



Vaccine as a treatment for gonorrhea and its main impasses



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ABSTRACT

INTRODUCTION: Gonorrhea is a disease caused by the bacterium *Neisseria gonorrhoeae*, it is a sexually transmitted infection, which manifests itself between men and women, with varied symptoms, therefore, for the diagnosis it is necessary microscopic examinations, cultures or nucleic acid amplification tests and regarding the treatment, its first line is the association of ceftriaxone with azithromycin. **METHODOLOGY:** This is a literature review, whose databases were taken from the SciELO and PubMed data platforms. The research period was from July 2023, meeting the inclusion criteria, which were articles from the years 2000 to 2023, in Portuguese and English, online texts,

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and in full texts. The following health descriptors (DeCS) were used as strategies for better evaluation of the texts: "Treatment", "Gonorrhea" and "Vaccine". **DISCUSSION:** The bacterium *Neisseria gonorrhoeae* is responsible for the sexually transmitted infection (STI) known as gonorrhea. Gonorrhea can manifest as urethritis in men, cervicitis, or urethritis in women, and can also affect extragenital sites such as the pharynx, rectum, conjunctiva, and, in rare cases, systemically, in both sexes. Confirmation of the diagnosis requires microscopic examinations of Gram-stained specimens, bacterial cultures, or nucleic acid amplification tests. The recommended first-line treatment is single-dose systemic therapy, usually with injectable ceftriaxone and oral azithromycin. However, a major public health concern on a global scale is the emergence of high levels of antimicrobial resistance (AMR) in *N. gonorrhoeae*, which compromises the effectiveness of available treatments for gonorrhea. *Neisseria gonorrhoeae* has been a historical challenge for vaccine development, due to the expression of variable surface molecules and its ability to cause repeated infections without inducing protective immunity. Current control measures are clearly insufficient and are threatened by the rapid emergence of antibiotic resistance. Currently, gonorrhea is considered a "superbug" as there is no reliable monotherapy for empirical treatment. Antibiotic resistance has increased treatment costs and led to the need for surveillance programs to track the spread of resistant strains. **FINAL COMMENTS:** Thus, it is extremely important to start discussions about alternative treatments for diseases caused by bacteria and viruses, without a preventive treatment specified yet. In the case of gonorrhea, it is interesting to study more and more, studying the possibilities and main factors about the obstacles to the creation of the vaccine.

Keywords: Gonorrhea, Prophylactic Treatment, Vaccine.

INTRODUCTION

Gonorrhea is a disease caused by the bacterium *Neisseria gonorrhoeae*, it is a sexually transmitted infection, which manifests itself between men and women with varied symptoms, so for diagnosis it is necessary microscopic examinations, cultures or nucleic acid amplification tests and regarding treatment, its first line is the association of ceftriaxone with azithromycin. Due to the resistance of the bacterium to medications and its suitability to the human host, other therapeutic forms have been studied and in this field the vaccine for gonorrhea is a good option for this disease but also challenging due to the varied expression of surface molecules, currently there are studies for the development of an effective vaccine that induces an efficient immune response and that has a response by the multiple variants of the microorganism, so far there is no vaccine licensed for use in the general population, but GSK's gonorrhea vaccine is in the intermediate phase of clinical trials and will soon have the results about its effectiveness.

METHODOLOGY

This is a literature review, whose databases were taken from the SciELO and PubMed data platforms. The research period was from July 2023, meeting the inclusion criteria, which were articles from the years 2000 to 2023, in Portuguese and English, online texts, and in full texts. The following health descriptors (DeCS) were used as strategies for better evaluation of the texts: "Treatment", "Gonorrhea" and "Vaccine".

DISCUSSION

The bacterium *Neisseria gonorrhoeae* is responsible for the sexually transmitted infection (STI) known as gonorrhea. Gonorrhea can manifest as urethritis in men, cervicitis, or urethritis in women, and can also affect extragenital sites such as the pharynx, rectum, conjunctiva, and, in rare cases, systemically, in both sexes. Confirmation of the diagnosis requires microscopic examinations of Gram-stained specimens, bacterial cultures, or nucleic acid amplification tests. The recommended first-line treatment is single-dose systemic therapy, usually with injectable ceftriaxone and oral azithromycin. However, a major public health concern on a global scale is the emergence of high levels of antimicrobial resistance (AMR) in *N. gonorrhoeae*, which compromises the effectiveness of available treatments for gonorrhea.

Neisseria gonorrhoeae has been a historical challenge for vaccine development, due to the expression of variable surface molecules and its ability to cause repeated infections without inducing protective immunity. Current control measures are clearly insufficient and are threatened by the rapid emergence of antibiotic resistance. Currently, gonorrhea is considered a "superbug" as there is no

reliable monotherapy for empirical treatment. Antibiotic resistance has increased treatment costs and led to the need for surveillance programs to track the spread of resistant strains.

N. gonorrhoeae is highly adapted to its human host and its ability to evade host defense mechanisms and suppress immune responses is critical to its success as a pathogen. Most gonococcal infections affect the lower urogenital tract, such as urethritis or cervicitis, but the most serious complications occur in ascending infections in women.

In 2016, an international workshop promoted by NIAID discussed research into vaccines against gonorrhea. Current steps include modeling the impact of vaccination, identifying sites and logistics for clinical trials, antigen discovery, investigating immune responses in humans, testing animal models, and creating genomic databases. These steps aim to develop an effective vaccine against gonorrhea and tackle growing antimicrobial resistance.

A retrospective case-control study conducted in New Zealand showed that the group B meningocemia vaccine, known as MeNZB, was associated with a lower risk of gonorrhoea in adolescents and young adults (15-30 years). Compared to cases of chlamydia, the vaccine showed an estimated efficacy of 31% against gonorrhea in this group. However, the protection offered by the vaccine waned over time, and its effectiveness was lower (14%) in individuals who also had a chlamydia infection. These results are important because they are the first evidence in more than 40 years to suggest the possibility of vaccination against gonorrhea.

Among the challenges faced for the gonorrhea vaccine are the various host constraints that limit the ability of mice to fully mimic human infection. Some limitations of mouse models include the absence of human transferrin and lactoferrin, soluble negative regulators of the complement cascade (such as factor H and C4b-binding protein), and receptors for several known gonococcal adhesins and invasins (such as CEACAMs, C3R integrin, CD46, and the elusive penis receptor). However, transgenic mice are currently available that express these host-restricted factors. In addition, mouse models for pelvic inflammatory disease (PID) are being developed and should allow the investigation of immune responses and the efficacy of vaccines against upper reproductive tract infections.

The lack of long-lasting immunity after natural infection makes it difficult to develop a vaccine against gonorrhea. Repeated infections are common, and the presence of specific antibodies and the absence of blocking antibodies are associated with reduced upper reproductive tract infection in high-risk women. The presence of blocking antibodies reduces the effectiveness of antibodies against bacterial proteins, while the absence of these antibodies is considered a protective factor against gonorrhea.

Currently, research for the development of a vaccine against gonorrhea is ongoing, but it faces several challenges. The antimicrobial resistance of *Neisseria gonorrhoeae* has driven the need

for an effective vaccine. However, the complexity of the infection-induced immune response and the pathogen's ability to evade the immune system make vaccine development difficult.

Vaccination strategies are focusing on identifying effective immunogenic targets that can induce a protective immune response against gonorrhea. Some of the main potential targets include surface proteins, such as pilin and porin proteins, which play a crucial role in the adhesion and invasion of the bacteria.

In addition, advances in the understanding of the immune evasion mechanisms of *N. gonorrhoeae* have provided valuable insights to direct the immune response. Researchers are exploring approaches that aim to improve the adaptive immune response, including inducing specific T cell responses and producing neutralizing antibodies.

Another challenge is the antigenic variation of *N. gonorrhoeae*, which means that the vaccine needs to be able to provide protection against multiple strains and serotypes of the pathogen. Vaccination strategies are being explored to overcome this variation and ensure a comprehensive immune response.

Currently, several vaccine candidates are being tested in animal models and, in some cases, in early clinical studies. However, there is still a long way to go before a safe and effective gonorrhea vaccine is available for widespread use. Continued commitment to vaccine research and development is critical to addressing the global threat posed by gonorrhea and combating the associated antimicrobial resistance.

To date, there is no licensed vaccine available for the prevention of gonorrhea in 2023, however GSK's gonorrhea vaccine has received the "Fast Track" designation by the FDA, the agency that regulates drugs in the United States, this potential immunizer is currently in phase II clinical trials, which is an intermediate stage in the vaccine development process. The objective of this phase is to evaluate the effectiveness of the vaccine in healthy adults, aged between 18 and 50 years, who are at high risk of contracting the infection. The study began in November 2022 and involves approximately 750 volunteers from eight countries, including Brazil. This research is an important step in the development of a vaccine against gonorrhea, but more studies and tests are still needed to confirm its efficacy and safety.

FINAL CONSIDERATIONS

Thus, it is extremely important to start discussions about alternative treatments for diseases caused by bacteria and viruses, without preventive treatment yet specified. In the case of gonorrhea, it is interesting to study more and more, studying the possibilities and main factors about the obstacles to the creation of the vaccine.

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