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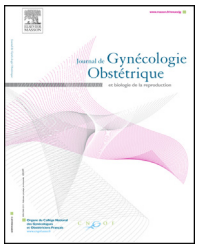

LATEST DEVELOPMENTS

To what extent do English language RCT meta-analysis justify induction of low-risk pregnancy for postdates?

Dans quelle mesure les méta-analyses d'essais randomisés contrôlés de la littérature anglo-saxonne peuvent-elles justifier l'induction du travail pour grossesse prolongée à bas risque ?

J.S. Cohain

Alon Shvut 37, 90433, Israel

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KEYWORDS
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Maternal morbidity

Summary Induction for postdates in low-risk pregnancy was adopted with the intent to prevent post-term antepartum stillbirth, the most common cause of perinatal death, based on evidence derived in English language RCT meta-analysis. Systematic English language meta-analysis of RCT studies of induction for postdates in low-risk pregnancy report perinatal mortality rates (PMRs) for low-risk pregnancy ranging from 2.6 to 7.6/1000, based on 2—5 stillbirths among 13—16 perinatal deaths, including diabetic pregnancies as well as other high-risk pregnancies irrelevant to the study question. Baseline PMR ≥ 41 weeks in large international databases for high and low risk pregnancies before routine induction 1998—2003 range from 0.9 to 2.4/1000 or about 300% lower than the reported PMR rates for postdate pregnancies in the expectant management arm in English language RCT meta-analysis. Deaths in the first week far exceed stillbirths in the RCT meta-analysis, the opposite of what is expected. These 2 implausible results bring into question the evidence used to justify induction for postdates ≥ 41 weeks.

MOTS CLÉS
Induction du travail ;
Mort-né
ante-partum ;

Résumé L'induction médicale du travail pour grossesse prolongée à bas risque est une pratique courante dont l'objectif est de prévenir la mortalité anténatale à terme dépassé, la cause la plus fréquente de mortalité périnatale. Cette pratique est acceptée comme valide au vu des résultats de méta-analyses de publications de la littérature anglo-saxonne. Selon ces méta-analyses

E-mail address: judyslome@hotmail.com

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Mortalité périnatale ;
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Morbidité maternelle

sur l'induction du travail pour grossesse prolongée à bas risque, le taux de mortalité varie entre 2,6 et 7,6 pour 1000 naissances, basé sur 2 à 5 mort-nés parmi 13 à 16 décès périnataux, y compris les grossesses diabétiques et autres grossesses à haut risque, sans rapport avec l'objet de l'étude. Si l'on regarde les grandes bases de données internationales de 1998 à 2003, la mortalité périnatale à ≥ 41 semaines est de 0,9 à 2,4 pour 1000 naissances, c'est-à-dire 300 % plus basse que la mortalité périnatale des grossesses prolongées dans les bras « wait-and-see » des études anglo-saxonnes prises en compte dans les méta-analyses. Dans ces méta-analyses, les décès de la première semaine dépassent de beaucoup les mort-nés, le contraire de ce à quoi l'on pourrait s'attendre. Ces deux résultats peu plausibles mettent en question la validité du choix d'une induction du travail pour les grossesses à ≥ 41 semaines.

Introduction

Previous to 1999, induction for low-risk pregnancy was carried out where the foetus showed signs of distress [1]. The potentially life-threatening risks which can result from artificially inducing labor, such as increased chorioamnionitis, cord prolapse, postpartum haemorrhage, tachysystole, failed induction, caesarean delivery, and accidental delivery of preterm foetus [2] were only taken when they outweighed the risks of continuing the pregnancy.

The protocol to induce for postdates was initially fuelled by the 1999 observational study [3] tenuously associating two variables that might have no relationship: a decrease of 1.9/1000 in antepartum stillbirth from 2.8/1000 to 0.9/1000 in Canada reported for all births between the years 1980 and 1995, with an increased induction rate reported at 2 Canadian hospitals and at the health departments of 6 provinces for births more than or equal to 41 weeks at various intervals between 1980 and 1995. This observational study did not control for any of the variables known to decrease stillbirth in all risk women, such as increased quality and availability of prenatal care, birth control and induced abortions; better controlled diabetes; decreased smoking, violence, and car accidents; increased intake of micronutrients and use of seat belts, to name a few.

Another impetus fuelling the acceptance of the protocol to induce for postdates was the publication of stillbirth rates after 41 weeks in large databases 1998—2003. These articles showed that about 1/1000 antepartum stillbirths occur after 40 weeks and about 2/1000 stillbirths after 41 weeks [4—6].

After the excess post-term stillbirths were documented, it was optimistically hoped that the excess 1/1000 stillbirths after 41 weeks among low-risk pregnancies could be lessened by induction of labor. It was not only hoped that induction could prevent some or all of the excess 1/1000 stillbirths after 41 weeks, but also hoped or assumed that it would do so without causing excess long-term harm to mother and child. It was also assumed that the extra 1/1000 born alive, saved by induction, would not die in the first month. Systematic meta-analyses were set out to test the first of these optimistic hopes.

The PMR rates in the meta-analyses for expectant management arm for low-risk pregnancy (not inducing for postdates) would be expected to be similar to expectant management rates of low-risk pregnancy, and lower than PMR rates of all risk pregnancies reported in large databases. PMR ≥ 41 weeks was defined as stillbirths after 41 weeks plus perinatal deaths in the first week after live birth/1000 births.

The aim of this study is to compare the PMR reported in the expectant management arms of the English language RCT meta-analyses 2009—2012 to baseline PMR rates before induction for postdates routines were established.

Results

The 3 English language meta-analyses of induction for postdates published after 2008 are Gulmezoglu et al. [7], Hussain et al. [8] and Wennerholm et al. [9]. The 3 systematic reviews combine the results of more or less the same 3000—3700 pregnancies delegated to expectant management in about 17 RCT studies, and report on the same 13—16 babies who reportedly either died in the uterus late in the pregnancy ($n = 2$—5) or died in the first week of life ($n = 8$—14). The reported PMR rates of the expectant management arm in the English language studies were:

- Gulmezoglu: 3.5/1000, (13/3700), (C.I 0.09—0.99);
- Hussain: 4.9/1000, (16/3282), (C.I 0.11—0.88);
- Wennerholm: 2.6/1000, (8/3097), (C.I 0.10—1.09).

About half of all births analysed in all 3 RCT meta-analyses derived from one study [10], which had the lowest rate of adherence to protocols, reporting that 50% of those randomised to expectant management were induced. Since Hannah's 1992 observational study [3] is biased in favor of induction and the Hannah study had a 50% rate of non-compliance to protocol, it was logical to extract the PMR rates without the Hannah study. When Hannah study [10] is excluded from the analysis, the perinatal mortality rates for the RCT meta-analysis expectant management arm are:

- Gulmezoglu: 4.3/1000;
- Hussain: 5.7/1000;
- Wennerhold: 7.6/1000.

These rates are compared to baseline rates reported in the literature in Table 1 and Fig. 1.

Gulmezoglu et al. is the most careful about itemizing each instance of perinatal mortality. Four perinatal deaths occurred ≥ 41 weeks in the expectant management arm (2 stillbirths and 2 deaths in first week) or 4/3700 or PMR = 1/1000, which is a credible PMR for low-risk pregnancy, and equivalent to the PMR for inductions, which