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Review

Comparison of the lateral flow immunoassays (LFIA) for the diagnosis of *Helicobacter pylori* infection

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ABSTRACT

Helicobacter pylori infection is the most common human infection where approximately 50% of the world populations are infected. The diagnosis of such infection is mainly done by endoscopy where gastric biopsies are examined for the presence of *H. pylori*. Such invasive approach is costly, time consuming and generally requires more than one test to confirm the infection. Serology on the other hand is a non-invasive approach that can detect *H. pylori* exposure. The lateral flow immunoassays (LFIA) support the serological approach and have the advantage of being fast, economic and require no additional equipment or experience. In this review the principles, components of the LFIA, sensitivities and specificities of the commercially available *H. pylori* test strips were compared and discussed.

Contents

1. Introduction

It is well known that half of the world populations are infected with *Helicobacter pylori* mainly those of the developing countries (Kimmel et al., 2000). The majority of subjects however are asymptomatic and only few percentages develop peptic ulceration that might progress to gastric cancer (Sipponen, 1998; Sipponen and Marshall, 2000). The diagnosis of *H. pylori* infection in such patients is an important approach for the selection of therapy and for the follow up of eradication success. *H. pylori* infection can be diagnosed by invasive and non-invasive techniques. The invasive technique (endoscopy) relies on the collection of gastric biopsy specimen to detect *H. pylori* by rapid urease test, culture, PCR and/or histopathology

Abbreviations: LFIA, lateral flow immunoassay; ICA, immunochromatographic assay; PCR, polymerase chain reaction; RUT, rapid urease test; UBT, urea breath test; ELISA, enzyme-linked immunosorbent assay; hCG, human chorionic gonadotropin.

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(Ricci et al., 2007). This is a time consuming and expensive approach unlike the non-invasive tests such as ^{13}C-urea breath test (UBT), stool antigen test and serology tests. The UBT and stool antigen tests detect the presence of *H. pylori* and are called active tests. Serology however (e.g. the ELISA test) detects anti-*H. pylori* antibodies which is an indicator for *H. pylori* exposure and is called passive test (Sciortino, 1993; Kimmel et al., 2000; Ricci et al., 2007). The lateral flow immunoassay (LFIA) is another alternative for the ELISA test used in serological and fecal diagnosis of *H. pylori* infection. It is intended particularly for a quick diagnosis and as a single use supporting test at a health care unit. Kato et al. (2004) compared the widely used stool antigen ELISA test with the lateral flow stool antigen test and reported that the later showed good specificity and sensitivity in the detection of *H. pylori* infection in children. The LFIA is an immunochromatographic assay (ICA) that is commercially available for a wide array of targets such as infectious agents (bacteria, viruses) (Nakasone et al., 2007; Cui et al., 2008; Kawatsu et al., 2008; Peng et al., 2008), hormones (Posthuma-Trumpie et al., 2008), drugs (Zhang et al., 2006; Zhu et al., 2008; Xie et al., 2009), pesticides (Zhou et al., 2004; Guo et al., 2009) and mycotoxins (Kolosova et al., 2007; Wang et al., 2007b). A visual qualitative (on/off) signal is enough for most applications. The best-known and first developed (LFIA) was the pregnancy test for the detection of human chorionic gonadotropin (hCG) hormone in urine sample (Leuvering et al., 1980; van Amerongen et al., 1993). Several investigators have also developed their own lateral flow test strips for the detection of various target molecules (Tanaka et al., 2006; Kolosova et al., 2007; Wang et al., 2007a, 2011; Chiao et al., 2008; Kawatsu et al., 2008; Peng et al., 2008; Zhao et al., 2008; Li et al., 2009; Xie et al., 2009; Xu et al., 2009; Omidfar et al., 2010; Yu et al., 2011). In general the lateral flow test strips have the advantages of being rapid (2–5 min), easy to use (self-performing), cost effective, portable, highly sensitive and specific. They do not require complicated equipment and technical expertise that are critical parameters for point-of-care, and have long shelf life at room temperature (12–24 months) (Posthuma-Trumpie et al., 2009; Ngom et al., 2010). The aim of this article is to review the components and the principles of lateral flow immunoassay (LFIA) devices and to compare the currently available rapid *H. pylori* commercial test devices.

2. Principles of the LFIA

The LFIA strips are designed to detect the presence of an analyte (antigen or antibody) by a specific labeled-antigen or labeled-antibody.

2.1. Test strip

The test strip consists of four sections; sample pad (cellulose), conjugate pad (glass fiber), membrane (nitrocellulose) and absorbent pad (cellulose) which are laminated onto a sheet of plastic backing orderly to allow cutting and handling. The pads overlap the membrane to allow a continuous flow path for the sample. The sample pad allows the diffusion of the sample into the conjugate pad that is impregnated with detector reagent (labeled-antigen or labeled-antibody) depending on the application. If the sample contains an analyte, it will bind to the detector reagent and the complex will continue to flow and then irreversibly binds capture reagent (antigen or antibody) at the test line on the membrane and forms a colored line. A continuous flow of the sample through the strip toward the control line will always form a colored line an indicator for a proper function of the test device. The absorbent pad at the end of the strip wicks the fluid through the membrane to ensure a continuous flow and thus maintains a clear background. Strips can be housed in a plastic holder (cassette), where only the sample application window and a reading window are exposed, for protection and easier handling (Millipore, 2008; Posthuma-Trumpie et al., 2009; Ngom et al., 2010).

2.2. Antibodies

The affinity of the specific antibody mostly influences the sensitivity of the test. Both monoclonal and polyclonal antibodies have been used in these tests; however the type of such antibodies used in commercial LFIA strips were not usually referred to in the manufacturer data sheets. Several investigators used either monoclonal antibodies or polyclonal antibodies both in the conjugate pad and on the test line (Shyu et al., 2002; Chiao et al., 2004, 2008; Kawatsu et al., 2006, 2008; Tanaka et al., 2006; Nakasone et al., 2007; Peng et al., 2008; Jiang et al., 2011; Yu et al., 2011). Others used both monoclonal and polyclonal antibodies on the same strip (Wang et al., 2011; Yang et al., 2011). The control line is coated with primary or secondary (anti-IgG) antibody depending on the application to capture excess detector reagents regardless of the presence or absence of target analyte (Posthuma-Trumpie et al., 2009; Ngom et al., 2010). The control line and the clear background that appear on the reading window are the indicators of an internal positive and internal negative procedural control.

2.3. Label particles

The majority of the available commercial LFIA strips (around 94%) use colloidal gold particles (red–pink color) for labeling, while the rest uses colored latex particles. According to the recent review articles many investigators also used colloidal gold particles for labeling (Posthuma-Trumpie et al., 2009; Ngom et al., 2010) while few others used colored latex particles (Gussenhoven et al., 1997; Greenwald et al., 2003). The size of the gold particles varies between 2 and 150 nm, but generally 15–25 nm particles were used (Zhou et al., 2004; Zhang et al., 2006; Nakasone et al., 2007; Zhao et al., 2008; Li et al., 2009; Xie et al., 2009; Omidfar et al., 2010). The advantages of gold particles are being stable, easy to use and have convenient surfaces to accelerate the antibody–antigen recognitions, which increases the immunoassay signals and allows a smooth flow through the membrane (DiScipio, 1996).

3. LFIA strips for the diagnosis of *H. pylori*

Several LFIA strips are currently commercially available for the diagnosis of *H. pylori* infection. This is a qualitative test that is used either to detect anti-*H. pylori* antibodies in blood samples (whole blood, serum and/or plasma) or to detect *H. pylori* antigens in stool samples. Both are intended to aid in the diagnosis of *H. pylori* infection in adult patients with