Relevance Of Antibiotic Overuse: Covid 19: Super Gonorrhea: A Review

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ABSTRACT:
Uncontrolled use of antibiotics to treat Covid-19 has unfortunately led to a revolt in cases of super gonorrhoea, a sexually transmitted infection (STI) which may even become incurable. "Gonorrhea "superbug" had been reported by several countries, including France, Japan and Spain, and this year also in the UK and Australia. The WHO states that cases of gonorrhoea may become even more resistant to the most common recommended treatment like azithromycin. These are extensively drug-resistant gonorrhoea with high-level resistance to the current recommended treatment for gonorrhoea like (ceftriaxone and azithromycin) including resistance to penicillin, sulphonamides, tetracycline, fluoroquinolones and macrolides. New cures for gonorrhea are urgently needed as people who are infected with it will infect others and accelerate microbial resistance.

KEYWORDS: N.gonorrhea, STD, COVID 19, antibiotics, overuse and drug resistant.

1. INTRODUCTION:

These are unprecedented times. A novel coronavirus (SARSCov2) is circulating the globe and has much of the world's population affected. At the same time, people continue to be exposed to, acquire, and/or display symptoms of sexually transmitted infections (STI).Among these STD a super gonorrhea is been exposed due to overuse of antibiotic usage which led to the development of antibiotic resistance to gonorrhea creating a growing worldwide burden.[1]

Neisseria Gonorrhoeae:

Neisseria gonorrhoeae is an obligate human pathogen and is the etiological agent of gonorrhea. Gonorrhea is among the most common sexually transmitted infections and all reflecting in longer-term trends. Risk factors for gonorrhea include sexual contact with an infected person or someone from an endemic area; previous gonorrhea, STIs or human immunodeficiency virus (HIV), being a sexually active youth; having multiple partners; and being a sex worker, street youth and/or man who has sex with men. Geographic clustering of gonococcal infections is associated with minority ethnic groups, low socioeconomic status and lack of education[2] Decreasing condom use, increased urbanization and travel, poor infection detection rates and inadequate or failed treatment all contribute to this increase. *N. gonorrhoeae* infection can also facilitate the transmission of HIV.[3,4] Gonorrhea affects high-, middle and low-income countries. The African region has the highest rates of gonococcal infections worldwide, with some 50 and 100 new infections per 1,000 women and men, respectively, every year[5]. In the US, it is the second most frequently reported notifiable infectious disease, in Canada a similar rise is also seen. Gonorrhea is a debilitating disease, globally now an urgent problem because *N. gonorrhoeae* is capable of rapidly developing resistance to multiple antibiotic classes.

Cases Research:

Overtime, *N. gonorrhoeae* has become less susceptible to numerous antibiotics, including the sulfonamides, penicillins, tetracyclines and fluoroquinolones. More recently, cases of resistance to cephalosporins, the current first-line treatment, have also been reported.[6] Urogenital gonorrhea may be asymptomatic in 40% of men and manifests most commonly as urethritis [7,8]. It is also asymptomatic in more than half of women[9]. In men, untreated urethral infection can lead to epididymitis, reduced fertility, and urethral stricture. In women, when present, symptoms are nonspecific and include abnormal vaginal discharge, dysuria, lower abdominal discomfort, and dyspareunia. The lack of discernible symptoms results in unrecognized and untreated infections, which can lead to serious complications.[10]

Complications:

Overall, 10% to 20% of female patients develop pelvic inflammatory disease (PID) and, consequently, are at risk for infertility[11]. Pregnancy complications associated with gonorrhea include chorioamnionitis, premature rupture of membranes, preterm birth, ectopic pregnancies, and spontaneous abortions. Infants of mothers with gonococcal infection can be infected at delivery, resulting in neonatal conjunctivitis (ophthalmia neonatorum). Such untreated conjunctivitis may lead to scarring and blindness.[12,13] Extra-genital infections are common in both sexes and frequently occur in the absence of urogenital infection[14,15]. Rectal infections are usually asymptomatic but can manifest as rectal and anal pain or discharge. Pharyngeal infections are mostly asymptomatic, but mild sore throat and pharyngitis may occur. Although bacterial concentrations are generally lower than in other infection sites, the pharynx is thought to be a favorable site for resistance emergence due to acquisition of resistance traits from commensal *Neisseria* spp. Disseminated gonococcal infections with gonococcal arthritis also occur. Because they are frequently asymptomatic, extra-genital infections often remain untreated, despite their key role in disease transmission[16].

Antibiotic Resistance:

Almost all antibiotic classes used against gonorrhea have lost their efficacy because of resistance.[17] Sulfonamides, penicillins, early-generation cephalosporins, tetracyclines,

macrolides, and fluoroquinolones can no longer be relied upon. The extended-spectrum cephalosporins (ESCs, i.e., cefixime and ceftriaxone), which represent the last remaining option for first-line empirical monotherapy, are also under threat, with resistance reported worldwide[18,19]. The WHO Gonococcal Antimicrobial Surveillance Programme (GASP) found that resistance is spreading especially in Asia, North America, Europe, Latin America and the Caribbean, and Australia, with large data gaps in Africa and Central Asia[20]. Reports of treatment failures with ESC are on the rise[21], and the first case of treatment failure with a dual therapy has recently been reported. Fluoroquinolone, high-level azithromycin, and cephalosporin resistance have now been found in several countries. *N. gonorrhoeae* displays extraordinary genetic versatility to achieve antimicrobial resistance (AMR), allowing horizontal gene transfer events with nonpathogenic *Neisseria* species that reside in different anatomical sites, particularly the pharynx[22,23].

Insufficient Research And Development For An Urgent Public Health Threat:
As a disease that is not usually deadly but affects millions of people, gonorrhea control initiatives
lack sufficient coordination and investment. With increasingly limited treatment options in the wider context of AMR, there is now growing concern that the threat of untreatable gonorrhea will become a reality. In February 2017, WHO listed *N. gonorrhoeae* among "High Priority" pathogens for research and development (R&D) of new antibiotics[24]. While hospital acquired pathogens may have been highest on the list because of the high rates of mortality they cause, *N. gonorrhoeae* was notably included because infections are extremely widespread, cause substantial morbidity with a significant health cost for countries, can affect pregnant women and their babies, and develop AMR at a particularly rapid pace. Gonorrhea was also listed by the US Centers for Disease Control and Prevention (CDC) in the top "Urgent Threat" category of 18 drug-resistant threats to the US and is included in similar AMR priority lists in the UK and Canada.

Newer Drugs:
The current pipeline for gonorrhea treatments is severely depleted, with only 3 new chemical entities in various stages of clinical development. Two of these candidates are also being developed for other indications.[25]
1. Solithromycin (Cempra Inc.) is an oral fluoroketolide with activity against gram-positive and fastidious gram-negative bacteria, including *N. gonorrhoeae*, *M. genitalium*, and *C. trachomatis* . It targets 3 different prokaryotic ribosomal sites and showed good efficacy in a Phase II study, with a 100% efficacy for genital, oral, and rectal sites of infection in men and women. A Phase III trial is ongoing.[26]
2. Zoliflodacin (Entasis Therapeutics) is a first-in-class spiropyrimidinetrione topoisomerase II inhibitor with activity against several pathogens, including *N. gonorrhoeae*, and *C. trachomatis*. Zoliflodacin has been shown to be highly effective in vitro against a large collection of geographically and genetically diverse *N. gonorrhoeae* isolates. Results from a Phase II trial showed high efficacy against urogenital infections (98%±100% microbiological cure rate, dependent on dose; clinicaltrials.gov NCT02257918). Over 90% of participants were male.[27,28]
3. Gepotidacin (GlaxoSmithKline) is another bacterial topoisomerase II inhibitor, a novel triazaacenaphthylene with good in vitro activity against a wide range of drug-resistant bacteria, including MRSA (methicillin-resistant *Staphylococcus aureus*), ESBL (extended-spectrum β-lactamases)-producing *Enterobacteriaceae*, and *N. gonorrhoeae*. A Phase II trial was recently completed, and 96.7% and 94.8% cure rates were achieved with doses of 1500

mg and 3000 mg, respectively (clinicaltrials.gov NCT02294682). As before, over 90% of the participants were male.[29]

2. CONCLUSIONS:

During this extraordinary time, we need to find a balance between providing necessary STI care and maintaining physical distancing to prevent unnecessary loss of life from COVID-19.The number of gonococcal infections is rapidly rising worldwide. Most worrisome, *N. gonorrhoeae* is an important member of the bacterial community that spreads AMR. Just 3 new clinical entities are in various stages of clinical development for treatment of gonorrhea today, in a therapeutic area that lacks a strong commercial interest.

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