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Does the Respiratory Distress Syndrome in Twins and Singletons Run Different Risks of Persistent Ductus Arteriosus?

V. Zanardo[1], P. Foti[1], D. Trevisanuto[1], P. Zambon[1], G. Stellin[2], O. Milanesi[1]

[1] *Department of Pediatrics, and* [2] *Institute of Cardiovascular Surgery, University of Padua, Italy*

Abstract. The incidence and evolution of patent ductus arteriosus (PDA) was evaluated in twins and preterm singletons with birth weight $\leq$ 1750 g admitted to our Department in 1987 for respiratory distress syndrome (RDS). Screening by echocardiography and Doppler-flow studies (AT MK 600) was performed on the third day of life. Out of 91 neonates who needed intubation and ventilation during this 12-month period (23.8% of admissions), 40 weighed less than 1750 g and of these 40, 14 were twins (35%). Hemodynamically significant PDA was documented in 13 patients; of these, only 5 were preterm singletons and 8 were twins. Two twins weighing < 1000 g received no therapy for ductus closure; one ductus closed spontaneously, the other had an early demise. Three twins and 2 preterm singletons received indomethacin; one of the twins needed a second cycle for definitive ductus closure. Three twins and three preterm singletons underwent surgery, while one twin died on the 10th postoperative day. Screening and early therapy of PDA during RDS could be of great clinical importance. Twinning seems to play a role in the incidence and evolution of PDA and this needs to be evaluated in further studies.

Key words: Respiratory distress syndrome, Patent ductus arteriosus, Premature twins

INTRODUCTION

Preterm birth and respiratory distress syndrome (RDS) are relatively frequent in twin births [1,7,9,11]. The spontaneous closure of Botallo's ductus in RDS usually occurs on the third day after birth [3]. After the third day, the preterm with

patent ductus arteriosus (PDA) needs therapy to close it. In fact, early therapy determines a more favorable course of RDS, a reduction in complications, and a better therapeutic response [4,5].

On evaluation of the results of the first year of screening and early therapy of PDA in patients with RDS, we found a high incidence of this complication in twins. Therefore, we considered the possibility that twinning may be associated to a higher risk of PDA.

MATERIAL AND METHODS

In 1987 we performed echocardiographic and Doppler-flow screening with an AT MK 600 (Advaced Technology Labs Inc., Bellevue, Washington) ultrasound apparatus, on the third day of life in all RDS preterm infants weighing $\leq$ 1750 g. Of 91 neonates treated for RDS (23.8% of admitted patients), 40 weighed $\leq$ 1750 g, and 14 of these were twins (35%). Each neonate was evaluated for birth weight, therapy received and the clinical course of PDA (see Tables 1-3).

Table 1 - Incidence of PDA in preterm singletons and in twins in relation to birth weight

Birth weight (g)	<1000	1000-1250	1250-1500	1500-1750	Total (<1750)
Twins	3/4	1/3	1/3	3/3	8/13 (61.5%)
Premature singletons	1/4	2/3	2/3	0/3	5/13 (38.5%)

Table 2 - Medico-surgical therapy of PDA in preterm singletons and twin with RDS and birth weight $\leq$ 1750 g

Birth weight (g)	<1000	1000-1250	1250-1500	1500-1750
PDA	4/13	3/13	3/13	3/13
Pharmacologic treatment	0	0	3	2
Surgical treatment	1	3	0	1

Table 3 - Incidence of PDA and mortality in preterm singletons and in twins with RDS weighing $\leq$ 1750 g

	PDA		Mortality
Preterm singletons	5/26 (12.5%)	P < 0.01	0/26
Twins	8/14 (61.8%)		2/14

The therapeutic protocol procedure in a hemodynamically significant PDA was medical therapy with indomethacin (0.2 mg/kg, 3 doses i.v. every 12 hr) associated with fluid restriction. If contraindications for using indomethcin were present (renal failure, hemorrhagic diathesis, NEC, thrombocytopenia) or conservative medical therapy failed, the ductus was closed surgically. Each neonate was also evaluated at the end of therapy for hematochemical and echocardiographic parameters.

RESULTS

The results are summarized in Tables 1-3. Hemodynamically significant PDA was found on the third day of life in 13 of the 40 RDS neonates having a birth weight $\leq$ 1750 g: only 5 of the 26 singletons and 8 of the 14 twins, the difference being highly significant ($P < 0.001$).

Treatment with indomethacin was always effective, although one twin needed a second cycle for definitive closure, with no side effects. Of those operated, 3 twins and 3 singletons, in whom the use of indomethacin was contraindicated, only 1 twin died from an extensive intracranial hemorrhage after 10 days of life.

DISCUSSION

Cardiovascular malformations are the largest category of major congenital defects, and yet an understanding of their pathogenesis is limited. Specific heart malformations have been associated with the twinning process, and conjoined twins often share a heart or cardiovascular anomalies [2,6,10]. However, most studies did not give sufficient details of cardiac diagnoses and did not exclude PDA [2].

The frequency of PDA in premature births is inversely proportional to birth weight and has been calculated to be about 20% in newborns of $\leq$ 1750 g with RDS [4]. This is obviously subject to variation depending on the methods used for different patient samples, with different mortality, different therapy and different diagnostic methods used for neonates with low birth weight.

With echocardiography and Doppler-flow studies we had a 35% incidence of PDA on the third day. In a high number of patients, PDA was undetected at auscultation. The higher frequency of PDA in twins with RDS obviously needs to be confirmed in larger numbers of cases. But, if it is true that high-risk pregnancies are not only those of twins, the high frequency of PDA in our twins may have relevant implications [2]. Screening for PDA is therefore useful in the early therapy of ventilated singleton or twin neonates who show a good and safe response to therapy with indomethacin, an inhibitor of prostaglandin synthetase, which also has a preventive effect on intracranial hemorrhage [8].

The PDA mortality during RDS in our patients was confined to twins. This may be simply due to small numbers, but nonetheless underlines how low-birth-weight twins are at risk for hemodynamic complications during RDS. The influence

of PDA on prognosis as well as the immediate outcome of premature twins, should be the subject of further study.

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Correspondence: Dr. V. Zanardo, Dipartimento di Pediatria, Università di Padova, Via Giustiniani 3, 35128 Padova, Italy.