hypertensive when the limits of the blood pressure were defined according to the birth weight, but not to the gestational age.

There were no significant differences in weight gain, plasma creatinine, the use of vasoactive drugs or the timing of surgery between the hypertensive and non-hypertensive groups in either the G or the O groups (data not shown). Hypertensive O patients were given diuretics significantly more often than non-hypertensive O patients (P=0.036).

Discussion

The occurrence of HTN has been described in newborns after closure of an AWD [1, 14], but its exact incidence and characterization have not been published. To the best of our knowledge, this is the first study demonstrating that patients with surgically corrected O present significantly more HTN than patients with G. HTN in the O group lasted an average of four times longer than in the G group. Two patients were on anti-hypertensive medication in the O group; this was never the case in the G group. The origin of hypertension after closure of an AWD in the newborn period remains unclear. Adelman postulated in his report [1] that patients might develop hypertension because of possible compression of the renal vascular pedicle and secondary release of renin, renal ischemia, increased cathecolamine production or transient hydronephrosis. Increased intra-abdominal pressure has been associated with adverse effects on cardiac, gastro-intestinal, hepatobiliary, pulmonary, central nervous system and renal functions [21]. Lacey et al. [22] clearly demonstrated that an increased abdominal pressure of 20 mmHg or higher was associated with a markedly decreased cardiac output and renal perfusion. This, in turn, might produce renal ischemia and secondary release of renin. Increased plasma renin activity and aldosterone have indeed been described in animals with increased intra-abdominal pressure [23]. Every child except one developed HTN after surgery was done, which made us postulate that the surgical closure of the AWD (and possibly a secondary increase in the intra-abdominal pressure) may have played a role in the occurrence of HTN in these patients, although one might argue that the rather long 2-week delay between the surgical closure of the AWD and the occurrence of HTN should allow the increased intra-abdominal pressure, if present, to decrease. G patients developed hypertension slightly earlier (although not significantly) than O patients. We were unable to correlate HTN with increased plasma renin activity. Plasma renin activity was measured in one single patient with HTN, and it was found to be normal. This issue clearly needs more prospective investigation, with serial plasma renin activity measures and simultaneous measure of the intra-abdominal pressure in patients with AWD, with and without HTN. As the heart rate was not recorded, we cannot rule out that an increased sympathetic activity was responsible for the transient hypertension in these children.

HTN could also be secondary to acute renal failure with volume overload. Intra-abdominal pressure is followed by an increase in the right atrial pressure, secondary to increased transmural pressure from the abdomen. Pressure in the inferior vena cava also increases with increased intra-abdominal pressure. This results in a decreased compliance of the right ventricle and a decreased cardiac output [24], which, if severe enough, induces acute renal failure [10, 12, 24]. Harmon reported that intra-abdominal pressure >20 mmHg in adult dogs caused significant decreases in the glomerular filtration rate and renal blood flow [25]. However, acute renal failure in the clinical setting of neonatal abdominal surgery is usually due to poor renal perfusion and acute tubular necrosis from hypovolemia and depressed cardiac output [24]. The good response to volume challenge and vasoactive drugs in some cases confirms that hypothesis [26, 27]. None of our patients developed renal failure, as assessed by weekly serum creatinine. Acute renal failure should therefore not play a major role in the genesis of hypertension in our patients.

Urinary tract obstruction, when severe enough, is known to increase renin production and release [28]. Three of our patients developed transient hydronephrosis secondary to mild uretero-pelvic junction obstruction. None of them developed HTN, and the obstruction resolved spontaneously.

Umbilical artery catheter use is associated with an increased incidence of renal artery thrombo-embolisms and secondary HTN. Only one of the O patients had an umbilical artery catheter. Fifteen G patients had umbilical artery catheters, which were removed in the first 2 to 3 days of life after central venous line placement. Two patients in the G group with umbilical artery catheter developed HTN lasting 1 day. Therefore, we feel that umbilical artery catheters did not play a role in the genesis of HTN in these patients.

Although term G patients were born with a significantly lighter birth weight, the incidence of HTN did not change when the blood pressure limits were set according to the birth weight and not the gestational age. The significantly higher incidence of HTN in the O patients compared to the G patients is not explained at this point. We can only speculate that O patients might have an increased intra-abdominal pressure secondary to the replacement of the liver in the abdominal cavity and that the increased intra-abdominal pressure leads secondarily to a transient HTN [23]. Simultaneous measurements of the blood pressure and the abdominal pressure are needed in further prospective studies to clarify this issue.

Conclusions

In this retrospective study, approximately 40% of O patients developed transient arterial HTN after closure of their defect. This contrasts sharply with only 10% of the G patients having HTN. It is our experience that HTN is usually mild (mean BP in the HTN group: 103.2±7.2 mmHg vs. 80.1±13.9 mmHg in the non-HTN group), non-symptomatic as well as transient, and rarely needs therapy. Therefore, unless the patient becomes symptomatic from HTN or the HTN is severe, we would recommend observation for several days before starting anti-hypertensive therapy. This is especially important in the immediate postoperative period when prolonged episodes of hypotension can end up in acute renal failure/anuria [24] with disastrous consequences if hemodialysis or peritoneal dialysis is impossible to perform. The cause of the HTN in patients with AWD remains unknown.

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