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CORRESPONDENCE

Anaphylaxis in late pregnancy: plasma concentrations of histamine, tryptase and IgE in the neonate

Anaphylaxis in pregnancy is a rare event and a potential cause of fetal cerebral hypoperfusion.¹ The biological features of anaphylaxis in the pregnant woman are well-known by obstetric anesthetists but so far no data exists about plasma markers in the newborn.

A 39-year-old woman, gravida 3, para 2, with no medical history or allergies, was treated with amoxicillin for a few days in early pregnancy. She was admitted with premature rupture of the membranes at 40 weeks' gestation. Since her cervical score was low and no uterine contractions were present, prophylactic antibiotic therapy with 2 g amoxicillin was commenced in accordance with the local protocol. A few seconds after beginning administration she complained of itching, burning and nausea, associated with skin flushing and a mild fall in blood pressure from 130/70 to 100/50 mmHg without tachycardia. She then developed widespread skin edema and uterine hypertonia, and this was considered a grade two reaction in the four-level system of the World Allergy Organisation. The fetal heart rate was approximately 50 beats per minute (bpm) and as this did not change when she was placed in the lateral position, an emergent cesarean section was called. An infusion of 1 L of normal saline was started and 120 mg methylprednisolone given. The fetal heart rate remained non-reassuring. The operation was performed under spinal anesthesia, after co-loading with 500 mL colloid (Pentastarch) and 50 µg epinephrine intravenously to manage bronchospasm. No circulatory collapse occurred. Eighteen minutes after the onset, a female infant weighing 3090 g and with Apgar scores of 6, 10, and 10 at 1, 5, and 10 min respectively, was delivered. A mixed acidosis (arterial cord blood pH 6.97, pCO₂ 100 mmHg, pO₂ 7.4 mmHg, base excess – 9.6, lactate 9.9 mmol/L) was noted. The infant recovered and her blood gases normalised after two hours of continuous positive airway

pressure. Tests for an infective source were negative. Plasma assays of histamine and tryptase were performed at delivery and 120 minutes later in both the mother and neonate; and specific IgE was assayed two months later (Table 1).

Fetal distress in anaphylaxis is widely acknowledged to be due to placental hypoperfusion, especially after inappropriate or delayed treatment. However, some newborns suffer from severe brain damage despite a low grade of maternal anaphylaxis, suggesting other mechanisms.^{1,2} A balance between histamine and histamine degradation by the enzyme diamine oxidase (DAO) appears to be crucial for an uncomplicated pregnancy.³ In animal models, excessive histamine levels have fatal effects during pregnancy. The activity of DAO, which is largely produced by the placenta, increases during normal pregnancy by up to 1000-fold and this barrier prevents excessive entry of histamine into the fetal circulation. Thus maternal plasma histamine does not increase in the case of anaphylaxis. The DAO is also present in the full-term infant and in amniotic fluid. In an uncomplicated pregnancy, the concentration of DAO is elevated in the newborn's serum at birth: it does not decline until after a week of life.⁴ The only data on plasma histamine concentrations in the normal neonate pertains to umbilical cord blood. This is below the lowest limit of detection of 1.8 ng/ml in a bioassay.⁵

Mast cells are largely present within the uterus and the placenta. A case report detailing the postpartum examination of the placenta found massive degranulation of mast cells and severe vasoconstriction of the umbilical arteries.⁶ In an isolated cotyledon, histamine induces contraction by activation of H1-receptors and secondary relaxation of placental chorionic plate arteries.⁷ Umbilical vessels are not innervated so control of flow depends on vasoactive substances either released locally or within the circulation. On isolated human umbilical vessels, the major mediators of anaphylaxis such as bradykinin, endothelin, histamine, 5-hydroxytryptamine

Table 1 Serum markers measured in the parturient, umbilical cord and neonate

	Histamine (N <10.0 nmol/L)		Tryptase (N <11.0 µg/L)		Specific IgE (N <0.10 kU/L) 2 months
	T0	T120	T0	T120	
Maternal	<1.0	<1.0	5.9	8.3	<0.10
Umbilical cord	17.8	–	2.1	–	–
Neonate	–	18.5	–	4.6	<0.10

Histamine, tryptase and specific IgE are respectively determined by radioimmunoassay, fluoroenzyme immunoassay and Immucap™. Units and normal values (N) in non-pregnant adults are shown at the head of each respective column. T0: assay at delivery. T120: assay at 120 min from delivery. –: not measured.

and thromboxane A2 produce appreciable maximal contractions and the last two are considered to be physiologic mediators of umbilical artery closure.⁸ It should be noted that epinephrine and norepinephrine generate weak contractions. IgE is a key component of typical anaphylaxis and it has been generally accepted that only IgG can cross the placental barrier, while other antibody isotypes are blocked.

My hypothesis is that diverse anaphylaxis mediators may cross the placenta, producing transient vasoconstriction of the umbilical vessels. This could occur even in low grade maternal anaphylaxis, explaining unexpected fetal distress in these cases. These effects could exacerbate those due to maternal hypotension. For a better understanding of this pathology, I advocate the extension of biological screening to the neonate, as well as further studies on histamine at birth in the normal neonate.

J.C. Sleth

*Polyclinique Saint-Roch, 560, Montpellier Cedex 3,
France*

E-mail address: jean-christian.sleth@wanadoo

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