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Amniocentesis for threatened preterm labor with intact membranes and the impact on adverse outcome in infants born at 22 to 28 weeks of gestation

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ABSTRACT

Background: It remains unclear whether performing amniocentesis to detect intra-amniotic infection is useful for improving neonatal outcomes.
Aims: To determine the efficacy of amniocentesis on the neonatal outcomes in women exhibiting threatened preterm labor and intact membranes.
Study design: Retrospective cohort study
Subjects: A total of 174 women with threatened preterm labor and intact membranes at 22 to 33 weeks of gestation. Women with obvious clinical chorioamnionitis, multifetal pregnancy and/or major anomalies were excluded.
Outcome Measures: Neonatal short- and long-term outcomes
Results: Sixty-seven women underwent amniocentesis (Tap group), while the remaining 107 did not. The prevalence of a positive Gram stain or a positive culture result was 10% in the Tap group. The overall outcomes were not statistically different between the two groups, with the exception of borderline significance ($p = 0.052$) in long-term outcomes, favoring the Tap group. We performed a subgroup analysis focusing on infants born at 22–28 weeks of gestation. Consequently, the Tap group had better neonatal outcomes than the no-Tap group with respect to both short-term (OR 0.19, 95%CI 0.07–0.55) and long-term (OR 0.15, 0.05–0.46) outcomes. A multivariate analysis revealed that after adjusting confounding factors, the gestational age at delivery (OR 0.4, 0.3–0.7) and amniocentesis (OR 0.1, 0.02–0.3) remained significantly different.
Conclusions: Amniocentesis is useful for improving neonatal outcomes in infants born at 22–28 weeks of gestation to women exhibiting preterm labor and intact membranes.

1. Introduction

It is estimated that 25% to 40% of preterm births are due to chorioamnionitis [1], and chorioamnionitis is associated with higher neonatal morbidity and mortality, including long-term neurodevelopmental impairment, in preterm infants [2–5]. Therefore, amniocentesis is often used to diagnose intra-amniotic infection/inflammation based on the results of amniotic fluid cultures, Gram staining, and measurements of the white blood cell count, glucose concentration, and cytokine levels [6]. Although intra-amniotic infection/inflammation is associated with adverse neonatal outcomes, it remains unclear whether performing amniocentesis to detect intra-amniotic infection is useful for improving neonatal outcomes as a result of the paucity of clinical trials. Hence, it has been reported that there is no evidence to support the routine use of amniocentesis to detect intrauterine infection in women exhibiting preterm labor with or without membrane rupture [7]. However, there have been significant improvements in neonatal intensive care within the last decade, and the intact survival rate of extremely premature infants has increased. Therefore, we sought to evaluate the effects of amniocentesis on the neonatal outcomes in women with threatened preterm labor and intact membranes.

2. Materials and methods

This study was approved by the ethics committee of the University of Miyazaki, Faculty of Medicine. Informed consent was obtained from all women prior to undergoing amniocentesis.

The study protocol is depicted in Fig. 1. We enrolled 1,690 women who were admitted to and delivered at the University of Miyazaki Hospital between 2007 and 2012. Among them, we diagnosed 260 women as having preterm labor and intact membranes at 22 to 33 weeks of gestation. Patients with obvious clinical chorioamnionitis ($n = 1$), multifetal pregnancy ($n = 82$), and major fetal anomalies ($n = 3$)

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were excluded, and the remaining 174 women were included as study subjects.

The 174 women demonstrated regular uterine contractions at intervals of 10 min or more, with or without cervical dilatation. No patients displayed apparent clinical signs of intrauterine infection, such as a maternal temperature of ≥38 °C, maternal tachycardia of ≥100 beats/min, uterine tenderness, a maternal white blood cell count of ≥15,000/mm^3, or foul-smelling vaginal discharge [8].

We offered transabdominal amniocentesis to all women in preterm labor with intact membranes before 34 weeks' gestation. We performed amniocentesis (Tap) after obtaining informed consent, unless other comorbid conditions were present. The major reason for inclusion in the no-Tap group was the placental position ($n = 50$). Since there were no clinical signs of chorioamnionitis, we balanced the risk of placental trauma over the benefits of the procedure. Other reasons included infection ($n = 13$), advanced labor ($n = 11$), relatively large bag protrusion into the vagina ($n = 14$), and the attending physician's choice ($n = 19$). As a result, 67 women were allocated to the Tap group and the remaining 107 women were allocated to the no-Tap group.

Amniotic fluid was cultured to detect aerobic and anaerobic bacteria. Mycoplasma and Ureaplasma species were not cultured due to technical difficulties in our laboratory at the start of the study. The glucose concentration (<15 mg/dL), Gram staining findings, and white blood cell count (>2/high-power field on microscopy) were evaluated (6). When Gram staining was positive for bacteria or fungi, we diagnosed the patient with chorioamnionitis and terminated the pregnancy via labor induction or Cesarean section. When Gram staining was negative, or in the no-Tap group, we started tocolytic agents. We first administered 50 μg/min of ritodrine intravenously, which was titrated to a maximum dose of 200 μg/min. When ritodrine was not sufficient to reduce uterine contractions, we added magnesium sulfate at a rate of 1–2 g/h. Tocolytic agents were stopped when the regular uterine contractions had subsided for more than 24 h.

We did not basically administer antenatal corticosteroids based on the protocol of other studies. After the end of the study in 2012, we routinely administered steroid to women with threatened preterm labor between 24 and 34 weeks of gestation, and five of these women were included in this study (Table 1).

Neonatal intensive care specific for gestational age was provided to all newborns. Infants born to mothers with positive Gram staining were treated with higher doses of antibiotics, while the remaining neonates were given routine antibiotics (ampicillin: 100 mg/kg, and amikacin sulfate: 7.5 mg/kg). Antifungal antibiotics (fluconazole) were also given routinely to all infants.

The two groups were compared with respect to neonatal early-onset sepsis, short- and long-term outcomes, and placental pathology. Since the incidence of an adverse neonatal outcome was gestational age dependent, we divided the infants into two subgroups: those born at

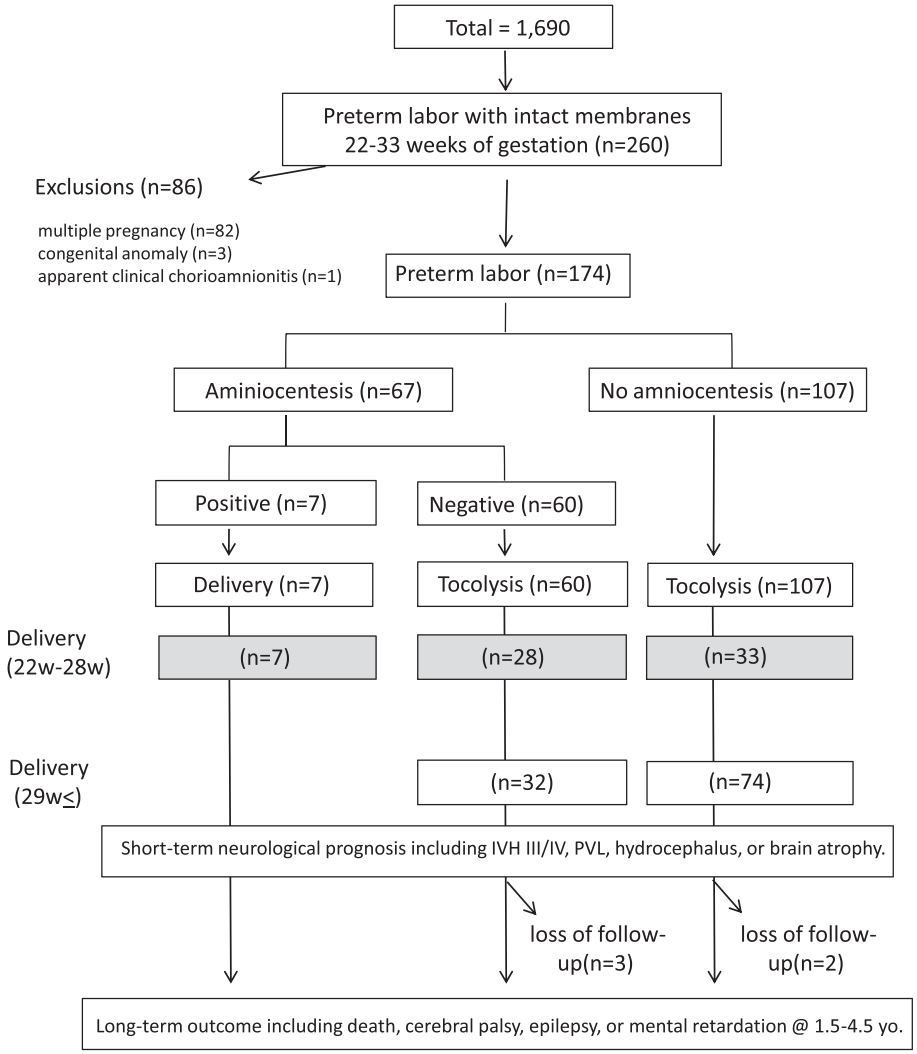

Fig. 1. Flow chart of the study.