

Serum (1->3)-B-D-Glucan Assay for Diagnosis of Pneumocystis Pneumonia in Immunocompromised Patients

Li-Chao Fan¹, Jie-Ming Qu², and Jin-Fu Xu^{1*}

¹Department of Respiratory Medicine, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, 200433, China

²Department of Respiratory Medicine, Huadong Hospital, Fudan University, Shanghai, 200040, China

Pneumocystis Pneumonia (PCP) is one of the most prevalent infections in Human Immunodeficiency Virus (HIV)-Infected Patients [1]. PCP also occurs in non-HIV patients who receiving transplantation, immunosuppressive therapy and anti-tumor chemotherapeutic agents [2]. The diagnosis of PCP is usually based on the microscopic detection of cysts by certain stain in respiratory specimens among patients at risk with fever, progressive dyspnea, nonproductive cough and relevant pulmonary infiltrates. However, the methods are limited to the quality of the respiratory specimens and the skill of the observer. Novel tests with greater sensitivity, such as Polymerase Chain Reaction (PCR) of respiratory samples, are potentially promising, but not yet widely available [3]. Emerging data from recent years have pointed to serum (1->3)- β -D-Glucan (BG) measurement as a promising tool for the diagnosis of PCP [4-6].

The peripheral measurement of (1->3)- β -D-glucan is based on detection of β -glucan, a polysaccharide present in the wall of Pneumocystis cysts and in other fungi [7,8]. The tests commercially available for the detection of BG are varied like the Fungitell assay (Associates of Cape Cod Inc., East Falmouth, MA, USA), the Fungitec G-test MK assay, the G-test assay (both are developed by Seikagaku Corp, Tokyo, Japan), b-glucan test Wako (Wako Pure Chemical Industries Ltd, Osaka, Japan) and so on. Among them Fungitell assay is approved in 2003 by the U.S. Food and Drug Administration for the presumptive diagnosis of invasive fungal infection. BG value of 80 pg/ml was considered positive according to the manufacturer's indications. The accuracy of BG maybe varies owing to the cutoff value of BG.

A meta-analysis made of fourteen studies reported that the average (95% confidence interval) sensitivity and specificity of BG were 94.8% (90.8-97.1%) and 86.3% (81.7-89.9%), respectively. The positive and negative likelihood ratios were 6.9 (5.1-9.3) and 0.06 (0.03-0.11), respectively. The area under the HSROC curve was 0.965 (0.945-0.978) [9]. The pooled specificity was moderate for PCP because the BG assay could be positive for various fungal infections and the presence of factors such as use of intravenous amoxicillin-clavulanic acid, treatment of patients with immunological preparations (albumins or globulins), use of cellulose membranes and filters made from cellulose in hemodialysis, and use of cotton gauze swabs/packs/pads and sponges during surgery [10]. If the aim is to increase the specificity of the test, slightly higher cut-off level than the one used in invasive fungal infections may potentially provide higher specificity, without unacceptable loss in sensitivity [4].

One report shows an excellent diagnostic performance, with a sensitivity of 98% and a specificity of 94%, the positive predictive value was only 64.7% and the negative predictive value is 99.8% [5]. The unsatisfactory PPV is possibly owing to affect by prevalence rate of local people, concurrent infection of other invasive fungi, intravenous injection of albumins or globulins, use of cellulose membranes and so on. So diagnosis of PCP should combine with clinical context. However, with a negative predictive value of 99.8%, a BG level \leq 85 pg/mL almost rules out PCP. Moreover, Serum BG could potentially be of value in differentiating between colonization and infection of PCP [11,12].

The severity and mortality of PCP, as well as BG levels, have been

reported to be lower in HIV-positive patients than in non-HIV patients [13,14]. However other studies didn't show significant difference between them [5, 6,15]. Further evaluation is needed to develop this controversy.

As regard to the value of prognosis of BG, a study shows that decreasing BG levels show a good correlation (88%) with a favorable treatment response [16]. This may assist in deciding whether to continue first-line therapy in cases of missing clinical improvement. Meanwhile, the kinetics of measured BG (Fungitell; Associates of Cape Cod) suggest that whereas increasing levels soon after treatment may not associated with treatment failure for b-d-glucan levels seldom return to the normal level within a 21-day treatment [17]. The increasing BG levels maybe the lysis of fungi after treatment.

In conclusion, the BG test is helpful for the diagnosis of PCP with a high accuracy, especially for patients with severe respiratory failure who are unable to undergo bronchoscopy and other invasive examinations owing to severe hypoxemia.

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*Corresponding author: Jin-Fu Xu, Department of Respiratory Medicine, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, 200433, China, E-mail: jfxu@ymail.com

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