



Resistance of *Neisseria gonorrhoeae* on oral and mucosa : A Review Article

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Abstract

Introduction: Gonorrhea is one of the four most common sexually transmitted diseases worldwide. Globally, the highest incidence of gonorrhea cases is in the African and Western Pacific regions (including China, Indonesia and Australia). Gonorrhea is a sexually transmitted disease caused by the bacteria *Neisseria gonorrhoeae*. These bacteria are gram-negative bacteria in the form of diplococci located intracellularly from PMN cells. Infection from *Neisseria gonorrhoeae* can be transmitted by sexual intercourse or vertical transmission at the time of delivery. In children, infection can occur as a result of sexual abuse by an individual infected with Gonorrhea or it can also occur from touching items contaminated with *N. gonorrhoeae* bacteria.

Discussion: Gonococcal infection occurs by invading the mucosa, so that gonococcal infection can occur in many places. Gonococcal infection can occur in male and female external genitalia, anorectal, pharynx and eyes. There can be a local infection in the genital area (most common), infection in the abdominal cavity (peritonitis), infection around the liver (perihepatitis), meningitis, endocarditis, dermatitis, arthritis and can spread to the bloodstream and cause a Disseminated Gonococcal Infection (DGI) which can spread systemically. The manifestations of gonococcal infection in the female external genitalia can be asymptomatic but may also include periurethral edema and urethritis. There may be a purulent discharge from the cervix but it does not represent vaginitis, dysuria or painful urination, dyspareunia or pain during sexual intercourse and lower abdominal pain. There can also be a vulvovaginitis, bartolin abscess, and in gonococcal infections that are not treated properly, a complication can occur in the form of pelvic inflammatory disease (PID), characterized by lower abdominal pain, increased body discharge from the vagina and urethra, dysuria and intermenstruals. bleeding accompanied by signs of peritonitis, endocervicitis, endosalpingitis and endometritis, causing a deep pelvic or lumbar pain. Currently, the resistance rate of *Neisseria gonorrhoeae* to antibiotics is increasing rapidly. This condition is not good for prognosis.

Conclusion: The administration of dual therapy with this drug regimen is expected to increase the cure rate so that it can prevent more serious complications and reduce the possibility of resistance to cephalosporins.

Keywords: Gonorrhoea; Resistance; Oral Management

Introduction

Gonorrhea is an infectious disease of the mucosa caused by gram-negative cocci bacteria *Neisseria gonorrhoeae* which can be transmitted through sexual or perinatal contact. This infection occurs co-infection with *Chlamydia trachomatis* [1,2]. Gonorrhea can occur in men or women, generally at productive age, but

infection by bacteria in women is asymptomatic. This infection can also occur in newborns due to vertical media from the mother during labor. Most gonorrhea manifests as infection of the genital tract, but it can also cause pharyngitis, proctitis and conjunctivitis in certain groups. Clinical findings of conjunctivitis were found in infants

with a history of perinatal infection[1-3]. Gonococcal infection is the most common cause of urethritis in men, who experience complaints of pus from the genitals. In women, gonococcal infection causes cervicitis, but this condition manifests asymptotically so that patients present after a pelvic inflammatory disease (PID), infertility, ectopic pregnancy, or a chronic pelvic inflammation. Diagnosis of a gonococcal infection is done by taking pus from the genitalia, rectum, oropharynx or eye secretions in conjunctivitis gonorrhea and doing a gram examination, where an image of gram-negative diplococcal bacteria can be found in PMN cells, which is confirmed by culture on gonococcal selective media such as Martin-Lewis medium and Thayer-Martin medium [1,4].

The management of gonorrhea is done by administering antibiotics with a recommended treatment regimen using Ceftriaxone 250 mg IM in a single dose, plus offering Azithromycin 1 gram orally in a single dose. In patients with cephalosporin allergy, an alternative therapeutic regimen can be used using a single dose of Gentamycin 240 mg IM and Azithromycin 1 g orally as a single dose [1,2,4,5]. Currently, the resistance rate of *Neisseria gonorrhoeae* to antibiotics is increasing rapidly. The high rate of Gonorrhea resistance to the penicillin, tetracycline and quinolone classes has made this drug class no longer accepted for use as a Gonorrhea therapy in most countries in the world. Even in some countries, it has been found that Gonorrhea resistance to cephalosporin therapy creates the 3rd that is given orally[6,7].

Discussion

Gonorrhea is one of the four most common sexually transmitted diseases worldwide. In 2015, the World Health Organization (WHO) estimated that around 357 million new infections from one of the four infectious diseases occurred each year [8]. In an epidemiological study based on data collected from 2005 to 2012, it was found that the global incidence of gonorrhea in women was 0.8%, while in men, it was found that the global incidence of gonorrhea was 0.6% of the worldwide population in 2012, so that if converted in total, there were 26,819,000 cases of gonorrhea worldwide in men and women aged 15-49 years, where there were 19 cases per 1000 women and 24 cases per 1000 men based on World Bank data in 2012 [9,10]. Globally, the highest incidence of gonorrhea cases is in the African and Western Pacific regions (including China, Indonesia and Australia). There are several potential causes for the increased incidence of Gonorrhea globally. One possible cause of this is the increasing prevalence of HIV infection in developing countries. Improvements in diagnostic capabilities and case reporting systems in several countries can also contribute to increasing the incidence of Gonorrhea globally [3].

Gonorrhea is a sexually transmitted disease caused by the bacteria *Neisseria gonorrhoeae*. These bacteria are gram-negative bacteria in the form of diplococci located intracellularly from PMN cells. Infection from *Neisseria gonorrhoeae* can be transmitted by sexual intercourse or vertical transmission at the time of delivery.

These bacteria mainly attack the columnar epithelium of the host, so that all mucous membranes can be infected by these bacteria[1,2]. There are many factors that influence *N. gonorrhoeae* bacteria on their virulence and pathogenicity. Fli help the attachment of bacteria to the mucosal surface thereby contributing to the resistance that occurs by preventing ingestion and destruction of bacteria by neutrophils. Opacity-associated (Opa) protein increases the adhesion between gonococcal bacteria and phagocytes, thereby increasing the ability of bacteria to invade host cells and can cause a decreased immune response [4].

Clinical Manifestation

Manifestations of gonococcal infection in male external genitalia can be urethritis, which is the most common manifestation of Gonorrhea in male external genitalia, balanoposthitis, balanitis, prostatitis, epididymitis, vesiculitis or cystitis, often characterized by a purulent and thick body body, sometimes accompanied by complaints of pain when urinating or dysuria. The manifestations of gonococcal infection in the female external genitalia can be asymptomatic but may also include periurethral edema and urethritis. There may be a purulent discharge from the cervix but it does not represent vaginitis, dysuria or painful urination, dyspareunia or pain during sexual intercourse and lower abdominal pain. In gonococcal infection that is not treated properly, a complication can occur in the form of pelvic inflammatory disease (PID) [1,5]. Anorectal manifestations include proctitis accompanied by pain and a purulent fever. In some cases complaints of burning or pain during defecation, tenesmus, and blood in the stool may also be found. Gonorrhea diagnosis is done by taking anamnesis and physical examination that leads to a gonococcal infection and finding an intracellular gram-negative diplococcal image from the results of gram staining of the secretions or body fluids of a patient suspected of a gonococcal infection and the growth of *N. gonorrhoeae* from culture results. The differential diagnosis of a gonorrhea urethritis includes urethritis caused by genital herpes, urethritis due to *C. trachomatis*, urethritis due to *Ureaplasma urealyticum*, urethritis due to *Trichomonas vaginalis*, bacterial vaginosis, Reiter's syndrome [11].

The manifestations of gonococcal infection in the male external genitalia can be in the form of urethritis which is the most common manifestation of Gonorrhea in male external genitalia, balanoposthitis, balanitis, prostatitis, epididymitis, vesiculitis or cystitis. This condition is often characterized by the presence of a body discharge that varies from clear and clear to purulent and thick, sometimes accompanied by complaints of pain during urination or dysuria. In some cases, edema may also be found in the external urethral meatus, prepuce or penis. Gonorrhea manifestations of the pharynx occur due to sexual exposure to oral-genital contact. It can also occur as a result of an inoculation after holding an infected limb or object and then putting the hand in the mouth. In this condition, there is erythema of the pharynx,

mild sore throat, and often an infection of the genitalia is also found [1,2]. There is a hyperemic pharynx and swelling of the tonsils and there is a purulent white discharge on the wall of the pharynx. It

is important to dig for the coitus suspectus with orogenital sexual intercourse and to do a throat swab to check with gram stain or for culture (Figure 1).



Figure 1: Gonorrhoea of the pharynx (Pharyngitis Gonorrhoea).

Gonorrhoea manifestations in the eye may include conjunctivitis, palpebral edema, chemosis and profuse and purulent discharge. In some cases, this gonococcal infection can even cause a corneal ulcer to perforate which can lead to permanent blindness. In neonates, ophthalmia neonatorum can occur, which is a bilateral conjunctivitis condition characterized by eye pain, conjunctival hyperemia, and the presence of purulent secretions[1]. Diagnosis of gonorrhoea is carried out by taking anamnesis and physical examination that leads to a gonococcal infection and finding an intracellular gram-negative diplococcal image from the gram stain of the secretions or body fluids of a patient suspected of a gonococcal infection. However, because the sensitivity is low, a negative gram test result is not sufficient to rule out a diagnosis of gonorrhoea, so it is necessary to have another gram-test or a culture examination done. Swab culture examination of the infected area is currently. The standard for diagnosis of Gonorrhoea, which is very useful especially in cases with unclear clinical picture, when there is a condition of failure of therapy or when it is difficult to extract the history of the disease. However, empiric therapy can be done first considering the culture results take 24-48 hours [2,4].

Gonorrhoea Resistance

Antibiotic resistance, especially in the case of Gonorrhoea, is a threat in reducing the consequences of sexually transmitted diseases worldwide. Based on data from WHO, the incidence of gonorrhoea infection that is resistant to antibiotics is increasing every year. This is of particular concern to public health observers, especially for the prevention of infertility in women [8]. Gonorrhoea is currently still one of the four largest sexually transmitted diseases

worldwide that can be cured. However, in recent years, Gonorrhoea has become increasingly resistant to antibiotics that were previously sensitive, which has led to fears that Gonorrhoea will not cure. Gonorrhoea with multiple drug resistance (MDR) was reported by more than 36 countries in the world in 2015 [9-10]. Untreated gonorrhoea can lead to more severe complications, such as female infertility, complications in pregnancy and blindness in newborns who are infected during pregnancy. the delivery process [12]. Resistance of *Neisseria gonorrhoeae* to penicillin and tetracyclines was first discovered in Asia in 1970. The high rate of resistance to quinolones (Ciprofloxacin) emerged since mid-2000. Recent data shows that there is an increase in resistance and failure of *Neisseria gonorrhoeae* treatment against third generation cephalosporins given orally. Several serotypes of *N. gonorrhoeae* that have been associated with failed cephalosporin therapy have also been shown to have resistance to other antibiotics and have been classified as multi-drug resistant gonococci [13].

Therapeutic Management

Initially, the therapeutic regimen given in cases of gonorrhoea can be done by providing single therapy using cephalosporins. However, due to the resistance of these bacteria to oral cephalosporins as monotherapy, dual therapy using ceftriaxone and azithromycin is recommended as the standard therapy for gonorrhoea cases worldwide, especially in the United States. Dual therapy with ceftriaxone and azithromycin should be given simultaneously on the same day and under direct supervision. Since most *N. gonorrhoeae* infections are co-infected with *C. trachomatis*, the principle of dual therapy is also considered quite effective

because basically azithromycin is a class of antibiotics given to *C. trachomatis* infections [14]. In recent years, gonorrhoea has become increasingly resistant to previously sensitive antibiotics, which has led to fears of incurable gonorrhoea. Gonorrhoea with multiple drug resistance (MDR) was reported by more than 36 countries in the world in 2015. Untreated gonorrhoea can lead to more severe complications, such as female infertility, complications in pregnancy and blindness in newborns who are infected during pregnancy. childbirth process. Due to the resistance of these bacteria to oral cephalosporins as monotherapy, dual therapy using ceftriaxone 250 mg IM single dose and azithromycin 1 g PO single dose is recommended as the standard therapy in cases of gonorrhoea worldwide. The administration of dual therapy with this drug regimen is expected to increase the cure rate so that it can prevent more serious complications and reduce the possibility of resistance to cephalosporins [15,16].

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