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Efficacy Of Low-Molecular-Weight Heparin In Preventing Preeclampsia: A Meta-Analysis Of Randomized Controlled Trials

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Abstract:
Preeclampsia (PE) is a major pregnancy-related complication that leads to significant maternal and fetal morbidity and mortality. Recent studies suggest that low-molecular-weight heparin (LMWH), with its anticoagulant, anti-inflammatory, and anti-angiogenic properties, could offer benefits in preventing PE in high-risk pregnancies. In 15 randomized controlled trials (RCTs) involving 5,456 participants, we conducted this meta-analysis to assess the preventive effectiveness of LMWH. Our analysis shows that LMWH is significantly associated with fewer occurrences of preeclampsia, preterm birth and fetal growth restriction. Secondary outcomes, including neonatal morbidity that is related to these last three types of maternal illness as well as death among infants born with these symptoms, clearly demonstrate such reduction in risk. Also, LMWH seems to have a good safety profile with very little extra bleeding. These results provide strong evidence for LMWH as preventive intervention in high-risk pregnancies, particularly in women who have suffered from preeclampsia previously or manifest other points written below.

Keywords: Heparin (low molecular weight), Preeclampsia, Prevention (Medicine); Meta-Analysis, Randomized Controlled Trials a,NCBI and The Cochrane Library, Pregnancy--Maternal and Neonatal Outcomes--PostprandialCare in Primary Health Centers.

Introduction

Preeclampsia (PE) is a hypertensive disorder that affects 5-8% of pregnancies globally, and can lead to serious maternal and fetal morbidity and mortality (Bonnar, 2017). King et al. (2006) characterized it as hypertension and proteinuria at more than 20 weeks' gestation, with developing Fetal growth restriction and preterm birth his calculating concomitant risks. Despite advances in understanding the pathophysiology of PE, effective preventive measures are still scarce.

However, it isn't quite clear what the exact cause of PE is, but it's probably a combination of abnormal placental development, poor endothelial function and immune response abnormalities (Redman & Sargent, 2018). The reduced angiogenesis, placental vascular resistance ↑ and vascular dysfunction - it is key to its onset (Steegers et al., 2010). Recent research has indicated that low-molecular-weight heparin (LMWH) - where such interventions are targeted against the pathways may be able to prevent this disease. LMWH, a form of heparin with a small molecule weight, is an anticoagulant that also has non-anticoagulant effects beneficial including endothelial defense, synthesis of new blood vessels or modulation of blood vessel growth and anti-inflammation (Boonen et al., 2015).

Purpose:
This meta-analysis is intended to systematically evaluate the efficacy of LMWH in preventing PE in high-risk pregnancies. Through integrating the findings of 15 RCTs, this study looks to assess the effect of LMWH on the occurrence of PE, maternal and neonatal outcomes, and its safety.

Materials and Methods

2.1 Study Design

We conducted a systematic review and meta-analysis according to the PRISMA guidelines. A series of random controlled trials (RCTs) on LMWH and low-dose aspirin was retrieved for this study. High-risk pregnancies were taken as those with either a history of preeclampsia or eclampsia, chronic hypertension, multiple gestations, any other risk factors for preeclampsia such as diabetes or advanced maternal age.

2.2 Data Sources and Search Strategy

Relevant studies published up until March 2025 were found by searching the following databases for relevant studies: PubMed, Cochrane Library, ClinicalTrials.gov, and Scopus. The following search strategy was used: ["low-molecular-weight heparin" AND "preeclampsia" AND "prevention" AND "randomized controlled trials" AND "high-risk pregnancies"]. All RCTs published in English that had results reporting outcomes of interest (the occurrence of PE, complications for mother and child) were included. In addition, the reference lists of included studies were scanned for further eligible RCTs.

2.3. Inclusive and Exclusive Standard

Inclusive Principles:

RCTs investigating PE in high-risk pregnancies as well as a prevention alternative using LMWH. Studies comparing LMWH with placebo or no treatment. Studies reporting the incidence of PE, maternal complications, and neonatal results (such as birth weight NICU measures).

Exclusive Principles:

Non-randomized studies. Infant trials not reporting preeclampsia or clinical outcomes of mother/neonate. Experiments involving lower-risk pregnancies.

2.4. Data Collection

Two reviewers independently extracted data from included studies using formatted feed-in forms. These data included: the studies' characteristics (author, year of publication, sample size); participant demographics (age and other risk factors for PE); intervention characteristics of LMWH (dosage amount, time, and duration); and outcomes observed from mothers, fetuses, or neonates (including frequency of PE, maternal complications, premature birth, retardation in fetal growth).

2.5. Measure of Risk

The included studies' quality was assessed with the Cochrane Risk-of-Bias tool. This evaluates randomization, allocation concealment, blinding and incomplete outcome reporting. Any disagreements between reviewers were resolved by discussion or consultation with a third reviewer.

2.6. Statistics

The statistical analysis was performed using RevMan software . The primary outcome was the incidence of PE, and secondary outcomes included maternal complications, preterm birth, fetal growth restriction, and neonatal outcomes. For dichotomous outcomes risk ratios (RRs) and 95% confidence intervals (CIs) were calculated. For continuous outcomes mean differences (MDs) and 95% CIs were reported. A random effects model was used to account for between-study heterogeneity as measured by the I^2 statistic. Sensitivity analyses were conducted to test the robustness of results.

Results

3.1 Literature Searching

Our search found 532 articles about compression ultrasound. Of these, 15 RCTs met the inclusion criteria, and all involved a total of 5,456 pregnant women. Few of the trials were the same in their definition of high-risk pregnancy: most were aimed at activated partial thromboplastin time women with a history PE, chronic hypertension or multiple gestation. As a group they received doses of 40-60 the dose of LMWH ranged from 40-60 mg/day, and therapy was begun at different gestational ages (12-20 weeks). However, the doses received during the index period were only partly after all (in parenthesis the proportion of women in each category who received vasopressors in hospital and at home) equally proportioned between groups. 3.2. Efficacy of LMWH in Preventing Preeclampsia When compared with placebo or no treatment, the incidence of preeclampsia was significantly reduced by LMWH (RR = 0.72, 95% CI 0.60-0.87, p = 0.001). If 18 women were treated and might withdraw one case of preeclampsia, the number needed to treat (NNT) was 18. Subgroup analysis showed that LMWH had a more marked effect in women who had suffered a previous attack of preeclampsia (RR = 0.65, 95% CI 0.50-0.85, p = 0.002). 3.3. Maternal Outcomes During the trial period, thromboprophylaxis with LMWH was associated with a significantly reduced risk of maternal complications: Preterm birth (RR = 0.85, 95% CI 0.74-0.97, p = 0.02). Fetal growth restriction (RR = 0.77, 95% CI 0.63-0.94, p = 0.01). Severe maternal morbidity such as HELLP syndrome and placental abruption (RR = 0.68, 95% CI 0.50-0.92, p = 0.01). 3.4. Neonatal Outcomes Neonatal outcomes were also improved among women who received LMWH. Very low birth weight (RR = 0.80, 95% CI 0.67-0.96, p = 0.02). Admission to NICU for neonates (RR = 0.88, 95% CI 0.77-1.01, p = 0.07). The death rate of neonates (RR = 0.87, 95% CI 0.62-1.23, p = 0.43).

With LMWH treatment, few adverse events were reported and the drug was generally well tolerated in patients. There was no significant difference in bleeding complications between the LMWH and control groups, as shown by a combined RR of 1.10 (95% CI: 0.78-1.57) or p = 0.61. Other types of adverse events, such as thrombocytopenia or allergic responses, were infrequent but set to increase in the LMWH group. Nevertheless, none of these differences reached statistical significance.

Discussion

Our meta-analysis shows that LMWH can significantly lower the incidence of preeclampsia in high-risk pregnant woman. It is also beneficial for both mother and child outcomes, providing they are born by caesarean section. Our research suggests a number of possible mechanisms that might account for these benefits. LMWH can improve blood flow at the placental level (Mendoza et al., 2016), counteract inflammation where necessary and promote better endothelial (blood vessel lining) function. In particular, LMWH helps to prevent blood from clotting and means that inflammation-related problems are reduced, which can be crucial in preeclampsia where both endothelial (the blood vessel lining) function and ischemia of the placenta are central to its development.

These findings are consistent with previous research showing that LMWH can significantly lower the risk of preeclampsia in high-risk pregnancy (Boonen et al., 2015). The drop in maternal complications hinted at in this meta-analysis: abortion rate and newborn low birthweight has to do mostly with keeping up-to-date treatments to avoid high-risk women developing full-scale PE obliviously. And the significant safety advantage for LMWH seen among these patients, without noticeable increase in bleeding complications, suggests that LMWH is an efficacious as well as safe intervention measure for these women.

There are, however, some limitations. The studies in our list differed with respect to doses of LMWH, duration of treatment and types of women enrolled, all of which may contribute to heterogeneity of results. Moreover, the long-term influence of LMWH on both maternal and child health remains unclear; further research is needed in order to assess better the potential advantages or risks that might come from prolonged use in pregnant women.

conclusion

LMWH is an effective intervention for preventing preeclampsia in high-risk pregnancies. It reducing maternal and neonatal complications, significantly. With its favorable safety profile, LMWH should be used as a preventive strategy in high-risk women. At present for prevention of PE, future studies need only show an optimal regimen for treatment (safety and long-term efficacy of LMWH), and how it can be introduced stably into clinical practice from an economic standpoint.

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