

Concerning the Article by L. Capasso et al.:

## Early Cord Clamping Protects At-Risk Neonates from Polycythemia

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Dear Sir,

We read with interest the article by Capasso et al. 'Early Cord Clamping Protects At-Risk Neonates from Polycythemia' [Biol Neonate 2003;83:197–200]. We have a few concerns about some of the information presented in the above referenced article [1]. First, the authors' review of the literature is incomplete. There is only one actual report of a study relating cord clamping and symptomatic polycythemia [2] from 1977. We have found that the older study lacks the methodological rigor expected today and was not a randomized controlled trial (RCT). The results have not been replicated. They do not mention this study, nor do they review it.

An extensive review of the literature of all randomized controlled and controlled trials on cord clamping from 1980 to 2001 looked for evidence that delayed cord clamping caused harm [3]. The data from trials over the last two decades do not support the theory that delayed cord clamping causes symptomatic polycythemia in spite of the fact that hematocrit levels are higher in late clamped term and preterm infants. There have been 4 RCTs and 5 controlled trials with term infants and 8 RCTs with preterm infants [3]. A total of 531 term infants experienced late clamping ranging from 3 min to cessation of pulsations without symptoms of symptomatic polycythemia. For preterm infants, there was also no evidence of the condition in the children with delayed cord clamping [3].

There is not consensus about the long-term outcomes found in children who have had polycythemia. In 1992, Bada et al. [4],

using a RCT, found no differences in neurologic outcome at 30 months when polycythemic infants and control infants returned for follow-up evaluation. In 1997, Liem et al. [5] found that hemodilution in polycythemia did not improve cerebral oxygenation despite possible improvement of cerebral perfusion demonstrating the continuing complexity of the issue of polycythemia.

In this study, the groups are markedly uneven in size and group selection was made subjectively by one author. Also the protocol is too narrow to result in a discrete grouping of infants. The fact that 1 infant in group 1 had seizures and 4 infants had cyanotic spells raises the question of harm from the early cord clamping. These outcomes are much more serious than the others with which they are grouped. Group 3 appears in one figure but is not referred to in the text.

There is a large volume of research on cord clamping [3] involving over 200 studies, and yet controversy remains. Randomized clinical trials with long-term follow-up of infants (at least 18 months) are essential if we are ever to solve this puzzle. Providers' behaviour at birth can result in the loss of 10–40% of the fetal/neonatal blood supply [6]. In 2002, Rajnik et al. [7] found that withdrawing 25% of a rat's blood volume resulted in the presence of pro-inflammatory cytokines in lungs and liver after only 3 h. Grether et al. [8] has shown a link between the presence of these cytokines and children that were later found to have cerebral palsy. These findings should raise our index of suspicion about potential harmful effects of immediate cord clamping.

Most importantly, prescription for clinical practice should not be based on one non-random observational study [9].

### References

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0006-3126/04/0862-0108\$21.00/0

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## Reply

Letizia Capasso Francesco Raimondi Antonio Capasso Valeria Crivaro Rachele Capasso Roberto Paludetto  
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Dear Sir,

We acknowledge the interest of Dr. Rabe and Dr. Mercer for our paper about an early cord clamping in neonates at risk for polycythemia and appreciate their criticisms.

Most of the literature quoted by Dr. Rabe and Dr. Mercer refers to the effects of a delayed cord clamping to interrupt fetal blood supply and polycythemia in the general neonatal population (term or preterm). We believe, however, that there is a substantial difference about the effect of blood volume shift (as implied by a delayed interruption of placental-fetal connection) in unselected neonates when compared to infants of diabetic mothers or with IUGR. The latter populations are often *already* polycythemic at birth for, most likely, an erythropoietin-independent and blood volume-independent mechanism [1, 2]. Hemoconcentration soon after birth further increases the hematocrit [3] and the chances to become symptomatic in these babies.

There is no previous study, to the best of our knowledge, on the hemodynamic effects

of blood volume movements in this particular setting. It is reasonable to believe that averting an average 7–10% total body blood volume contained in the cord (far from the critical volumes cited by Dr. Rabe and Dr. Mercer) at birth before hemoconcentration could help to prevent symptomatic polycythemia.

Our intervention at birth was therefore to prevent the cord blood content to enter the circulation with a second cord clamp (i.e. no intervention was done on the interruption of placental-fetal connection) close to the abdomen in a selected population of at-risk neonates. Patients in the study were not randomized. However, 'selecting patients most at risk for polycythemia in the treatment group was an expected act rather than in favour of the studied treatment'. Seizures and cyanotic spells have been described as part of the clinical picture of polycythemia/hyperviscosity syndrome [3, 4]. There is little ground, on the basis of our limited numbers, to think that treatment might have played a role. If anything, our intervention

might have been ineffective in those individual neonates.

We completely share Dr. Rabe and Dr. Mercer's call for further research on the open issues of neonatal polycythemia and its clinical consequences and thank them for their attention.

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## Erratum

The wrong figures were printed in the article by L. Capasso et al.: Early Cord Clamping Protects At-Risk Neonates from Polycythemia [Biol Neonate 2003;83:197–200]. The correct ones are shown here:

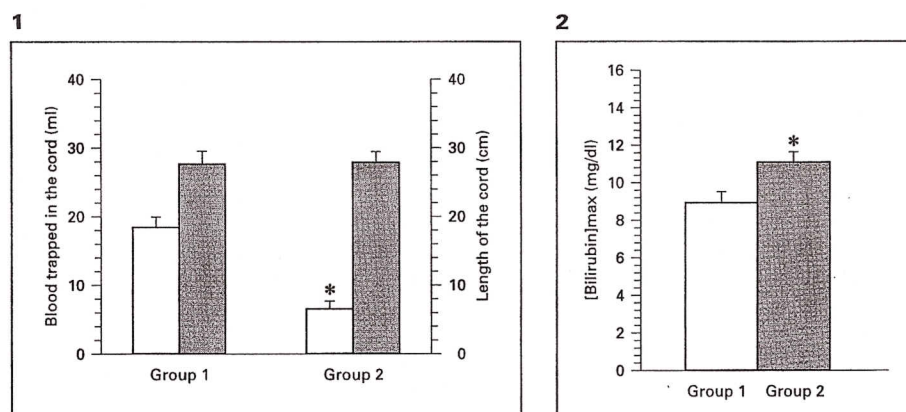


Fig. 1. Cord length and its blood content. While the length of the cord between clamps is similar among groups (grey bars), its blood content significantly decreases for longer clamping times (\*  $p < 0.00$  vs. group 1) (white bars), indicating that longer clamping times allow cord blood to flow into the neonatal circulation.

Fig. 2. Clamping time and bilirubinemia. Longer clamping times (group 2 – grey bars) are associated with a higher value of peak bilirubinemia (\*  $p < 0.04$ ).