Maternal and fetal β endorphin: effects of pregnancy and labour

The recent discovery of specific opiate receptors in the brain and the pituitary gland and of endorphins that bind to these receptors led to many studies on the role and effects of these substances. The pituitary gland secretes β endorphin at the same time as β lipotrophin, and adrenocorticotrophic hormone (ACTH).¹

β endorphin in pregnancy and labour

Various workers have measured peripheral plasma β endorphin concentrations in women during pregnancy, labour, and delivery. Their reported absolute β endorphin concentrations and their conclusions about whether or not pregnancy is associated with a rise in maternal plasma β endorphin concentrations, are at considerable variance. The differences in absolute β endorphin concentrations may be largely due to differences in methods and antibody specificity.

Goland *et al*² measured maternal plasma β endorphin concentrations during pregnancy. They reported marginally but not significantly higher concentrations in pregnant women. When measuring plasma concentrations in relatively large groups of non-pregnant controls and first, second, and third trimester pregnancies, we found a significant nadir during the second trimester (table 1).³ Genazzani *et al*⁴ reported a significant decrease in maternal plasma β endorphin at 9-12 weeks' gestation and an increase near full term (36-37 weeks' gestation)

when compared with those found in non-pregnant controls. These discrepancies may be attributed to the selection of study subjects, the number of patients studied, and the stringent classification of subjects.

In our study venous blood samples from pregnant and non-pregnant volunteers were taken between 8 and 10 am, and none of the study subjects was to undergo any surgical operation or induction of labour unless stated otherwise. The increase in maternal plasma β endorphin concentrations in women at full term reported by Genazzani *et al*⁴ was because their subjects were about to undergo elective caesarean section. Our data indicated that the psychological stress that is associated with preparation for a major operation such as caesarean section without premedication is enough to induce increased pituitary release of β endorphin.³ Thus, one may conclude that in the absence of specific stress, maternal plasma β endorphin is decreased rather than increased throughout pregnancy until labour ensues.

During labour, maternal plasma β endorphin concentrations rise and remain high during the early postpartum period (table 1). This is most consistent with the increase in secretion of ACTH that has been reported to occur during labour and to peak at delivery.^{5,6} Csontos *et al*⁷ reported parallel increases in maternal plasma β endorphin and ACTH concentrations. Our observation that maternal plasma β endorphin concentrations remain raised for some

Table 1 Plasma β endorphin concentrations in non-pregnant women, women during pregnancy and labour, 30-60 minutes postpartum, and just before elective caesarean section in the absence of labour[†]

Subjects	No. of samples	Mean (SE) β endorphin concentration (pg/ml)	p Value (Mann-Whitney U test) compared with non-pregnant controls
Non-pregnant control subjects	17	58 (2.4)	
Women in first trimester	11*	47 (2.4)	<0.005
Women in second trimester	11*	33 (1.9)	<0.0005
Women in third trimester	10*	49 (2.7)	<0.02
Women in early labour (cervical dilatation <4 cm)	12	202 (32.0)	<0.00005
Women in advanced labour (cervical dilatation >4 cm)	10	389 (78.0)	<0.00005
Women 30-60 minutes postpartum	12	177 (22.0)	<0.00005
Women awaiting caesarean section	15	151 (23.0)	<0.005†

*Measurement on plasma pooled from four volunteers, representing 44, 44, and 40 subjects, respectively; †compared with women in the third trimester.

time after delivery, despite the short half life of β endorphin,⁸ indicates that the maternal pituitary continues to secrete increased amounts of β endorphin after delivery.

Plasma β endorphin concentrations fall in response to epidural analgesia during labour and delivery,⁹⁻¹² and after intrathecal morphine analgesia during labour.¹³ The decline in maternal plasma β endorphin concentrations after maternal analgesia while uterine contractions and progress in labour continue indicate that pain, stress associated with pain, or both, are major stimuli of pituitary β endorphin release rather than labour itself. These data have been validated by the use of appropriate controls in whom epidural catheters were placed but saline rather than an anaesthetic agent was initially injected.⁹ This significant decline in circulating β endorphin is probably due to decreased pituitary secretion of β endorphin in response to the alleviation of the stress induced by labour pain, and is consistent with the short half life of β endorphin measured as 4.1, 13.1, and 46.2 minutes, respectively, with its multiexponential disappearance curve.⁸

β endorphin and the fetus

Plasma β endorphin concentrations are a measure of stress not only in the mother but also in the fetus. β endorphin concentrations rise significantly in response to fetal distress (table 2). This increase of β endorphin in the fetal circulation in response to stress was shown to be paralleled by a concomitant rise in beta lipotrophin,¹⁴ a finding that is consistent with the fact that β endorphin originates from β lipotrophin by selective cleavage. Wardlaw *et al*¹⁵ showed a significant inverse correlation between umbilical plasma β endorphin concentrations and

PaO₂ and pH, indicating that fetal hypoxia or acidosis, or both, may be related to β endorphin release. Data have shown that umbilical venous plasma β endorphin concentrations are higher than umbilical arterial plasma β endorphin concentrations as measured in 22 paired samples without apparent fetal distress,³ suggesting that the placenta contributes to the pool of circulating fetal β endorphin. In the presence of fetal distress, however, umbilical arterial β endorphin concentrations seem to rise more extensively than umbilical venous concentrations, suggesting that the fetal pituitary is capable of secreting β endorphin in response to stress.

This conclusion is consistent with the findings of Fachinetti *et al* that β endorphin is present in the plasma of newborn babies during the first 24 hours of life.¹⁶ Considering that β endorphin has a short half life,⁸ the data of Fachinetti *et al*¹⁶ seem to indicate that the fetus born at full term is capable of producing β endorphin, probably by release from the pituitary. That corticotrophin releasing hormone secreted in response to stressful stimuli may not only initiate the selective cleavage of ACTH but also that of β endorphin from their common precursor pro-opiomelanocortin in the fetus and newborn, seems to be an attractive hypothesis. Hypoxia may be the overriding stress stimulus in the fetus, and opioid peptides in the fetal central nervous system may act as neurotransmitters that modulate fetal heart rate patterns and decrease fetal heart rate variability.¹⁷ It has been shown that neither the mode of anaesthesia,^{11 18} presence or absence of labour, nor the mode of delivery, affect umbilical vein plasma β endorphin concentrations.³ The latter finding contradicts that reported by Raisanen *et al* in which normal vaginal delivery without asphyxia increased β endorphin release into the fetoplacental circulation.¹⁹

Table 2 Umbilical venous plasma β endorphin concentrations in newborn babies delivered by various routes and modes with and without apparent intrapartum fetal distress³

Route and mode of delivery	Fetal distress	No of samples	Mean (SE) β endorphin concentration (pg/ml)	p Value (Student's t test) compared with spontaneous vaginal delivery
Spontaneous vaginal delivery	No	14	128 (19.8)	
Elective caesarean section	No	12	131 (20.5)	NS
Emergency caesarean section	No	18	109 (18.1)	NS
Forceps or vacuum delivery	No	10	161 (31.4)	NS
Forceps or vacuum delivery	Yes	6	366 (59.7)	<0.01
Emergency caesarean section	Yes	4	421 (138.0)	<0.05
Combined groups without fetal distress	No	54	133 (11.1)	
Combined groups with fetal distress	Yes	10	398 (62.4)	<0.001*

*Compared with the combined groups without fetal distress.

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