SHORT COMMUNICATION

Analytical Performance Evaluation of Goldstream Fungus (1-3)-β-D Glucan

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SUMMARY

Background: (1-3)-β-D-glucan (BDG) is a fast and simple assay to diagnose invasive fungal infection. In this study, we evaluated the performance of the Goldstream BDG assay (Beijing Gold Mountainriver Tech Development) performed on the automated analyzer, IGL-200 (Genobio Pharmaceutical).

Methods: The precision and linearity of the Goldstream BDG assay were evaluated according to Clinical and Laboratory Standards Institute procedures. BDG results performed on the IGL-200 were compared to a manual photometer, MB-80A (Genobio Pharmaceutical). The manufacturer-provided reference interval was verified.

Results: Within-laboratory imprecision (% Coefficient of Variation) was 9.4%. The best polynomial fit was third-order within the manufacturer’s claimed linear range (32.0 - 830.0 pg/mL). The BDG assay performed on IGL-200 and MB-80A showed a total agreement of 97.6%. All healthy subjects were within range of the manufacturer provided reference interval.

Conclusions: The analytical performance of the Goldstream BDG assay was clinically acceptable.


KEY WORDS

(1-3)-β-D-glucan, evaluation, performance

INTRODUCTION

Various methods are used to diagnose fungal infection. Since microbiological culture takes days to weeks to be reported and biopsy specimens need invasive procedures, several biomarkers are used to monitor and assist with the diagnosis of invasive fungal infection. BDG, (1-3)-β-D-glucan, is a major component of the fungal cell wall and is produced by clinically significant fungi [1-3]. BDG is a fast and simple assay with good diagnostic accuracy [4].

Currently, available BDG assays differ in various aspects such as reagent composition, measurement principle, and cutoff level. The approval status of BDG assay products varies from country to country, and the type of assay used varies greatly depending on the region. Fun-gitell (Associates of Cape Cod, East Falmouth, MA, USA) is the only assay that is cleared by the FDA and CE and largely used in the USA and Europe since 2004.

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Wako BDG assay (Fujifilm Wako Pure Chemical Industries, Osaka, Japan) is widely used in Japan and has obtained a CE mark relatively recently in 2018 [5]. Goldstream BDG assay (Beijing Gold Mountainriver Tech Development, Beijing, China) is predominantly used in South Korea and China [6]. While the clinical performance of BDG assays is well characterized, analytical performance reports of the Goldstream BDG assay are rare. In this study, the analytical performance of the Goldstream BDG assay using the newly developed automated analyzer IGL-200 (Genobio Pharmaceutical, Shanghai, China) was evaluated and compared with BDG assay results performed on the manual photometer MB-80A (Genobio Pharmaceutical).

**MATERIALS AND METHODS**

This study was approved by the Institutional Review Board of Ewha Womans University Mokdong Hospital (approval number: EUMC 2021-08-024).

**Precision**

The repeatability and within-laboratory imprecision of the Goldstream Fungus BDG assay was evaluated according to the Clinical and Laboratory Standards Institute (CLSI) document EP15-A3 [7]. Two concentrations of control sera (Beijing Gold Mountainriver Tech Development) were assayed five times per day for five days.

**Linearity**

The linearity of the BDG assay was evaluated based on the CLSI document EP06-A [8]. The linear interval of the manufacturer’s claimed range was 10 to 1,000 pg/mL. Five concentrations of control material and Fungus 1-3-β-D-Glucan Control (Gold Mountain River Tech Development) were used, which span the analytical measurement range of 32.0 - 830.0 pg/mL. All samples were measured in duplicate. The total allowable error for nonlinearity was defined as ± 10.0%.

**Method comparison**

A total of 42 patient samples were used to compare the Goldstream BDG assay results between the IGL-200 and MB-80A photometry analyzer according to the CLSI document EP12-A2 [9]. Total agreement, positive agreement, negative agreement, and Cohen’s kappa value were evaluated.

**Reference interval verification**

The reference interval was verified according to the CLSI document EP28-A3c [10]. A total of 22 healthy individual samples were used. The manufacturer-provided reference range was under 60 pg/mL.

**RESULTS**

The repeatability and within-laboratory imprecision of the Goldstream BDG assay were 6.6% and 9.4% for high-level control material, respectively (Table 1). For negative control material, all results were under the measurable range (< 10 pg/mL) and imprecision could not be calculated.

The linearity analysis showed that the best polynomial fit was a third-order and differences (95% confidence interval) between the third-order and linear equations were as follows: level 1, -46.5% (-51.6 to -41.4%); level 2, 30.9% (25.2 to 36.6%); level 3, 41.4% (36.9 to 45.8%); level 4, 10.4% (4.8 to 16.1%); level 5, -36.3% (-41.4 to -31.1%) (Figure 1). Compared with the results performed on the IGL-200 and MB-80A, the total agreement, positive agreement, and negative agreement rate was 97.6% (41/42), 95.5% (21/22), and 100% (20/20), respectively. There was one discrepant case with positive MB-80A (89.7 pg/mL) and negative IGL-200 (< 10 pg/mL) (Figure 2). When quantitative results of two assays were compared, the Passing-Bablok regression analysis showed that y (IGL-200) = 1.092 x (MB-80A) - 0.9236 (correlation coefficient (r) = 0.953).

**DISCUSSION**

Although the Goldstream BDG assay is one of the most commonly used BDG assays in Korea and China, its performance evaluation reports are rare. Furthermore, previously reported performance evaluation is limited to the method comparison [11]. The purpose of this study was to evaluate the analytical performance of the Goldstream BDG assay using IGL-200. Previous studies have used the MB-80A, which is a photometer that can run 128 samples simultaneously. It requires manual pretreatment and a reagent addition process. IGL-200 is an automated kinetic tube reader, which can run 30 samples simultaneously without a manual process. Since BDG is a component of the fungal cell wall and exists in the environment, manual treatment increases the possibility of contamination [12]. IGL-200 is an enclosed automatic analyzer, which can reduce possible contamination and operational error.

Within-laboratory imprecision (% Coefficient of Variation) of control material was 9.4%. This result was within a desirable specification (10.0%) which was suggested by the manufacturer. Previous reports with other BDG assays show better precision. Song et al. reported that the Wako assay’s within-laboratory imprecision was 5.9% [6]. Pruller et al. reported that the Fungitell assay’s imprecision ranged from 3.0% to 5.5% [13]. Linearity was evaluated within the ranges of 32.0 -
Table 1. Precision of the Goldstream (1-3)-β-D-glucan assay.

<table>
<thead>
<tr>
<th>Mean (pg/mL)</th>
<th>Repeatability</th>
<th>Within-laboratory imprecision</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>SD (pg/mL)</td>
<td>% CV</td>
</tr>
<tr>
<td>186.26</td>
<td>12.29</td>
<td>6.6</td>
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Abbreviations: CV - coefficient of variation, SD - standard deviation.

Figure 1. Linearity of the Goldstream (1-3)-β-D-glucan assay.

830.0 pg/mL. The best fit polynomial regression was a third-order polynomial, and the difference between the best fit third-order and linear equations was over ± 10.0%. BDG is a quantitatively measured and qualitatively reported item, and linearity evaluation is not essential in clinical laboratories. However, this evaluation did not confirm the linearity within the range claimed by the manufacturer.

There was an excellent correlation between IGL-200 and MB-80A, showing a total agreement of 97.6%. Of the 42 samples evaluated, only one sample showed a discrepancy between IGL-200 and MB-80A. This case was positive (89.7 pg/mL) with MB-80A and negative (< 10 pg/mL) with IGL-200. The patient was diagnosed with acute myeloid leukemia and was under chemotherapy. There was no sign of infection and follow-up BDG assays were all negative. Blood culture and Aspergillus antigen assay were also negative. The possibility of invasive fungal infection in this patient seemed to be very low, and the positive result from MB-80A could be caused by contamination.

Currently available BDG assays differ in many aspects such as pretreatment method, measurement principle (colorimetric vs. turbidimetric), reagent source (Limulus polyphemus vs. Tachypleus tridentatus), and cutoff level (11 pg/mL for Wako, 80 pg/mL for Fungitell and Goldstream). Although there are such differences between assays, there are few studies published on the comparison of each assay, possibly due to certain reagents being used in certain areas according to approval status. According to previous reports, the total agreement between Goldstream and Fungitell was 94.74% and the kappa between Goldstream and Wako was only 0.44 [6,11].

Since BDG is a pan-fungal diagnostic test, ubiquitous environmental fungi such as Penicillium spp. and Paecilomyces spp. could be a source of false-positive results. Therefore, it is important to use appropriate reagents and ensure proper quality control to minimize false-positive results.

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**CONCLUSION**

The Goldstream BDG assay was precise and IGL-200 and MB-80A had very good correlation. The manufacturer reference interval was also acceptable. Linearity evaluation showed a third-order polynomial fit within the manufacturer’s claimed linear range. Since the BDG assay is vulnerable to contamination, it is necessary for the clinical laboratory to control the quality of the assay. Analytical performance evaluation and comparative studies between assays are rarely performed; thus, additional studies are needed. In conclusion, the overall performance of the Goldstream BDG assay was clinically acceptable.

**Declaration of Interest:**
The authors have no conflict of interest to declare.

**References:**


