Fetal Heart Rate Response to Maternal Hypocapnia and Hypercapnia in Late Gestation

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Abstract

Objective: To examine the effects of acute maternal hypocapnia and hypercapnia on electronic fetal heart rate (FHR) patterns in late gestation.

Methods: Thirty-five women with healthy singleton pregnancies performed a modified carbon dioxide (CO_2) rebreathing procedure between 34 and 38 weeks of pregnancy. Prior to rebreathing, subjects hyperventilated for five minutes to reduce end-tidal CO_2 tensions ($PETco_2$) below 23 Torr (hypocapnia). During rebreathing, $PETco_2$ progressively increased from hypocapnia to hypercapnia ($PETco_2$ = 40–60 Torr) at a constant hyperoxic end-tidal O_2 tension of 150 Torr. FHR responses were classified using standardized guidelines over four periods: 20 minutes before rebreathing (pretest), during hypocapnia and hypercapnia, and 20 minutes after rebreathing (post-test).

Results: Mean baseline FHR measures (SD) over the four test periods were 138(8), 144(10), 132(11), and 137(9) beats per minute (bpm). All pairwise comparisons were statistically significant except the pretest versus post-test comparison ($P < 0.05$, Tukey-Kramer multiple comparisons test). A single tachycardia episode of 170 bpm was recorded in the post-test period. In 20 subjects FHR variability changed from moderate in the pretest period to minimal during hypocapnia and/or hypercapnia. All but two returned to moderate FHR variability in the post-test period. One other fetus with minimal post-test variability had moderate values in the three preceding test periods.

Conclusion: Electronic FHR parameters remained within normal limits for third-trimester fetuses with the exception of one fetus that experienced tachycardia. Acute maternal hypocapnia and hypercapnia over the range studied had no adverse effects on fetal well-being. These results support the safety of the modified CO_2 rebreathing procedure for research in healthy, low-risk pregnancy.

Key Words: Fetal heart rate, hypercapnia, hypocapnia, rebreathing, pregnancy

Competing Interests: None declared.

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Résumé

Objectif : Examiner les effets de l'hypocapnie et de l'hypercapnie maternelles aiguës sur les tracés électroniques du rythme cardiaque fœtal (RCF) au cours de la dernière partie de la gestation.

Méthodes : Trente-cinq femmes présentant une grossesse monofœtale en santé ont effectué une intervention modifiée de réinhalation du dioxyde de carbone (CO_2) entre la 34^e et la 38^e semaine de grossesse. Avant la réinhalation, les sujets ont été soumis à une hyperventilation pendant cinq minutes en vue d'abaisser les tensions de CO_2 de fin d'expiration (PCO_2 de fin d'expiration) en deçà de 23 torr (hypocapnie). Au cours de la réinhalation, la PCO_2 de fin d'expiration est progressivement passée de l'hypocapnie à l'hypercapnie (PCO_2 de fin d'expiration = 40–60 torr) à une tension d'O_2 de fin d'expiration hyperoxique constante de 150 torr. Les réactions du RCF ont été classées au moyen de lignes directrices standardisées pendant quatre périodes : 20 minutes avant la réinhalation (prétest), au cours de l'hypocapnie, au cours de l'hypercapnie et 20 minutes à la suite de la réinhalation (post-test).

Résultats : Les mesures moyennes du RCF de base (σ) pendant les quatre périodes d'essai étaient 138(8), 144(10), 132(11) et 137(9) battements par minute (bpm). Toutes les comparaisons par paire étaient significatives sur le plan statistique, sauf dans le cas de la comparaison prétest/post-test ($P < 0,05$, test de comparaisons multiples de Tukey-Kramer). Un seul épisode de tachycardie de 170 bpm a été enregistré au cours de la période post-test. Chez 20 sujets, la variabilité du RCF est passée de modérée au cours de la période prétest à minimale au cours de l'hypocapnie et/ou de l'hypercapnie. Tous ces sujets, sauf deux, ont connu un retour à une variabilité du RCF modérée au cours de la période post-test. Un autre fœtus connaissant une variabilité post-test minimale présentait des valeurs modérées au cours des trois périodes d'essai précédentes.

Conclusion : Les paramètres électroniques du RCF sont demeurés dans les limites normales pour ce qui est des fœtus du troisième trimestre, exception faite de ceux d'un fœtus ayant connu une tachycardie. L'hypocapnie et l'hypercapnie maternelles aiguës se situant dans la gamme de valeurs étudiée n'ont pas entraîné d'effets indésirables sur le bien-être fœtal. Ces résultats soutiennent l'innocuité de l'intervention modifiée de réinhalation du CO_2 à des fins de recherche dans le cas de grossesses en santé et n'étant exposées qu'à de faibles risques.

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INTRODUCTION

Previous studies have examined the effects of maternal hypocapnia and hypercapnia on fetal breathing movements, fetal gross body movements, and uterine, placental, or cerebral blood flow in laboratory animals.[1–3] However, there is limited information, particularly in humans, regarding the effects of experimentally widening or narrowing the maternal-fetal CO_2 gradient on electronic FHR patterns. Acute changes in fetal Pco_2 may be expected to influence electronic FHR patterns by altering fetal central and peripheral chemoreceptor activity. Central and peripheral chemoreceptors are active in the fetus. Changes in FHR patterns are mediated, at least in part, by sympathetic and parasympathetic pathways in response to chemoreceptor stimulation.

Studies in our laboratory have employed a modified CO_2 rebreathing procedure to examine the effects of human pregnancy on ventilatory control.[4] During this procedure, pregnant women are exposed to acute periods of systemic hypocapnia and hypercapnia lasting from five to 10 minutes, which may affect fetal well-being through changes in the maternal-fetal gradient for CO_2 and perhaps also fetal PCO_2. Although other laboratories have employed similar CO_2 rebreathing procedures for studies of ventilatory control throughout human pregnancy,[5–8] none have described their effects on electronic FHR patterns.

The purpose of the present study was to conduct a detailed analysis of the effects of the modified CO_2 rebreathing procedure on fetal cardiac parameters. We hypothesized that brief periods of maternal hypocapnia and hypercapnia would have transient effects on electronic FHR patterns (baseline FHR, FHR variability) but that these changes would remain within normal limits based on the guidelines developed by the NICHHD.[9]

METHODS

Prospective subjects were recruited via media advertisements, posted announcements, and contact with obstetricians and midwives for participation in an ongoing study in our laboratory designed to investigate the effects of human pregnancy on ventilatory control and acid-base regulation.

ABBREVIATIONS

FHR	fetal heart rate
NICHHD	National Institute of Child Health and Human Development
PCO_2	partial pressure of carbon dioxide
$PETCO_2$	partial pressure of end-tidal carbon dioxide

Inclusion criteria were the following: age 20 to 40 years, gestational age 34 to 38 weeks, singleton pregnancy, non-smoker, regularly active (= 30 minutes of walking three times per week), parity < 3, and not taking medications other than prenatal vitamin supplements. All subjects were screened for medical contraindications to study participation (cardiorespiratory disease, anemia, placenta previa, toxemia or preeclampsia, gestational diabetes) by the physician or midwife monitoring their pregnancies. A general medical-health questionnaire and the Physical Activity Readiness Medical Examination for Pregnancy[10] were used for this purpose. During the week before laboratory testing, subjects underwent a routine fetal ultrasound examination and biophysical profile to demonstrate normal fetal growth and behaviour, and amniotic fluid volume. All women who enrolled completed the study and none were excluded because of obstetric complications. The study protocol and consent form were approved by the Research Ethics Board, Faculty of Health Sciences at Queen's University. Each subject provided written consent before study participation.

Modified CO_2 Rebreathing Procedure

Subjects abstained from aerobic and muscular conditioning exercise as well as caffeine on the day of testing. A modified CO_2 rebreathing procedure that included five minutes of prior hyperventilation and maintenance of a constant (or iso-oxic) end-tidal O_2 tension ($PETO_2$) was used to evaluate the effects of human pregnancy on ventilatory control, as previously described.[4] Briefly, subjects voluntarily hyperventilated room air for five minutes, using a deep and deliberate breathing pattern to lower end-tidal PCO_2 ($PETCO_2$) between 19 and 23 Torr. $PETCO_2$ stability was achieved after approximately one minute of voluntary hyperventilation. Subjects were then switched from room air to a rebreathing bag containing a hyperoxic-hypercapnic gas mixture (6% CO_2–24% O_2-N_2 balanced). Rebreathing began with three to five deep breaths causing rapid equilibration of the PCO_2 in the bag, lungs, and arterial blood to that of the mixed-venous blood, thereby minimizing the arteriovenous PCO_2 difference.[11] This ensures that changes in $PETCO_2$ accurately reflect changes in arterial, pulmonary and venous PCO_2. Upon equilibration, subjects were asked to relax and breathe as they felt the need.

During rebreathing, $PETCO_2$ increased progressively from hypocapnia to hypercapnia at a rate determined by the metabolic production of CO_2, and iso-oxia was maintained, under computer control, at a hyperoxic $PETO_2$ of 150 mmHg by providing a flow of 100% O_2 to the rebreathing bag. Maternal arterial blood O_2 saturation and heart rate were monitored continuously throughout each test using an ear oximeter (OXI; Radiometer Copenhagen,