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Commentary

Prenatal Testing is Made More Accessible by Enhancing Blood Collection, Transport, and Storage Conditions for Cell Free DNA

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Abstract

Circulating cell free foetal DNA (ccffDNA) from maternal plasma can be analysed molecularly to identify foetal mutations and chromosomal abnormalities. The goal of this extensive study was to examine and confirm the blood shipping and collecting circumstances that enable noninvasive prenatal testing. The effects of shipping and storage, specifically, on the stability and quantity of circulating cell-free DNA (ccfDNA) in Streck® Cell-Free DNATM Blood Collection Tubes (Streck BCTs, Streck, Omaha NE). These BCTs were tested for their ability to successfully prevent foetal ccf DNA from being diluted by maternal genomic DNA by minimising cellular degradation (Alfirevic Z et al., 2017).

INTRODUCTION

Fetal cells acquired through invasive procedures like amniocentesis and chorionic villus sampling are frequently analysed to find chromosomal, genetic, and biochemical abnormalities of the foetus. Invasive sampling techniques provide a modest but real risk of harm to both mother and foetus. Circulating cell-free foetal DNA (ccffDNA), which is present in maternal plasma, provides an alternative source of genetic material that faithfully reflects foetal state. It is believed that the placenta is the primary source of ccffDNA, and as a result, clearance of ccffDNA from maternal plasma occurs shortly after birth. Recent advancements in non-invasive prenatal testing (NIPT) techniques, including the genotyping of foetal RHDs from maternal plasma and the diagnosis of foetal aneuploidies in high-risk pregnant women, have been made possible by the use of ccffDNA. However, it is important to take precautions to minimise an increase in circulating maternal DNA following phlebotomy (by the lysis of maternal white cells), since this might hamper quantitative applications like non-invasive aneuploidy testing (FF). Across different gestational ages, typical foetal fractions range from 2% to 40%, making up a mean of 10% of the total ccfDNA (Sekizawa A et al., 2003).

The Fetal Quantifier Assay (FQA), which is used as the QC cut-off, measures the least foetal fraction at which Trisomy 21 may be accurately determined to be present at 4%. So, in circumstances of low starting foetal fraction, a slight increase in maternal DNA might lower the foetal fraction below the 4% QC cut off. Test findings below 4% FF would not be published. Strong and established blood collection instruments and processing techniques are necessary to enable a large population of moms to use non-invasive prenatal diagnostic technologies. Processing guidelines for maternal blood collected into standard EDTA Tubes call for cold storage of the blood samples followed by plasma preparation within 6 hours in order to retain high foetal fraction. Low speed centrifugation of maternal blood is the first step in the process of making plasma (Rigo-Bonnin R et al., 2019).

The plasma layer is then taken off and centrifuged more quickly to pellet any remaining plasma debris. Because it is laborious, plasma processing is only done at collection locations when it is absolutely essential owing to geography or other factors. The need for fast plasma processing for blood taken in conventional EDTA tubes, together with the related processing expenses at collection sites, would unduly restrict the availability of NIPT to a large

population. Ideal blood collection equipment would allow transportation of whole blood at room temperature (6–37 °C) and lengthen the processing time for plasma in order to address these issues. A system like that would make analysis and processing more centrally located. There are a number of alternatives to EDTA tubes for blood collection and plasma preparation for molecular diagnostics (Siekmann L, 2013).

There are three different tube types that may be used to preserve foetal fractions: tubes that are intended to physically separate cellular blood components from non-cellular blood components (using a gel plug or mechanical separator), tubes that contain reagents to keep maternal blood cells active and intact for a predetermined amount of time, and tubes that contain cell-preserving reagents. Streck recently unveiled and began selling the Streck Cell-Free DNA BCT, a tube containing cell-preserving agents to stop white blood cell degeneration (which would release maternal DNA) and limit nuclease-mediated DNA degradation for up to 14 days at room temperature (Streck BCTs).

When held at room temperature for a period of 72 hours, the concentrations of "short-fragment" ccffDNA from blood obtained Streck BCTs remained stable, according to research by Barrett and colleagues. However, after being kept in EDTA tubes for 72 hours, it was found that the amount of "long-fragment" (maternal) plasma DNA had increased. According to findings by Hidestrand et al., total plasma DNA levels in blood that was drawn into EDTA tubes and delivered with or without frozen ice packs rose after 72 hours. The level of total DNA is reported to be stable when whole blood in Streck BCTs is transported without ice packs (72 h), while it is observed to rise when shipped with frozen ice packs (Armbruster D, 2017).

CONCLUSION

In conclusion, the examination of Streck Blood Collection Tubes found that they offer a useful substitute for blood collection in EDTA Tubes. Up to 7 days following blood collection, Streck BCTs allow ambient shipping to a processing location. In order to execute complicated molecular testing of ccffDNA and enhance patient access to safer non-invasive prenatal testing (NIPT) techniques, these tubes and approved protocols for their usage and handling are needed.

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