Amniocentesis for PPROM Management: A Feasibility Study

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Abstract

Objective: In Canada, most mothers whose amniotic membranes rupture before 34 weeks' gestation are hospitalized and delivered when signs of chorioamnionitis or fetal distress are observed or when a predetermined gestational age between 34 and 37 weeks is reached. This management approach can be questioned because in utero exposure to infection is a risk factor for cerebral palsy in neonates. Amniocentesis has the potential to detect markers of intra-amniotic infection. Our objective was to determine the acceptability of a randomized study comparing expectant management with amniocentesis-based management in women with premature rupture of the membranes.

Methods: Between November 2005 and January 2007, we conducted a qualitative study involving 40 patients admitted to a tertiary care centre with premature rupture of the membranes between 28 and 34 weeks. The participants read an information booklet and answered a questionnaire. They were asked if they would agree to participate in a randomized study comparing expectant management with amniocentesis-based management. They graded the importance of a series of statements in their decision-making process.

Results: Seventy percent (28/40) of patients would have participated in the proposed study. Determining the presence of amniotic fluid infection or lung maturity was the main reason motivating their choice. The reasons for refusing to participate were related to complications of amniocentesis (fetal trauma, iatrogenic preterm labour, infection, or pain).

Conclusion: The majority of patients with premature rupture of the membranes would participate in a study comparing expectant management to management based on amniocentesis results. This study helped us to better understand their motivations and fears.

Résumé

Objectif : Au Canada, la plupart des mères dont les membranes amniotiques se rompent avant la 34e semaine de gestation sont hospitalisées; de plus, leur accouchement est déclenché lorsque l'on constate des symptômes de chorioamnionite ou de souffrance fœtale, ou lorsqu'un âge gestationnel prédéterminé (entre 34 et 37 semaines) est atteint. Cette approche de prise en charge peut être remise en question puisque l'exposition *in utero* à l'infection constitue un facteur de risque d'infirmité motrice cérébrale chez les nouveau-nés. L'amniocentèse présente le potentiel de détecter les marqueurs de l'infection intra-amniotique. Notre objectif était de déterminer l'acceptabilité d'une étude randomisée comparant la prise en charge non interventionniste à la prise en charge fondée sur l'amniocentèse chez les femmes connaissant une rupture prématurée des membranes.

Méthodes : Entre novembre 2005 et janvier 2007, nous avons mené une étude qualitative portant sur 40 patientes admises à un centre de soins tertiaires et qui connaissaient une rupture prématurée des membranes entre la 28e et la 34e semaine de gestation. Les participantes ont lu une brochure d'information et ont rempli un questionnaire. On leur a demandé leur opinion quant à la participation à une étude randomisée comparant la prise en charge non interventionniste à la prise en charge fondée sur l'amniocentèse. Elles ont classé, en ordre d'importance, une série d'énoncés liés à leur processus de prise de décision.

Résultats : Soixante-dix pour cent (28/40) des patientes auraient participé à l'étude proposée. La détermination de la maturité pulmonaire ou de la présence d'une infection du liquide amniotique constituait la principale raison expliquant leur choix. Les raisons motivant le refus de participer étaient liées aux complications de l'amniocentèse (traumatisme fœtal, travail préterme iatrogène, infection ou douleur).

Conclusion : La plupart des patientes connaissant une rupture prématurée des membranes participeraient à une étude comparant la prise en charge non interventionniste à la prise en charge fondée sur l'amniocentèse. Cette étude nous a aidés à mieux comprendre leurs motivations et leurs peurs.

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INTRODUCTION

Preterm premature rupture of the membranes complicates 3% of pregnancies and is responsible for approximately one third of all preterm births.[1,2] PPROM is an important cause of perinatal morbidity and mortality because it is associated with chorioamnionitis, placental abruption, and neonatal sepsis.[2–5] While expectant management with antibiotics and steroids has been favoured in the past, preferred management in women with PPROM is the centre of a major debate. Moreover, it is likely that optimal management will differ according to gestational age at the time of PPROM.

Subclinical infection, characterized by colonization of amniotic fluid or membranes by pathogens without clinical evidence of overt infection, is found in one third of patients with PPROM.[6,7] In utero exposure to infection or inflammation is associated with greater neonatal morbidity and higher rates of clinical chorioamnionitis and neonatal sepsis, important risk factors for cerebral palsy.[8–11] Therefore, some authors have proposed performing amniocentesis prior to expectant management to rule out subclinical infection.[12–14]

A systematic review of four studies comparing expectant management with intentional delivery in cases of PPROM was published in 2006.[15–19] In those trials, where antibiotics and corticosteroids were not routinely used, intentional delivery was associated with a lower rate of chorioamnionitis and shorter maternal length of stay. Although expectant management was linked with greater gestational age at birth, the trials were unable to demonstrate any significant neonatal benefit.[20]

One RCT compared expectant management with an approach using weekly amniocentesis in patients with PPROM.[13] Delivery was planned when fetal lung maturity was detected or when MIAC was diagnosed by culture or gram stain. Management with weekly amniocentesis was associated with reduced neonatal length of stay. No RCT has compared the two management approaches (expectant management or intentional delivery) since use of antibiotics and corticosteroids became standard management in these patients.

The objective of the current study was to determine if women with PPROM between 28 and 34 weeks' gestation would agree to participate in a randomized trial comparing expectant management with management based on amniocentesis results. The second objective was to determine the role of several factors in their decision-making process.

METHODS

A qualitative prospective study was proposed to women who were admitted to our tertiary care centre between November 2005 and January 2007 at a gestational age of between 28 weeks 0 days and 34 weeks 6 days. Women were included if they were over 18 years of age, had a singleton pregnancy, and were able to read French. Women with a maternal or fetal condition that precluded expectant management (suspected chorioamnionitis, suspected fetal distress, or lethal fetal anomalies) were not eligible. The project was approved by the Scientific and Ethics Committees of the Sainte-Justine Hospital Research Centre.

Table 1. Patient demographic and obstetric characteristics

Age in years*	28.5 ± 6.0
Caucasian origin†	34 (85)
Married or with partner†	38 (95)
Education†	
Secondary	21 (52.5)
College	7 (17.5)
University	12 (30)
Smoking†	8 (20)
Gravidity‡	2 (1;8)
Parity‡	0 (0;4)
Gestational age at PPROM (in weeks)*	30.4 ± 3.6
Gestational age when answering the questionnaire (in weeks)*	31.8 ± 2.0
PPROM in a previous pregnancy†	4 (10)
Mid-trimester amniocentesis in the current or a prior pregnancy†	6 (15)

*Mean ± standard deviation; †n (%); ‡Median (minimum; maximum).

The first step of the study was the production of a booklet on PPROM for patients (containing information on PPROM, possible management strategies with their associated risks and benefits, differentiating between clinical and subclinical infections, amniocentesis technique, and the role and limits of markers in the detection of MIAC). A patient with PPROM, a resident in obstetrics and gynaecology, and a maternal-fetal medicine specialist reviewed the booklet to ensure that the information was clear to lay readers.

In the second step of the study, a questionnaire was developed using the same process. The first part of the questionnaire aimed to obtain demographic, medical, and obstetrical data, and the second part was designed to question the willingness of patients to participate in a hypothetical RCT that would compare expectant management with management based on amniocentesis results in patients with PPROM. In the latter situation, it was assumed that delivery would be indicated in cases when there was a high suspicion of MIAC based on direct (gram stain, cultures) or indirect (glucose, LDH, white blood cell count, or other potential available biomarkers) measures, or in which fetal pulmonary maturity was confirmed. Finally, women were asked to grade factors according to their importance in their decision-making process (0 = not important, to 5 = highly important).

ABBREVIATIONS

MIAC microbial invasion of the amniotic cavity
RCT randomized controlled trial
PPROM preterm premature rupture of membranes