Enferm Infecc Microbiol Clin. 2017;xxx(xx):xxx–xxx

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Continuing medical education: Methods of rapid diagnosis

Rapid diagnosis of sexually transmitted infections☆

Luis Otero-Guerra[a], Ana Fernández-Blázquez[b], Fernando Vazquez[b,c,d,*]

[a] Servicio de Microbiología, Hospital de Cabueñes, Gijón, Spain
[b] Servicio de Microbiología, Hospital Universitario Central de Asturias, Oviedo, Spain
[c] Departamento de Biología Funcional, Área de Microbiología, Facultad de Medicina, Oviedo, Spain
[d] Fundación de Investigación Oftalmológica, Instituto Oftalmológico Fernández-Vega, Oviedo, Spain

ARTICLE INFO

Article history:
Received 3 January 2017
Accepted 5 January 2017
Available online xxx

Keywords:
Point of care system
Screening assay
Sexually transmitted diseases

ABSTRACT

Sexually transmitted infections (STIs) are responsible for an enormous burden of morbidity and mortality. Worldwide, millions of cases of STIs, such as syphilis, chlamydia, or gonorrhoea occur every year, and there is now an increase in antimicrobial resistance in pathogens, such as gonococcus. Delay in diagnosis is one of the factors that justifies the difficulty in controlling these infections. Rapid diagnostic tests allow the introduction of aetiological treatment at the first visit, and also leads to treating symptomatic and asymptomatic patients more effectively, as well as to interrupt the epidemiological transmission chain without delay. The World Health Organisation includes these tests in its global strategy against STIs.

Diagnóstico rápido de las infecciones de transmisión sexual

Palabras clave:
Sistemas de diagnóstico a la cabecera del enfermo
Cribado de ITS
Infecciones de transmisión sexual

RESUMEN

Las infecciones de transmisión sexual (ITS) suponen una importante carga de morbimortalidad. A nivel mundial todos los años se producen millones de casos de ITS como sífilis, infección por clamidias o gonococia, y actualmente se asiste a un incremento de la resistencia a los antimicrobianos en patógenos como el gonococo. La demora en el diagnóstico es uno de los factores que justifica la dificultad para controlar estas infecciones. Las pruebas de diagnóstico rápido permiten instaurar el tratamiento etiológico en la primera consulta, lo que lleva a tratar a más pacientes, tanto sintomáticos como asintomáticos, de forma más efectiva, e interrumpir sin demoras la cadena epidemiológica de transmisión. La OMS incluye estas pruebas en su estrategia mundial contra las ITS.

Introduction

Worldwide, sexually transmitted infections (STIs) pose a significant morbidity and mortality burden as they compromise quality of life, sexual and reproductive health and newborn and child health. They also indirectly facilitate the transmission of the human immunodeficiency virus (HIV) and cause cell changes that precede some forms of cancer. The WHO provides data on a reality that seems far-removed from developed countries. Syphilis causes over 300,000 foetal and neonatal deaths per year and exposes another 215,000 children to premature death. It also estimates that 357 million new cases of four types of curable STIs are recorded every year: 131 million *Chlamydia trachomatis* (CT) infections, 78 million *Neisseria gonorrhoeae* (NG) infections, 6 million *Treponema pallidum* (TP) infections and 142 million *Trichomonas vaginalis* (TV) infections. Similarly, the human papillomavirus (HPV) is believed to be responsible for 530,000 cases of cervical and uterine cancer as well as 264,000 deaths. We also cannot forget the emergence of multidrug-resistant gonococcal strains that threaten us with untreatable gonorrhoea.

While it is true that progress has been made, such as the reduction of mother-to-child syphilis transmission in developing countries, globally the prevalence of STIs remains the same or is

DOI of original article: http://dx.doi.org/10.1016/j.eimc.2017.01.004
☆ Please cite this article as: Otero-Guerra L, Fernández-Blázquez A, Vazquez F. Diagnóstico rápido de las infecciones de transmisión sexual. Enferm Infecc Microbiol Clin. 2017. http://dx.doi.org/10.1016/j.eimc.2017.01.004
* Corresponding author.
E-mail address: opsklins@gmail.com (F. Vazquez).

Table 1
Differences between rapid tests and POCTs.

Characteristic	Rapid testing	POCTs
Difficulty	Simple	Simple (can be used in primary care)
Time	<30 min	<20–30 min
Electricity source	Yes, necessary	No
Trained personnel	Yes, necessary	No
Quality control	No, internal controls	Yes (more reliable)

POCTs: point-of-care tests.
Source: Adapted from Muralidhar.[3]

even on the rise. Numerous factors contribute to this, but the treatment delay that arises while patients await a diagnostic result is particularly important. By means of a mathematical model, it has been shown that using a rapid diagnostic test with a sensitivity as low as 63% successfully improves the percentage of treated patients, compared to waiting for the result of a high-sensitivity test available at a second consultation, which many patients fail to attend.[1] As such, diagnostic tests that provide immediate results will facilitate the administration of aetiological treatments to a larger number of infected patients and new transmissions will be avoided by breaking the chain of infection.

To that effect, it is necessary to reinforce the capacity of the laboratories and to also proceed with designing and implementing diagnostic tests at the point of care to facilitate systematic and early STI diagnosis of all suspected individuals, even if they are asymptomatic.

In this review, we will present the latest rapid diagnostic techniques for the main STI- and vulvovaginitis-causing pathogens, though we will leave viral hepatitis and HIV to one side.

History, concept and characteristics of the rapid tests in sexually transmitted infections

In STIs, diagnostic tests can serve several purposes: (a) diagnosis; (b) screening of high-risk groups; (c) treatment monitoring; (d) epidemiological surveillance; (e) investigation of outbreaks; (f) validation of syndrome management in countries with few resources; (g) detection of resistance patterns; (h) ensuring quality in laboratory tests; and (i) research.[2]

The diagnostic tests used in STIs are: (a) direct microscopy; (b) culture; (c) antigen detection; (d) serology; (e) detection of microbial metabolites (whiff test, for example), and (f) molecular methods. All of these may be considered rapid at least in some of their forms, except culture.

Rapid tests in STIs can be considered as such, or as point-of-care tests (POCTs). This review considers both types indiscriminately. POCTs can be defined as diagnostic tests that allow a diagnosis to be obtained and a treatment indicated at the same visit. The differences between them are detailed in Table 1 (adapted from Muralidhar[3]).

Rapid tests/POCTs aimed at STI diagnosis must meet the following requirements established by the WHO[4]:

ASSURED

- Affordable.
- Sensitive.
- Specific.
- User-friendly (few steps and minimum training).
- Rapid and robust (storable at room temperature, results in <30 min).
- Equipment-free.
- Deliverable to end-users.

POCTs must also comply with quality controls included in the tests and be environmentally safe and low cost.

An important aspect is what users think the qualities of rapid tests/POCTs should be in STIs. In a study on focus groups, it was found that the qualities of a rapid test should be high sensitivity and specificity, a short procedure time and a low cost.[5]

For POCTs, various types of technology are used[6]:

a) Precipitation/agglutination reactions such as the RPR test for syphilis.
b) Immunochromatography in different test formats: (b1) lateral flow; (b2) multiple, e.g. HIV + syphilis, HIV + syphilis + HBV/HCV, treponemal test + non-treponemal test; (b3) using a flow assay such as dot-blot; (b4) with readers/scanners to eliminate observer bias, thereby increasing sensitivity and facilitating quantification.
c) Emerging technologies such as microfluidic assays (which detect multiple analytes such as HIV and syphilis) and loop-mediated isothermal amplification technology (LAMP), which achieves amplification using four primers and polymerase enzyme in a constant temperature reaction (60–65 °C) and obtains results in less than 1 h.

POCTs were developed to complement centralisation in "core" laboratories, allowing for decentralised determinations that are available 24 h a day, 365 days a year. They are usually combinations of syndrome-based microorganisms, can be collected by the patients themselves, do not require trained personnel and are rapid so as to enable decision-making. Of all of them, the STI tests are among those that have been proven cost-effective.[7]

Irrespective of the terminology and discourse that may surround rapid tests or POCTs, in this review we include the types of tests we consider to be interchangeable, whether these are with or without equipment at the point of care or in a nearby laboratory, and which try to provide the fastest results possible.

The rapid response laboratory in sexually transmitted infections and needs in different settings: primary care, emergency departments, STI clinics, reference laboratories

Laboratory centralisation makes the presence of a rapid response laboratory difficult in our setting, but the following methods may be available in various working environments:

a) Primary care: e.g. Gram stain and Amsel criteria for bacterial vaginosis.
b) Emergency departments: normally have a support laboratory.
c) STI clinic: the above methods, dark-field microscopy, urine sediment.
d) Reference laboratory: all rapid techniques.

In developing countries, rapid tests/POCTs generate huge interest as they help to reduce the enormous disease burden that they endure. These tests allow a move away from syndromic treatments (targeted blindly and simultaneously at various pathogens causing the same syndrome) and a progression towards aetiological treatments (targeted specifically at the causal pathogen). The unnecessary use of antimicrobials and the emergence of resistances are avoided, costs are reduced and the chain of infection is broken more effectively. However, there are drawbacks, as aspects such as cost, the need for the refrigeration of reagents or electrical supply requirements (e.g. for a microscope) can mean that tests which prove very useful in one setting may be useless in another. As such, all of the ASSURED requirements are equally important.