Accelerated Titration of Oxytocin in Nulliparous Women with Labour Dystocia: Results of the ACTION Pilot Randomized Controlled Trial

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Abstract

Objective: The primary objective was to determine the feasibility of a large RCT assessing the effectiveness of an accelerated oxytocin titration (AOT) protocol compared with a standard gradual oxytocin titration (GOT) in reducing the risk of CS in nulliparous women diagnosed with dystocia in the first stage of labour. The secondary objective was to obtain preliminary data on the safety and efficacy of the foregoing AOT protocol.

Methods: This was a multicentre, double-masked, parallel-group pilot RCT. This study was conducted in three Canadian birthing centres. A total of 79 term nulliparous women carrying a singleton pregnancy in spontaneous labour, with a diagnosis of labour dystocia, were randomized to receive either GOT (initial dose 2 mU/min with increments of 2 mU/min) or AOT (initial dose 4 mU/min with increments of 4 mU/min), in a 1:1 ratio. An intention-to-treat analysis was applied.

Results: A total of 252 women were screened and approached, 137 (54.4%) consented, and 79 (31.3%) were randomized. Overall protocol adherence was 76 of 79 (96.2%). Of the women randomized, 10 (25.6%) allocated to GOT had a CS compared with six (15.0%) allocated to AOT (Fisher exact test $P = 0.27$).

Conclusion: This pilot study demonstrated that a large, multicentre RCT is not only feasible, but also necessary to assess the effectiveness and safety of an AOT protocol for labour augmentation with regard to CS rate and indicators of maternal and perinatal morbidities.

Key Words: Oxytocin, labour dystocia, labour augmentation, Caesarean section, randomized controlled trial

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Résumé

Objectif : Notre objectif principal était de déterminer la faisabilité d'un ECR de grande envergure qui comparerait l'efficacité d'un protocole d'ajustement accéléré de la dose d'ocytocine à celle d'un protocole habituel d'ajustement graduel de la dose d'ocytocine pour réduire le risque de césarienne chez les femmes primipares qui ont reçu un diagnostic de dystocie durant le premier stade du travail. Notre objectif secondaire était de recueillir des données préliminaires sur l'innocuité et l'efficacité du protocole accéléré.

Méthodologie : Nous avons mené un ECR pilote multicentrique à groupes parallèles et à double insu dans trois centres de naissance canadiens. Un total de 79 femmes primipares enceintes d'un seul fœtus étant en travail spontané et ayant reçu un diagnostic de dystocie ont aléatoirement fait l'objet d'un protocole graduel (dose d'attaque de 2 mU/min et incréments de 2 mU/min) ou d'un protocole accéléré (dose d'attaque de 4 mU/min et incréments de 4 mU/min), selon un ratio de 1:1. Une analyse selon l'intention de traiter a été effectuée.

Résultats : Au total, 252 femmes ont été repérées et abordées. Parmi celles-ci, 137 (54,4 %) ont accepté de participer à l'étude, et 79 (31,3 %) ont fait l'objet d'une répartition aléatoire. L'adhésion globale au protocole était de 76 femmes sur 79 (96,2 %). Dix

femmes (25,6 %) du groupe graduel ont subi une césarienne, de même que six femmes (15,0 %) du groupe accéléré (test exact de Fisher, $P = 0,27$).

Conclusion : Cette étude pilote a montré qu'un ECR multicentrique de grande envergure est non seulement faisable, mais également nécessaire pour évaluer l'innocuité et l'efficacité d'un protocole accéléré de stimulation du travail en ce qui concerne le taux de césarienne et les indicateurs de morbidité maternelle et périnatale.

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INTRODUCTION

Oxytocin use for augmentation of labour in dystocia is widely practiced and is recommended by different national guidelines.[1–3] There is a wide range of oxytocin regimens in use. These regimens can be broadly categorized as accelerated oxytocin titration (AOT), commonly known as high-dose oxytocin, or gradual oxytocin titration (GOT), commonly known as low-dose oxytocin.

Three systematic reviews identified that AOT, for the management of dystocia, was associated with fewer CSs, shorter duration of labour, and more spontaneous vaginal deliveries compared with GOT.[4–6] Dystocia is an important and common obstetrical complication, associated with increased risk of maternal puerperal and neonatal infections,[7,8] and it is the leading indication for primary CS, accounting for almost one half of all CSs in nulliparous women.[9–11] CS, in turn, is associated with maternal and neonatal morbidity and their long-term health outcomes.[12–14] It is known that 80% of women who undergo a CS will have a repeat CS,[15] and that elective repeat CS accounts for approximately 40% of all CSs in Canada.[10] Therefore, implementation of an AOT protocol may provide a good strategy to reduce not only the morbidity associated with dystocia in nulliparous women, but also the rate of primary CS and subsequent elective repeat CS, along with the morbidity associated with CS.

Although AOT seems to be a promising strategy in reducing the rate of primary CS resulting from dystocia, all systematic reviews that provided this evidence have limitations.[4–6] In addition, there have been concerns about side effects of oxytocin administration because a full safety profile for AOT has yet to be developed.[16–18] For these reasons, a larger trial is needed to provide solid evidence of the effectiveness and safety of an AOT protocol. The primary objective of this double-masked pilot RCT was to provide information on the feasibility and acceptability of conducting a large multicentre trial on AOT versus GOT. A secondary objective was to collect outcomes of effectiveness and safety on both interventions.

ABBREVIATIONS

AOT	accelerated oxytocin titration
EFM	electronic fetal monitoring
FHR	fetal heart rate
GOT	gradual oxytocin titration

METHODS

This pilot study was a double-masked, parallel-group RCT comparing an AOT protocol with the currently used GOT for labour augmentation in nulliparous women who were diagnosed with dystocia in the first stage of labour. The trial was conducted between April 2012 and October 2013, in the birthing units of three Canadian academic teaching centers: The Ottawa Hospital (Ottawa, ON), CHU Sainte-Justine Hospital (Montréal, QC), and Kingston General Hospital (Kingston, ON). Ethics approval was obtained from each participating institution before the initiation of the trial (Ottawa Health Science Network Research Ethics Board Protocol No. 2011471-01H). Consent was obtained on admission to the birthing unit, and participants were randomized when eligibility for labour dystocia was met. Participants were not subject to any trial interventions before consent and the diagnosis of dystocia and randomization were completed. The trial was registered in clinicaltrials.gov (Accelerated Titration of Oxytocin for Nulliparous Patients With Labour Dystocia: ACTION Pilot Study; NCT01397630).

Inclusion and Exclusion Criteria

Women were eligible to participate if they were able to comprehend English and/or French, able to comply with study requirements, ≥18 years of age, nulliparous, carrying a singleton pregnancy with the fetus in a cephalic presentation at term (37+0 to 42+0 weeks of gestation), had a spontaneous onset of labour, and had no contraindications to a trial of labour or vaginal birth.

Eligibility criteria at the time of randomization included active labour, cervical dilatation <10 cm, ruptured amniotic membranes of at least 30 minutes, normal fetal heart rate pattern, and labour dystocia. Active labour was initially defined as the presence of regular uterine contractions, cervical dilatation ≥4 cm, and cervical effacement of at least 80% (cervical length <1 cm). After trial commencement, the inclusion criteria were modified to define the active phase as cervical dilatation of ≥3 cm to reflect the clinically