1. INTRODUCTION

miRNAs (miRNAs) are non-protein coding RNA molecules of about 22 nucleotides long, with an essential role in post-transcriptional regulation. They regulate various biological processes, including embryonic development, cell death and cell proliferation. It is predicted that more than 60% of our genes are targets of them.

There are many evidences that miRNAs play an important role in spermatogenesis. They follow specific expression patterns inside the testis and some of them are specifically expressed by each cell population.

2. OBJECTIVES

The main objectives of this review are:

To provide a broad vision of the pathology (NOA) and to describe miRNAs, their generation and their implications in spermatogenesis.

To describe a miRNA or a set of miRNAs present in seminal plasma that may predict the possibility of obtaining sperm from the testes of a patient with NOA.

To relate the alteration of the miRNA selected in the context of infertility.

3. METHODOLOGY

The methodology consisted on a bibliographic search.

The most used databases were PubMed and Google Scholar. The articles selected were published from 2010 onwards.

Some keywords used were: non-obstructive azoospermia, miRNAs, successful sperm retrieval, microTESE.

The most important reviews and articles were read and summarized.

4. RESULTS

There is a correlation between the probability of having a successful sperm retrieval in each histology and their number of deregulated miRNAs, the more deregulated miRNAs, the more difficult to obtain sperm. Considering this, these miRNAs could evaluate the possibility of having a successful sperm extraction.

<table>
<thead>
<tr>
<th>Histopathological pattern</th>
<th>Sertoli cell-only syndrome</th>
<th>Maturation arrest</th>
<th>Hypospermatogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm retrieval rates (%)</td>
<td>22.5 – 41</td>
<td>36 – 75</td>
<td>81 – 100</td>
</tr>
<tr>
<td>Deregulated miRNAs (n)</td>
<td>46</td>
<td>27</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 1. Sperm retrieval rates after performing microTESE and number of miRNAs deregulated according to testicular histology of patients with NOA.

Two studies have focused on the ability of some miRNAs to predict a successful sperm retrieval. The expression of some miRNAs was compared between NOA patients with a successful obtaining of sperm and NOA patients without it.

![Image](image-url)

Figure 1. miRNA biogenesis and mechanisms of action. The precursors molecules of miRNAs (pri-miRNA) are transcribed in the form of long hairpin structures by RNA polymerase II from intergenic or intragenic (miRISC) regions.

The nuclear Drosha-DGCR8 complex processes the pri-miRNA into an intermediate called pre-miRNA. This pre-miRNA is transported to the cytoplasm where is processed by Dicer-TBP resulting in a double-stranded miRNA of about 20 bp. This miRNA duplex is unwound, and only one strand associates with Argonaute (AGO) proteins to form the RNA-induced silencing complex (miRISC). miRISC, as a part of miRISC, binds to the 3’UTR of a target miRNA by complementarity and leads to its translational repression or degradation.

There are many evidences that miRNAs play an important role in spermatogenesis. They follow specific expression patterns inside the testis and some of them are specifically expressed by each cell population.

5. CONCLUSIONS

There is a lack of biomarkers to predict a successful sperm retrieval in patients with NOA, and miRNAs are good candidates since they have been demonstrated to play an important role in spermatogenesis.

One possible miRNA to predict a successful sperm retrieval before practicing the microTESE is miR-34c-5p. Its expression in seminal plasma is significantly different between NOA patients with and without sperm retrieval: miR-34c-5p and its family are involved in spermatogenesis, but their redundant functions with other miRNAs make it necessary to focus not only on this single miRNA, but a profile of miRNAs.

Non-obstructive azoospermia (NOA) is the most severe diagnosis in cases of male infertility, and it is caused by a severely impaired spermatogenic function of the testes. There are different histopathological patterns of NOA.

- Hypospermatogenesis: tubules with a very reduced population of germ cells, but they are present.
- Sertoli only syndrome: because of the spermatogenic maturation sequence.

In some NOA cases, a sperm retrieval can be done by microdissection testicular sperm extraction (microTESE) in order to fertilize oocytes through intracytoplasmatic sperm injection (ICSI). However, there is a lack of possible biomarkers of spermatogenesis for a non-invasive diagnosis before the microTESE.

Non-obstructive azoospermia is the process in which spermatogonial cells become haploid spermatocytes. It can be divided into 3 steps: meiosis I, meiosis II, and spermiogenesis.

6. BIBLIOGRAPHY