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"Silent" Patent Ductus Arteriosus and Bronchopulmonary Dysplasia in Low-Birthweight Twins

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Abstract. During a screening protocol of early echocardiographic diagnosis (ATL MK 600) and treatment of "silent" PDA in RDS preterms with BW $\leq$1.750 kg, clinical data on premature twins were collected, including diagnosis of both PDA and BPD, to investigate whether twin birth influences PDA incidence and BPD development. Out of the 290 RDS preterms evaluated, 96 (33%) showed evidence of PDA, and a total of 79 (27%) developed BPD, 47 (16%) with associated PDA and 32 (11%) without PDA. Out of 238 singletons, 74 (31%) presented "silent" PDA and a total of 75 (31%) developed BPD, 44 (18%) with associated PDA, and 31 (13%) without PDA. In 52 other twins (18% of the total number of babies studied), 22 (42% of this subgroup) presented evidence of "silent" PDA, and 4 (8% of the subgroup), developed BPD, 3 with associated PDA (6% of the subgroup), and 1 without PDA (2% of the subgroup). From these data, it is inferred that that low-birthweight twins are at high risk for PDA hemodynamic complications during RDS, and may benefit from early induced ductal closure. Instead, in RDS twins, BPD was statistically less frequent (at the 99% C.L.) probably because twinning enhances fetal lung maturity, influencing enzymatic and nonenzymatic protective systems of lung defence.

Key words: Bronchopulmonary dysplasia, "Silent" PDA, Premature twins, Respiratory distress syndrome

INTRODUCTION

Preterm delivery and respiratory distress syndrome (RDS), common events in twin births, are considered important determinants of chronic lung disease associated with prematurity, or bronchopulmonary dysplasia (BPD) [1, 7, 13]. In a preliminary report, we found a high incidence of "silent" patent ductus arteriosus (PDA) in premature

twins affected by RDS, and we hypothesized that twin birth could play a role in the occurrence of PDA, and in the related chronic pulmonary sequelae [16]. The contribution of PDA to the pathogenesis of BPD is, in fact, supported by data demonstrating the potential of pulmonary edema in complicating the recovery phase of RDS and by the well documented improvement in lung function after symptomatic medical or surgical PDA closure [3, 10]. However, the most important support for the relationship between pulmonary edema and BPD comes from reports linking pulmonary edema and PDA directly to BPD [1, 6, 8, 13].

The purpose of the present study was, therefore, to investigate more widely, the question of whether twin births influence the occurrence of PDA and the development of bronchopulmonary dysplasia.

MATERIAL AND METHODS

During the course of a screening protocol on early diagnosis and treatment of "silent" PDA in RDS preterms with BW ≤ 1.75 kg, laboratory and clinical data of premature twins, including diagnosis of both PDA and BPD, were collected [16, 17].

The sample studied consisted of 52 preterm twins out of 290 infants ≤ 1.75 kg with RDS admitted to the NICU of the Pediatrics Department of Padua Unviersity, between January, 1987 and December, 1991. Serial 2-D echocardiographic and pulsed Doppler evaluations (ATL MK 600) were performed on the third day of life in RDS preterms, to detect the patency of the ductus and the direction of shunting ("silent" PDA) early on, before cardiac and ventilatory failure become progressive [8].

The decision to close the PDA, as we previously reported, was made by the attending neonatologist. If the indomethacin treatment was judged echocardiographically ineffective, after a second course, or in the presence of blood abnormalities that contraindicated the further use of the drug, ductus ligation was carried out in the NICU [17].

Statistical analysis was performed on DEC VAXSTATION 3100 M 76, using the BPD-Padova Programme, which contains all the standard statistical routines, produces an electronic clinical card for each premature infant, and draws histograms of the items of interest [9].

RESULTS

Out of 290 RDS preterm infants with BW ≤ 1.75 kg who were comprehensively screened on the third day of life, 96 had echocardiographic and pulsed Doppler evidence of "silent" PDA, 79 developed BPD, 47 with associated PDA, and 32 without PDA (33%, 27%, 16% and 11% of the sample respectively) (Table).

Out of the 238 singletons, "silent" PDA was detected in 74 (31%), and 75 (31%) comprehensively developed BPD. 44 of these (18%) had associated PDA, while 31 (13%) showed no echocardiographic evidence of PDA. Of the 52 twins, (18% of the total preterms studied), 22 (42% of the subgroup) showed echocardiographic and Doppler evidence of PDA. The development of BPD was found in 4 out of 22 twins (8% of the total twins), with 3 (6% of the total number of twins) found to have PDA and 1 (2% of the total number of twins) found not to have PDA.

Table - Overall occurrence of PDA and the development of BPD in screened premature twins and singletons with RDS

Prematures		%	Twins	%		Singletons	%
RDS	290		52			238	
PDA	96	(33)	22	(42)		74	(31)
BPD	79	(27)	4	(8)	..... *	75	(31)
-with PDA	47	(16)	3	(6)	..... *	44	(18)
-without PDA	32	(11)	1	(2)	..... *	31	(13)

* Occurrence significantly increased (more than the 99% CL)

Moreover, statistical analysis of the data showed that the gestational age and BW in the premature PDA singletons and twins were comparable (Mean ± SEM 29.2 ± 0.2 vs 29.8 ± 0.4 weeks, and 1.17 ± 0.03 vs 1.15 ± 0.05 kg respectively).

DISCUSSION

The twin and singleton low birthweight infants in this study were enrolled in an early treatment of "silent" PDA trial, and were screened on the third day of life by echocardiographic and Doppler evaluation. The occurrence of PDA in preterm twins and singletons confirmed the findings of our preliminary report and, in accordance with previous data, the incidence of "silent" PDA resulted higher in twins than in the singletons (42% vs 31%). This increased occurrence of "silent" PDA in twins was not of statistical significance, however. These variations in PDA incidence are obviously in part dependent on the patient sample homogenization during a five year period, and also reflect the diagnostic and therapeutic approach used in our NICU.

However, this increased occurrence of PDA was not associated with a worsening pulmonary prognosis for the twins. This observation argues against PDA as a major causative factor of BPD in premature low-birthweight twins [4, 11]. Moreover, the occurrence of BPD in premature twins without "silent" PDA is lower at the 99% C.L. compared to that of premature singletons (2% of premature twins versus 13% of premature singletons).

One possible explanation for this interesting data would be the twinning, which frequently represents per se a condition of malnutrition for the fetus [2, 5, 12, 14]. Fetal malnutrition enhances fetal lung maturity, and probably also that of the enzymatic and nonenzymatic antioxidant defence systems that influence the pathogenesis of the chronic lung disease bronchopulmonary dysplasia [5, 15].

In conclusion, low birthweight twins are at risk for PDA hemodynamic complications during RDS, and may benefit from early ductus closure. Nevertheless, the pulmonary sequelae are less frequent in premature twins, probably because the twinning enhances fetal lung maturity and influences enzymatic and nonenzymatic protective systems of lung defence.

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