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Advantages and disadvantages usage of Galactomannan ELISA assay for detection of Aspergillosis

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ABSTRACT

Aspergillosis is an important disease caused by Aspergillus spp. under specific conditions in the human body. It becomes very serious disease now days due to increased usage of immunosuppressive drugs in the treatment of various malignant diseases and in organ transplantation. Early stages of aspergillosis are usually difficult to diagnose. This will lead to high mortality rate among patients with aspergillosis, especially invasive forms. Galactomannan (GM) as one component of Aspergillus cell wall is preferred to use for diagnosis of aspergillosis. Its specificity and sensitivity are quite acceptable to give an indicator for aspergillosis. This review will explain the advantages and disadvantages of using GM antigen in the diagnosis of aspergillosis.

Keywords: NIL

INTRODUCTION

Aspergillosis is one of the most common diseases caused by various members of Aspergillus genus [1-3]. Soil is the natural habitat of Aspergillus species living on various organic materials as saprophytic fungi [4]. In the presence of many predisposing factors, entering of these non-harmful fungi into respiratory system will turn them into pathogenic organisms. This will be encouraged by occurring of any defect in the immune system as in immunocompromised patients or suffering from underlying conditions in immunocompetent individuals [5-7].

Galactomannan (GM) as one component of Aspergillus cell wall is successfully used for diagnosis of aspergillosis [8-13]. This antigen, which can find in various fluids of the human body can easily detect by using ELISA technique [8-9]. Serum is more suitable than other type of samples for detecting of GM [10], while bronchoalveolar lavage (BAL) in some cases of IPA shows more susceptibility than serum [14-17]. Assay for GM as an indicator for aspergillosis has many advantages and disadvantages outcomes. This will be discussed in this review after illustration the most characters of aspergillosis and its causative agents.

Aspergillus

Aspergillus is usually involved a great number of saprophytic fungi distributing in a wide range of environments [18]. Morphological characters are mostly used for identification of Aspergillus species which including colony and conidia colors and appearance of conidiophores, matulae, phialides and vesicle [19]. Hundreds of asexual spores and few of sexual type can produce by single fungal colony [18].

Satisfied levels of temperature, humidity and organic materials usually facilitate Aspergillus to grow very fast [20]. Medical places and internal sites of the human shelters are also contained various species of Aspergillus, which make them association with many effects on the human health [20-22]. Destruction of various types of organic materials gives the Aspergillus species an ability to live in more difficult environments than do by other organisms [18]. Approximately all of Aspergillus species can easily culturing on synthetic media such as Czapek Dox agar (CDA) and malt extract agar (MEA) [19].

Aspergillosis

The capacity of Aspergillus species to live in an environment with little amount of nutrients and low oxygen level make these fungi associations with various types of diseases in the human body [23]. Immunity stat of the host also play important role in the pathogenesis of Aspergillus when most of the infections development in immunocompromised individuals [3].

The specific term for the diseases caused by Aspergillus is aspergillosis which is involving various degrees of infections ranging from non-invasive to invasive effects in the human body [1-3]. A. fumigatus is considered the most frequent species of Aspergillus responsible for a wide range of aspergillosis [2, 5, and 24]. The virulence of this fungus and other species of Aspergillus to cause disease is mainly depended on the efficiency of the immune system. Although a huge number of fungal spores are entering our body every day by inhalation, aspergillosis has no chance to develop inside our body due to the defensive activity of the immune system [6, 24]. First line against inhaled spores is represented by the immunological activities of the components of the innate immune system which including recognition by pattern recognition receptors, phagocytosis, and antimicrobial action of many compounds stimulating by this system [25]. Thus, any defect in the immune system will give a chance to germinate entering spore and produce invasion hyphae that have the ability to cause various types of aspergillosis. Weakness in immune system usually results from using of immunosuppressive drugs in the treatment of cancers or organ transplantation, or from the presence of underlying conditions such as diabetes or infected by some types of virus such as HIV [5-7]. Recently, heavy used of immunosuppressive drugs increases the possibility to infect with aspergillosis [5]. Some of the cases show more severe infections with high motility rate [6, 26]. However, immunocompetent individuals can also get aspergillosis under specific conditions [14-16, 27]. Pulmonary aspergillosis is the most common type of Aspergillus infections that ranging from a mild disease as with aspergilloma to more severe disease as with invasive pulmonary aspergillosis (IPA) [25]. Generally, several types of aspergillosis that differ in location and severity levels can be included into four types; invasive pulmonary aspergillosis (IPA); aspergilloma; chronic pulmonary aspergillosis (CPA); and allergic bronchopulmonary aspergillosis (ABPA) [2, 24].

Galactomannan

Galactomannan (GM), which has a heteropolysaccharide structure with a mannan core and varying lengths containing immunodominant galactofuranosyl units, is one component of the Aspergillus cell wall [2, 29]. Analysis of the GM of A. fumigatus revealed the presence of mannan core in a linear form with an alpha-(1-2)-linked mannotetraose repeating unit attached via alpha-(1-6) linkage [30]. Detection of GM is one common application assay for diagnosis of fungal infections such as aspergillosis and invasive fusariosis [8-13]. GM is producing from the growing hypha of Aspergillus in the human body and not from colonization conidia [2]. Its solubility in various fluids of the human body makes it a recommending testing for diagnosing variable types of aspergillosis [8-13]. Double sandwich ELISA, which is used in Europe for decades ago and in the USA since 2003, currently considers the best detection method of GM [29]. Based on this assay, specificity of GM may variable toward different types of aspergillosis. It found about 99% when the ELISA is used for diagnosis of IA [31], while it significant in only 26% of aspergilloma that positively diagnosed by immunodiffusion assays [30].

Variable samples are usually used to detect GM in the human body, such as serum, which is commonly one, Bronchoalveolar lavage (BAL), urine, and biopsy [10-12]. Serum is usually more preferred than other type of samples for detecting of GM [10], while BAL in some cases of IPA with immunocompetent

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conditions showed more susceptibility than serum [14-17].

Advantages of GM test

Aspergillosis, especially invasive type, is usually very difficult to diagnose in early stage due to its non-specific characters [24]. Thus, a suitable diagnostic assay is always demand for obtaining a significant indicator to the initial development of aspergillosis. The GM can give a positive result for early diagnosis of invasive aspergillosis with 90% sensitivity and 84% specificity than other methods such as latex agglutination [9]. It can significantly diagnosis invasive aspergillosis in the serum sample for at least 39 days before the disease causing death [10]. Periods of IA or its primary development also can determine by measuring of GM level alone or in combination with the results of CT-scan [8, 13]. Its measurement in the fluid of the human body can also be useful to follow up the success of antifungal therapy against aspergillosis. It is found that detection of less than 1 ng/ml of GM in the serum sample will consider a sign for starting treatment by antifungal agents or for monitor treatment of aspergillosis [11].

The fact that most of patients with aspergillosis have one or more of immunosuppressive factors will decrease the efficiency of immunological diagnostic assays [2]. Antibodies against various antigens are usually considered the backbone for diagnosis of many pathogenic organisms. Thus, any defect in immune system will make immunological diagnosis more difficult. This problem can be passed by using GM ELISA. However, the sensitivity and specificity of GM have been found not affected by the immune deficiency in the patients with aspergillosis [32].

Disadvantages of GM test

As with other serological tests, false positive or negative results can be expected to get from GM detected by ELISA. A false-negative result may relate to the previous presence of antibodies for Aspergillus or to the treatment with antifungal agents [2]. Otherwise, false-positive result can also obtain during investigation of invasive aspergillosis by GM ELISA [33]. This may result from treatment by antibiotic or infection by fungi other than Aspergillus [32]. Thus, a new ELISA diagnostic tool called specific Aspergillus antigen-capture enzyme-linked immunosorbent assay (ELISA) with 100% specificity has been developed to reduce the false results of the ordinary GM ELISA kit [34]. However, false results cannot prevent using of GM ELISA for surveillance or diagnostic purposes of aspergillosis [35].

In conclusion; Detection of GM could be considered an acceptable assay for the diagnosis of more invasive type of aspergillosis. The advantage of using this assay, especially the ability of GM assay to detect early stages of invasive aspergillosis may cover its unsuitable characters.

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