Non-Invasive Prenatal Diagnosis (NIPD): Clinical applications in the early detection of fetal diseases. The case of thalassemia
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Introduction

Non-Invasive Prenatal Diagnosis (NIPD) is a low-risk genetic test carried out on a sample of maternal blood that allows for the detection of fetal defects and inherited diseases. However, fetal cells are usually scarce in the maternal circulation. To achieve an accurate diagnosis, they need to be enriched in order to isolate a sufficient amount of them.

One of the most common monogenic diseases is thalassemia, a hemoglobinopathy characterized by abnormal formations of hemoglobin. These include α- and β-globin mutations that result in the underproduction or even the absence of normal protein cells. These anomalies cause a variety of symptoms that may differ from one patient to another.

Objectives

- To develop, deepen and enhance specific scientific knowledge on NIPD for its evolution, its clinical applications, how it is said should be performed and the particular techniques and medical equipment usually involved in the testing process.
- To compose an accurate definition and a structured, research-based report on thalassemia, including a precise account of its types, world presence, and observable symptoms in order to determine the most suitable ways to detect and diagnose it.

Methodology

This paper is a literature review based on a guided online research in accordance with selected keywords: NIPD, Non-Invasive Prenatal Diagnosis and ‘thalassemia’. Retrieved medical databases were consulted (PubMed, ScienceDirect, Google Scholar) and papers were chosen according to their journal impact.

Results

Non-Invasive Prenatal Diagnosis

An accurate analysis of fetal material is crucial in order to perform an efficient prenatal diagnosis:

- **Intact fetal cells** that can be found in the maternal plasma:
  - Trophoblasts can be detected via the use of specific antibodies that are able to detect placental antigens. They usually are present in the maternal blood (and can therefore be isolated from it) during the first trimester of pregnancy only.
  - Leukocytes usually continue to circulate in the maternal blood long after pregnancy.
  - Nucleated red blood cells (NRBC) have a short half-life. They present an unmature, distinctive morphology.
  - Cell-free fetal DNA (cffDNA) originates in the placenta. It derives from the genetic material that is released after fetal cells undergo apoptosis or lysis, the latter being triggered by the mother’s immune system.
  - Cell-free fetal RNA (cffRNA) originates in active genes present in the placenta. It tends to appear in a smaller amount than cffDNA.

- Fetal DNA is then analyzed by screens for birth defects and inherited diseases.

NIPD stands out as a good screening prenatal test. If the results turn to be positive, it can then be followed by invasive procedures aiming to confirm the pathology.

- Usage of NIPD in the early detection of thalassemia is still going through an experimental phase. However, numerous research projects aiming to promote and spread NIPD procedures in clinical applications are currently being conducted.

- Thalassemia is confirmed to be one of the most common blood disorders. There exist two different types of this disease, each one of them entailing different levels of risk.

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Thalassemia

Most relevant diagnosis techniques:

- Fluorescent Immunohistochemistry (FHC) is a method for demonstrating the distribution of proteins in tissue sections. It is performed via specific antibodies that recognize the target protein.
- **Real-time PCR combined with fluorescence** testing is performed in order to determine whether a fetal globin chain is an ordinary or a mutated one.
- **PCR in two steps** is used when a paternal allele is concerned.
- **MPS** involves identifying single nucleotide differences in fractionated DNA in order to discriminate potential mutation points in the fetal genome.
- **Real-time quantitative PCR** is used to amplify, detect and/or quantify a targeted allele, be it a normal or a mutated one. Markers from paternal and maternal DNA are employed in the sample analysis.

- A well-trained genetic counselor who would be able to thoroughly explain the techniques, advice the couples and answer their questions stands out as a highly-recommended option.
- In order to respect the principle of autonomy, the women should be potentially tested need to be adequately informed before giving their consent.
- In order to respect the principle of justice, women should receive good medical care regardless of social, economic or ethnic reasons.

Bioethics

It is essential to have in consideration the legal framework of the country where the diagnosis is to be performed: in countries where abortion is an illegal practice, NIPD results could put pregnant women in a vulnerable, even dangerous position.

- In Spain, NIPD is being increasingly used in the private sector in order to detect Down’s syndrome and Edward’s syndrome.
- As for the future of non-invasive prenatal testing, studies show a tendency to implement the use of NIPD in the public health sector as well.
- A widespread practice of NIPD is thought to be followed by a decrease of invasive testing, resulting in a decline of miscarriage risks and improved safety for pregnant women.

Conclusions

- Non-Invasive Prenatal Diagnosis (NIPD) stands out as a good screening prenatal test. If the results turn to be positive, it can then be followed by invasive procedures aiming to confirm the pathology.
- Since it entails a simple blood test, NIPD emerges as a socially welcomed test.
- Thalassemia is confirmed to be one of the most common blood disorders. There exist two different types of this disease, each one of them entailing different levels of risk.
- Usage of NIPD in the early detection of thalassemia is still going through an experimental phase. However, numerous research projects aiming to promote and spread NIPD procedures in clinical applications are currently being conducted.

References