Low molecular weight heparin and noninvasive prenatal testing

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INTRODUCTION

Noninvasive prenatal testing (NIPT) for fetal aneuploidies by massively parallel sequencing has emerged as a powerful tool in the management of high-risk pregnancies. It is vital that patients receive pre-test counseling about limitations of the test. Here we note a correlation between low molecular weight heparin, (LMWH), and non-reportable NIPT results.

METHODS

Maternal blood samples submitted to Sequenom Laboratories for MaterniT21® PLUS testing were subjected to DNA extraction, library preparation, and whole genome massively parallel sequencing as described by Jensen *et al*.[1]

RESULTS

During routine follow up of non-reportable results, we identified 47 instances (spanning a 3 year period) where feedback from clinicians revealed that the patients were taking LMWH. In 37 cases analysis of two independent aliquots from each patient revealed very low fetal fraction, GC bias failure, library preparation failure or total sequencing count failure. In most of these cases, another specimen draw had been requested and obtained, the results of which mimicked the original results. For 30 out of the 37 patients, the samples failed for insufficient fetal DNA. Samples from 7 patients had a technical failure 2 of these were due to insufficient DNA amplification. For 10 other patients known to be on LMWH, all quality metrics passed, and a result was issued. Of these 10 samples, 5 were redraws where the initial sample was non reportable.

CONCLUSIONS

Although it is unclear if LMWH use, or an underlying biological condition, is impacting NIPT results, it is important that providers are educated about maternal conditions and therapeutic agents that have the potential to confound results. Heparin is a known inhibitor of PCR, and prior reports have indicated that LMWH use could increase the risk for false positive results due to high GC bias[2]. We have had no documented false positives or false negatives in patients with known LMWH use. Providers should be aware that some laboratories may not monitor GC bias as a quality control metric before reporting results, which could lead to false positive results in addition to non-reportable results. Labs offering cfDNA testing should monitor both fetal fraction and GC bias to mitigate potential effects of LMWH. LMWH dosage, as well as maternal BMI could also explain why some samples fail while others do not. The timing of the NIPT draw in relation to LMWH treatment could also impact the ability to receive a reportable result; we recommend drawing cffDNA samples just prior to the next LMWH dose. While providers should be aware of the potential impact of LMWH or the underlying biological condition on NIPT results, LMWH in itself is not a contraindication to NIPT.

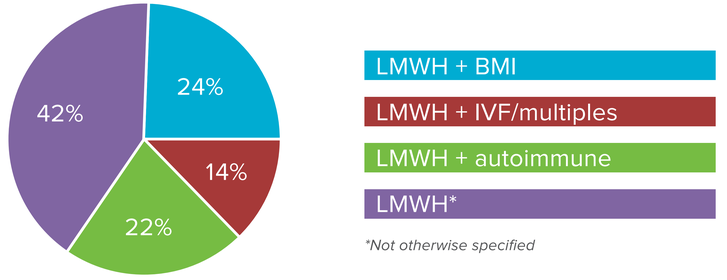
REFERENCES

1. Jensen TJ1, Zwiefelhofer T, Tim RC, et al. *High-throughput massively parallel sequencing for fetal aneuploidy detection from maternal plasma*. PLoS One. 2013;**8**(3):e57381. doi: 10.1371/journal.pone.0057381. Epub 2013 Mar 6.

2. Gromminger S, Erkan S, Schock U, et al. *The influence of low molecular weight heparin medication on plasma DNA in pregnant women*. Prenatal Diagnosis DOI: 10.1002/pd.4668 (2015)

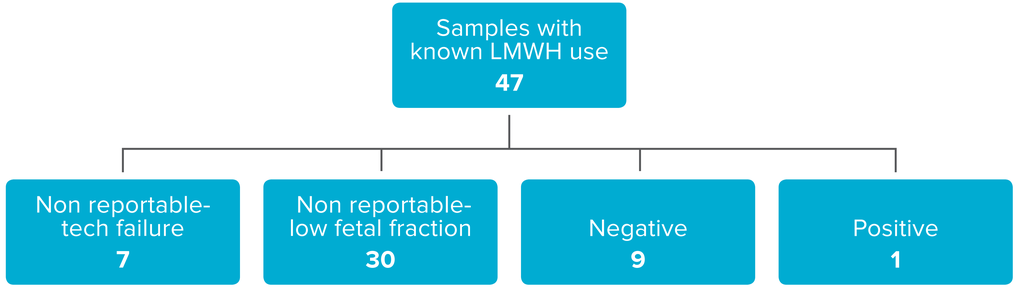
RESULTS

Samples with known LMWH use



*Not otherwise specified

Non-reportable samples with known LMWH use



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