STUDY PROTOCOL

Official Title:
Novel Use of Central Venous Pressure (CVP) Set With McDonald Cerclage Technique for Amnioinfusion in Preterm Premature Rupture of Membranes Improves Amniotic Fluid Index and Neonatal Outcomes

Protocol Number: AMNIO-PPROM-001
NCT Number: Not Yet Assigned
Document Date: 2 January 2021

Principal Investigator: Herlambang Herlambang
Institution: Faculty of Medicine and Health Science Universitas Jambi / Raden Mattaher General Hospital Jambi

Objective

To compare the effectiveness of CVP-set amnioinfusion combined with the McDonald cerclage technique versus conventional transabdominal amnioinfusion in restoring amniotic fluid volume and improving maternal, pregnancy, and neonatal outcomes among women with PPROM and oligohydramnios.

This study protocol was approved by the Faculty of Medicine Ethics Committee Review Board, Universitas Jambi. Written informed consent was obtained from all participants prior to enrollment. All procedures involving human participants were conducted in accordance with the ethical standards of the institutional research committee and the principles outlined in the Declaration of Helsinki (Approval No: 3069/UN21.8/PT.01.04/2021).

Study Design Research Subjects

This study was designed as a prospective, two-arm, comparative interventional study conducted between January 2021 and November 2024. The study was carried out in a tertiary referral hospital setting, where facilities for high-risk pregnancy management and neonatal care were available. A total of 40 pregnant women diagnosed with preterm premature rupture of membranes (PPROM) between 24 and 26 weeks of gestation, accompanied by oligohydramnios (amniotic fluid index [AFI] <2 cm), were recruited after fulfilling eligibility criteria.

Study Population and Allocation

Participants were recruited consecutively from antenatal clinics and emergency obstetric admissions. After obtaining informed consent, participants were allocated into two groups based on procedural feasibility and operator availability: the CVP-set amnioinfusion group (case) and the serial amnioinfusion group (control). Although randomization was not performed due to logistical limitations, efforts were made to ensure comparability between groups in terms of baseline characteristics such as maternal age, parity, and gestational age at diagnosis.

Baseline assessments included detailed obstetric history, physical examination, and ultrasound evaluation. The diagnosis of PPROM was established through clinical history of fluid leakage, sterile speculum examination demonstrating pooling of amniotic fluid, and ultrasonographic findings of reduced amniotic fluid volume. In selected cases, adjunctive tests such as nitrazine testing or fern pattern examination were used to support the diagnosis.

Eligibility Criteria

The primary aim of this study was to evaluate the effectiveness of amnioinfusion using a CVP set compared to serial amnioinfusion, both followed by cerclage, in relieving oligohydramnios and improving neonatal outcomes in mid-trimester PPROM (24–26 weeks gestation).

Inclusion criteria consisted of women with singleton pregnancies diagnosed with PPROM and oligohydramnios (AFI <2 cm) within the specified gestational age range. Exclusion criteria included the presence of uterine contractions, clinical or laboratory signs of intrauterine infection, and pregnancy complications requiring immediate termination, such as hypertension, preeclampsia, HELLP syndrome, or other significant maternal conditions.

Intervention Procedures

Serial Amnioinfusion

Under sterile conditions, and with ultrasound guidance, an 18-gauge needle was inserted into the intra-amniotic cavity following local anesthesia. After confirming correct placement by aspirating a small amount of fluid, 500–750 mL of Ringer's lactate solution was infused manually. Antibiotic prophylaxis (cefotaxime 1 gram) and corticosteroids (10 mg) were administered, followed by cervical cerclage. The procedure was repeated weekly if oligohydramnios persisted or recurred.

CVP-Set Amnioinfusion

In the intervention group, a central venous pressure (CVP) set was used to enable controlled and continuous infusion of fluid into the amniotic cavity. This technique allowed for gradual and regulated delivery of fluid, potentially improving retention and minimizing rapid leakage. The infusion rate was adjusted according to maternal tolerance and uterine response, under continuous ultrasound monitoring.

Peri-Procedural Management

All participants received prophylactic antibiotics according to institutional protocols to reduce the risk of ascending infection. Maternal monitoring included regular assessment of vital signs, uterine activity, and laboratory parameters such as leukocyte count and inflammatory markers when indicated. Fetal well-being was evaluated through serial ultrasound examinations and cardiotocography where feasible. Post-procedure, patients were observed for at least 24–48 hours for complications, including uterine contractions, vaginal bleeding, and signs of chorioamnionitis. Tocolytic therapy was administered when necessary, and corticosteroids were considered to promote fetal lung maturity based on gestational age and clinical condition.

Follow-Up and Outcome Assessment

Participants were followed weekly or more frequently depending on clinical condition. At each visit, AFI measurements were performed using standardized ultrasound techniques. The need for repeat amnioinfusion was determined based on persistent or recurrent oligohydramnios. The primary outcome of the study was the degree of increase in AFI following intervention. Secondary outcomes included gestational age at delivery, neonatal birth weight, Apgar scores, and maternal length of hospital stay. Additional observations included procedural feasibility, maternal tolerance, and complication rates.

Delivery Management

The timing and mode of delivery were determined based on standard obstetric indications. In the absence of complications, expectant management was continued to prolong pregnancy. However, delivery was indicated in cases of intrauterine infection, non-reassuring fetal status, or onset of active labor. Mode of delivery (vaginal or cesarean section) was decided based on clinical judgment and obstetric indications.

Data Collection and Quality Control

All data were recorded prospectively using standardized case report forms. Ultrasound measurements were performed by experienced clinicians using consistent techniques to minimize inter-observer variability. Data were subsequently entered into a secure database for analysis.

Statistical Analysis Plan (SAP)

The primary outcome was the degree of AFI increase. Secondary outcomes included gestational age at delivery, neonatal birth weight, Apgar scores, and maternal length of stay. Statistical analysis was performed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro–Wilk test and expressed as mean ± standard deviation (SD). Independent sample t-tests were used to compare continuous variables between groups. A p-value of <0.05 was considered statistically significant. Missing data were handled conservatively, and incomplete cases for primary outcomes were excluded from final comparative analysis. Sensitivity analyses were conducted where appropriate to ensure the robustness of results.

INFORMED CONSENT FORM

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Protocol Number	AMNIO-PPROM-001
Ethics Approval Number	3069/UN21.8/PT.01.04/2021
Ethics Committee	Faculty of Medicine Ethics Committee Review Board, Universitas Jambi
NCT Number	Not Yet Assigned
Document Date	2 January 2021
Principal Investigator	Herlambang herlambang
Institution / Hospital	Faculty of Medicine and Health Science Universitas Jambi, Raden Mattaher General Hospital Jambi
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Invitation to Participate

You are invited to participate in a research study involving pregnant women diagnosed with preterm premature rupture of membranes (PPROM) accompanied by a very low amount of amniotic fluid (oligohydramnios). Before deciding whether to participate, please read the following information carefully. You may ask the research team any questions about the study before making your decision. Participation in this study is voluntary.

Purpose of the Study

The purpose of this study is to compare the effectiveness of amnioinfusion using a central venous pressure (CVP) set combined with the McDonald cerclage technique with conventional transabdominal amnioinfusion in restoring amniotic fluid volume and improving maternal, pregnancy, and neonatal outcomes among women with PPROM and oligohydramnios. The study involves 40 pregnant women with PPROM occurring between 24 and 26 weeks of gestation and an amniotic fluid index (AFI) of less than 2 cm.

Study Procedures

If you agree to participate and meet the eligibility criteria, you will undergo an initial assessment that includes obstetric history, physical examination, and ultrasound evaluation. The diagnosis of PPROM will be assessed using clinical history, sterile speculum examination, and ultrasound examination. Additional diagnostic tests may be performed when clinically indicated.

1. CVP-Set Amnioinfusion

A central venous pressure (CVP) set will be used to provide controlled infusion of fluid into the amniotic cavity. The infusion will be performed with ultrasound monitoring, and the infusion rate will be adjusted according to maternal tolerance and uterine response.

2. Conventional Transabdominal Amnioinfusion

Under sterile conditions and ultrasound guidance, an 18-gauge needle will be inserted into the amniotic cavity after local anesthesia. After correct placement is confirmed, 500-750 mL of Ringer's lactate solution will be infused. The procedure will be followed by appropriate obstetric management, including cervical cerclage as specified in the study protocol.

All participants will receive appropriate peri-procedural management according to institutional protocols. Maternal condition and fetal well-being will be monitored during and after the procedure.

Follow-Up

You will be followed regularly according to your clinical condition. Ultrasound examinations will be performed to assess the amount of amniotic fluid. Maternal and fetal conditions will also be monitored throughout follow-up. The study will evaluate changes in amniotic fluid index (AFI), gestational age at delivery, neonatal birth weight, Apgar scores, maternal length of hospital stay, procedural feasibility, maternal tolerance, and complications.

Possible Risks and Discomforts

Amnioinfusion and the associated obstetric procedures may involve discomfort and potential complications. Participants will therefore be monitored for uterine contractions, vaginal bleeding, signs of infection including chorioamnionitis, and other maternal or fetal complications. Participants will be observed following the procedure, and appropriate medical management will be provided when clinically indicated. The study protocol specifies post-procedure observation for at least 24-48 hours.

Possible Benefits

The procedure may help restore or maintain amniotic fluid volume. However, improvement cannot be guaranteed for an individual participant. Information obtained from this study may contribute to a better understanding of the management of oligohydramnios associated with PPROM.

Voluntary Participation and Right to Withdraw

Your participation is voluntary. You may choose not to participate or may withdraw from the study at any time without affecting your right to receive appropriate medical care.

Confidentiality

Information collected during this study will be handled confidentially. Research data will be recorded and stored for analysis, and participants will not be personally identified in reports or publications resulting from this study.

Questions About the Study

If you have questions about this research, the procedures, or your rights as a research participant, please contact:

Principal Investigator: Herlambang Herlambang

Institution: Faculty of Medicine and Health Science Universitas Jambi, Raden Mattaher General Hospital Jambi

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Statement of Consent

I have read or have had explained to me the information provided above. I have had the opportunity to ask questions about the study, and my questions have been answered satisfactorily.

I understand the purpose and procedures of the study, as well as the possible risks and benefits. I understand that participation is voluntary and that I may withdraw from the study at any time without affecting my medical care.

By signing below, I voluntarily agree to participate in this study.

Participant Name: _____

Participant Signature: _____

Date: _____

Researcher/Person Obtaining Consent: _____

Signature: _____

Date: _____

Witness (if applicable): _____

Signature: _____

Date: _____