OBSTETRICS WORLD PREMATURITY DAY

Transabdominal amnioinfusion for preterm premature rupture of membranes: a systematic review and metaanalysis of randomized and observational studies

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OBJECTIVE: The purpose of this study was to review systematically the efficacy of transabdominal amnioinfusion (TA) in early preterm premature rupture of membranes (PPROM).

STUDY DESIGN: We conducted a literature search of EMBASE, MEDLINE, and ClinicalTrials.gov databases and identified studies in which TA was used in cases of proven PPROM and oligohydramnios. Risk of bias was assessed for observational studies and randomized controlled trials. Primary outcomes were latency period and perinatal mortality rates.

RESULTS: Four observational studies (n = 147) and 3 randomized controlled trials (n = 165) were eligible. Pooled latency period was 14.4 (range, 8.2–20.6) and 11.41 (range −3.4 to 26.2) days longer in the TA group in the observational and the randomized controlled trials, respectively. Perinatal mortality rates were reduced among the treatment groups in both the observational studies (odds ratio, 0.12; 95% confidence interval, 0.02–0.61) and the randomized controlled trials (odds ratio, 0.33; 95% confidence interval, 0.10–1.12).

CONCLUSION: Serial TA for early PPROM may improve early PPROM-associated morbidity and mortality rates. Additional adequately powered randomized control trials are needed.

Key words: amnioinfusion, latency period, oligohydramnios, PPROM, pulmonary hypoplasia

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Preterm premature rupture of membranes (PPROM) complicates approximately 3% of all pregnancies.[1] It is a major cause of neonatal death and morbidity, primarily because of preterm birth. Lack of amniotic fluid may lead to pulmonary hypoplasia, infection, and restrictive joint deformities. Chorioamnionitis negatively affects neonatal prognosis at all gestational ages and warrants prompt delivery. The standard management approach to mid-trimester PPROM includes antibiotic treatment[2] and corticosteroids[3] to accelerate fetal lung maturity between 24 and 32 weeks of gestation.[4] Delivery is warranted if there is clinical evidence of chorioamnionitis or fetal distress. Termination of pregnancy may be offered for previable PPROM (<22-23 weeks of gestation) because of the poor prognosis. Despite the relatively high frequency of this condition, controversy regarding the optimal management persists.

★ EDITORS' CHOICE ★

In recent years, attempts to decrease neonatal mortality and morbidity rates were undertaken with different strategies that included intracervical fibrin application,[5] amniopatch,[6] fetal endoscopic tracheal occlusion,[7,8] antioxidant treatment,[9] gelatin sponge,[10] and progesterone treatment.[11] None of these strategies have proved to be consistently effective, reproducible, or applicable for most centers.

Amnioinfusion or instillation of physiologic solution into the amniotic cavity was attempted initially to reduce intrapartum variable decelerations.[12] Later, it was suggested as a treatment modality to prolong the latency period and prevent the oligohydramnios-related sequelae in cases of early PPROM.[13,14] Both transcervical[15,16] and transabdominal[14] routes have been attempted. One of the hypothetic disadvantages of the transcervical route is the nonsterile environment through which the infusion catheter passes, therefore increasing the risk of the introduction of infectious organisms from the vaginal flora into the amniotic sac. Transabdominal amnioinfusion (TA) theoretically surmounts this pitfall. Several articles have described serial TA as a plausible treatment modality to prolong the latency period between rupture of membranes and birth.[17] Recently, a Cochrane review assessed the efficacy of TA for PPROM with the use of data from 2 randomized trials and concluded that the small number of subjects in those studies precluded a definitive answer in regards to the efficacy of the intervention.[18] However, additional data are available from observa-

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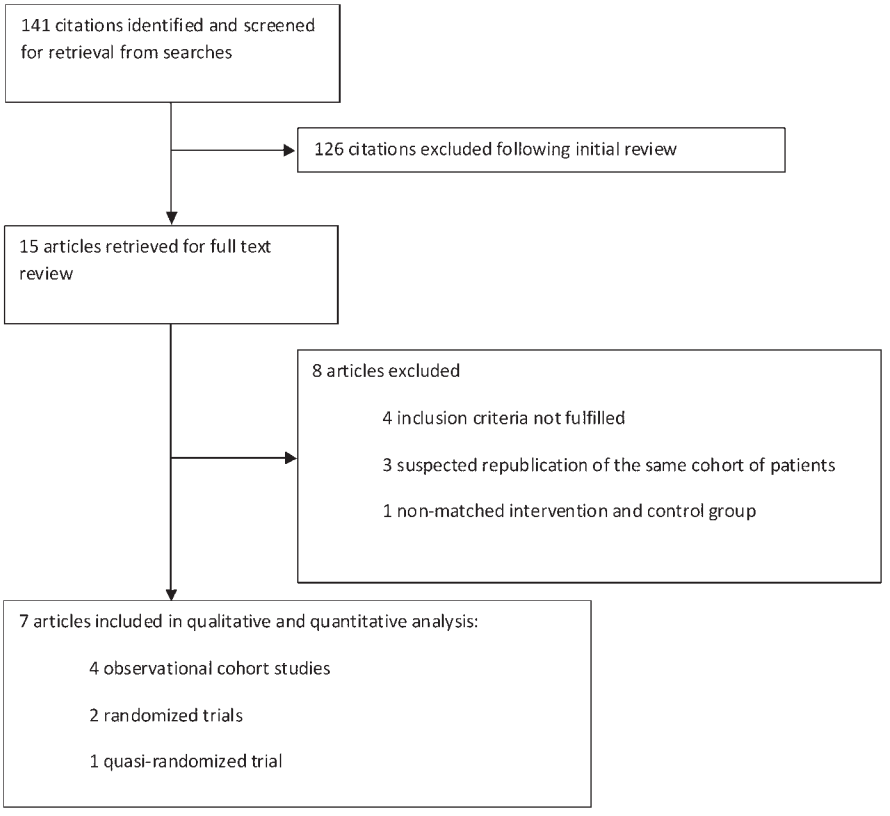
FIGURE 1
Study selection process



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tional studies of TA that can shed further light on this topic.

Our objective was to review systematically and metaanalyze studies that have assessed efficacy and safety of TA in women with PPROM. This systematic review provides results of separate qualitative and quantitative analyses of randomized controlled trials (RCTs) and observational studies.

METHODS

Search strategy

We performed a comprehensive literature search, assisted by an experienced librarian, using the MEDLINE from 1950 to December 2011 and EMBASE from 1980 to December 2011. We also searched the ClinicalTrials.gov database for studies that finished recruitment. We used the terms *fetal membranes, premature rupture, rupture, membrane*, pregnancy, amnioinfus*, premature fetus membrane rupture,* and *amnioinfusion*. There were no language or geographic restrictions. Bibliography of identified articles was used to screen for additional related articles.

Study selection

We included both comparative observational and RCTs in which TA and conventional treatment were compared with conventional treatment alone. Case reports, case series, and abstract publications were excluded. Studies that included patients with a confirmed diagnosis of PPROM-associated oligohydramnios were included. Studies that included oligohydramnios from other causes (eg, intrauterine growth restriction, renal anomalies) were excluded. Two reviewers (S.P. and H.A.) independently evaluated studies for inclusion; disagreements were resolved through consensus among the authors.

Outcome measures

The primary outcomes of interest were latency period (interval from PPROM to birth) and perinatal death. Secondary outcomes of interest were pulmonary hypoplasia, neonatal death, gestational age at birth, birthweight, chorioamnionitis, early onset (<72 hours from delivery) neonatal sepsis, bronchopulmonary dysplasia, and cesarean delivery. Two investigators (S.P. and H.A.) independently abstracted the relevant data from selected articles.

Assessment of risk of bias

Risk of bias in observational studies was assessed with the Newcastle-Ottawa scale[19] and in RCTs with the Cochrane collaboration's tool.[20] For observational studies, the domains of assessment included selection, comparability, and outcome assessment biases. For RCTs, the domains included selection, performance, detection, attrition, reporting, and other biases. Two investigators (S.P. and H.A.) independently assessed risk of bias; discrepancies were resolved through discussion and involvement of third author.

Data extraction

Data were extracted in duplicate from published reports by 2 authors who used a standardized data collection form. A third reviewer was consulted in case of disagreement between the 2 data extractors; discrepancy was resolved by consensus. We did not contact authors for missing information. For continuous outcomes, means and standard deviations were obtained from studies. When they were not reported, they were calculated from range, median, and sample size according to the method described by Hozo et al.[21] For categoric outcomes, event rates were obtained.

Statistical analysis

Statistical analyses were performed with the Review Manager (RevMan) software (version 5.1.4; The Nordic Cochrane Centre, København, Denmark). Metaanalyses were performed separately for cohort studies and the RCTs. Where data were sufficiently homogenous, metaanalysis was conducted with the use of a random effects model, with weighting of studies according to the DerSimonian-Laird method. Random-effect model was used to account for between and within study heterogeneity. Cochran's Q