



MULTI DRUG RESISTANT GONORRHOEA: WINNING BACK A LOST BATTLE

Clinical Research

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ABSTRACT

Gonorrhoea is a very ancient disease characterized by urethritis, epididymo orchitis and salpingitis sometimes leading to infertility in females. The disease used to be simply treated with penicillin and macrolides. However the emergence of drug resistant gonorrhoea means we are left with very few options to combat this scourge.

Since the first report of multi drug resistant gonorrhoea was reported in united kingdom , it has widely spread across continents. There are also two other multi drug resistant gonorrhoea has been reported in Australia. However newer antibiotics such as Zoliflodacin , solifenacin etc which are currently in trial phases 2 and 3 offer hopes of cure. This together with formulation of basic antibiotic use guideline will work to ensure gonorrhoea does not become untreatable sexually transmitted disease.

Development of multi drug resistance in gonorrhoea is a serious threat to the world at large and urgent research is needed at the cellular and subcellular level to control this infection. Countries and governments should work together to formulate comprehensive policies for such a disease.

KEYWORDS

INTRODUCTION

Gonorrhoea is a sexually transmitted disease (STD) in man that predominantly involves the genitourinary system with the potential to spread to virtually any system of the body if left untreated. Gonorrhoea is characterised by dysuria, pus discharge from urethral meatus and testicular pain. Women may present with vaginal discharge, vaginal bleeding and pelvic pain.^[1]

The causative agent of gonorrhoea is a Gram negative diplococcus *Neisseria gonorrhoea*. Pus culture from urethra and endocervical swab remains the mainstay of diagnostic aids throughout the world but newer diagnostic modalities like PCR is increasingly coming into play.^{[2][3]}

Gonorrhea affects about 0.8% of women and 0.6% of men.^[4] An estimated 33 to 106 million new cases occur each year, out of the 498 million new cases of curable STI – which also includes syphilis, chlamydia, and trichomoniasis.^{[5][6]} Infections in women most commonly occur when they are young adults. In 2015, it caused about 700 deaths.

A Brief History of Gonorrhoea

Gonorrhoea was originally referred to as the clap. This nickname came about because the person infected would feel a clapping sensation when urinating. There is also a few group of workers who feel that the word clap is derived from the word French word for brothels called les clapiers. Men who often visited these brothels frequently got this malady.^[7]

The bacteria responsible was first discovered by Albert Neisser, in 1879 who gave his name to this newly discovered bacteria.^[8]

Emergence of Multidrug resistant Gonorrhoea: An emerging threat

Gonorrhoea has progressively developed resistance to the antibiotic drugs prescribed to treat it. Following the spread of gonococcal fluoroquinolone resistance, the cephalosporin antibiotics were widely used to treat gonorrhoea. The emergence of cephalosporin-resistant gonorrhoea means we now have fewer antibiotic options left that are simple, well-studied, well-tolerated and highly effective.

Since the case reports of isolate strains of resistant *Gonococcus* started appearing across the world, various agencies, including the CDC Atlanta's the Gonococcal Isolate Surveillance Project has been monitoring U.S. antibiotic resistance trends in gonorrhea. Through the collaborative effort of selected STD clinics and their local laboratories,

regional laboratories, and CDC, GISP's collected data help monitor trends in Gonococcal resistance spread throughout the world and the United states.^[9]

High rates of penicillin, tetracycline, and quinolone resistance have long been detected and these medicines are currently not recommended for the treatment of gonorrhoea in the majority of countries in the world. Gonococcal resistance to third-generation cephalosporins given orally has emerged in Japan, Norway and elsewhere, with even wider spread of gonococci that have determinants for Cephalosporin resistance.^[10]

This emergence of decreased susceptibility of *N. gonorrhoeae* to the "last line" treatment option of cephalosporins together with resistance already shown to penicillins, sulphonamides, tetracyclines, quinolones and macrolides (including azithromycin) make *N. gonorrhoeae* a truly multidrug-resistant organism.^[10]

Multi drug resistant gonorrhoea – few anecdotal reports

In early 2018 Dr. Gwenda Hughes et al reported a case the case of multi-drug resistant gonorrhoea in UK which was resistant to azithromycin and ceftriaxone that has been successfully treated with ertapenam.^[11] Similar such reports have been coming from other parts of the world .Two cases of multi-drug resistant gonorrhoea infection have been detected in Australia. The emergence of this strain, resistant to ALL antibiotics that have been in routine use to treat gonorrhoea, is a major public health concern.^[12] Drug-resistant gonorrhoea exists in many countries, including Australia. However, these latest cases and a recent one in the United Kingdom, appear to be the first reported that are resistant to all of the antibiotics that have been in routine use against gonorrhoea. Many such cases continued to be reported across the world.

MDR gonorrhoea – is there a light at the end of tunnel?

The illicit, widespread and sometimes overuse of antibiotics has significantly contributed to the problem. A solution could be framing policies and guidelines about rational use of antibiotics. Each hospital should have its own antibiotic use policy and possible legislation curbing such use of antibiotic is the need of the hour. Three new candidate antibiotics show promise in the treatment of MDR gonorrhoea and include Zoliflodacin (currently completed phase II trial), Solithromycin (currently completed phase III trial) and Gepotidacin (currently completed phase II trial).^[13]

another new avenue which looks promising is a development of new

vaccine against gonorrhoea A vaccine for gonorrhea has been developed that is effective in mice.^[14] It will not be available for human use until further studies have been completed. Development of a vaccine has been complicated by the ongoing evolution of resistant strains and antigenic variation.

The sharing of surface antigen with *Neisseria meningitidis* makes the use of the available vaccine against *Neisseria meningitidis* plausible to develop cross protection against drug resistant gonorrhoea.^[15]

The development of antibodies against the surface receptors of gonorrhoea coccus holds promise in that it will prevent the attachment of the bacteria to the uroepithelial cells and hence infection. However, at present, the development of such antibodies is awaited.

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