A Diagnostic Stewardship Intervention to Improve Utilization of 1,3-β-D-glucan Testing

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Abstract

Background
1,3-β-D-glucan (BDG) is a cell wall component of fungi such as *Aspergillus* spp., *Candida* spp., and *Pneumocystis jirovecii*. BDG assay is used as a screening test to aid early diagnosis of invasive fungal infections (IFI) that are associated with significant morbidity and mortality in immunocompromised patients. The diagnostic performance varies depending on IFI risks among study populations, thus it is important to appropriately select patients with risk factors for IFI to optimize utilization of the BDG test.

Methods
An intervention to improve BDG test utilization was initiated at Truman Medical Center on November 28, 2018. The BDG test order was replaced by a BDG test request. The request was sent to the inbox of an on-call pathology team. Patient information was reviewed and the on-call pathology team called the ordering physician to discuss the case based on the approval algorithm chart. The criteria for BDG test approval were 1) immunocompromised or ICU patient, and 2) on empiric antifungal therapy, or inability to perform specific diagnostic tests such as bronchoscopy. If approved, a BDG test order was immediately processed. Retrospective chart review was conducted for 1 year pre- and post-intervention to obtain demographic, clinical, and laboratory data for 4 patient groups. Group 1 included patients who had BDG tests during pre-intervention period. Group 2 was composed of all patients who had BDG test requests during post-intervention period. Group 2a and 2b were the post-intervention patients with approved and rejected BDG test requests, respectively.

Results
The number of BDG tests performed per year decreased from 156 pre-intervention to 24 post-intervention. The number of test requests was 65 and 41 of them were rejected which led to $7,380 direct cost savings. There was no significant difference in age or the proportion of immunocompromised and ICU patients between Group 1 and 2. The test positivity rate was significantly higher in Group 2-a compared to Group 1 (45.8 % vs. 25.3%, p=0.038). There was no delay in IFI diagnosis or IFI-related mortality in patients for whom BDG test requests were rejected.

Conclusion
We successfully and safely implemented a diagnostic stewardship intervention for BDG testing and improved test utilization.

Introduction

- Invasive fungal infections (IFI) are common causes of morbidity and mortality in immunocompromised patients[1, 2]
- Early diagnosis of these infections can improve survival outcomes[3]
- BDG assay is used as a screening test to aid early diagnosis of invasive fungal infections[4]
- However, BDG diagnostic performance varies depending on IFI risks among study populations and it is important to appropriately select patients with risk factors
- Inappropriate use of test can contribute to:
  - Increased healthcare costs
  - Overutilization of antifungal agents[5]

Methods

- A new protocol for BDG test orders was implemented on November 28, 2018 with BDG test order being replaced by a BDG test request order
- The test request order and patient information were reviewed by an on-call pathology team
- Request approval was performed based on the following criteria:
  - Being in the intensive care unit AND currently on empiric antifungal therapy[3,6,7,8]
  - Immunocompromised status AND fungal infection suspected (with consideration of whether or not bronchoscopy to be performed)[9, 10, 11]

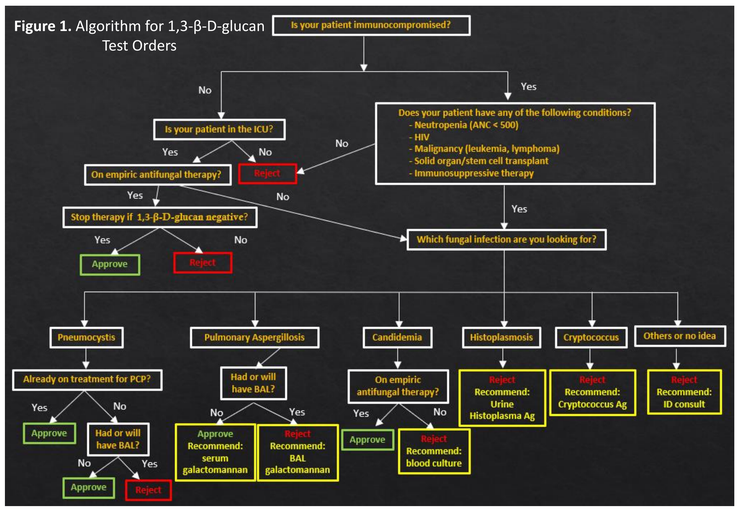

Figure 1. Algorithm for 1,3-β-D-glucan Test Orders

- Retrospective chart review was conducted for 12 month period pre- and post- intervention for clinical data.
- The results were summarized for 4 patient groups including: all BDG orders during pre-intervention period (Group 1), all BDG requests during post-intervention period (Group 2), approved BDG requests during postintervention (Group 2a), and rejected BDG requests during postintervention (Group 2b)

Results

- BDG tests performed decreased from 156 tests in the pre-intervention period to 24 approved tests post-intervention
- Of the 65 tests requested during post-intervention, 41 were rejected which led to direct cost savings of $7,380
- The test positivity rate was significantly higher in Group 2a compared to Group 1 (45.8 % vs. 25.3%, p=0.038)

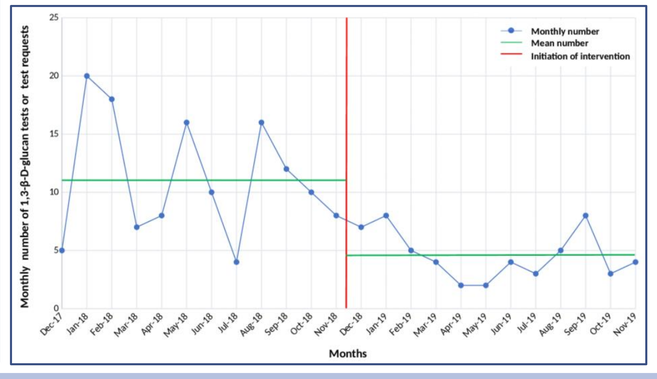

Figure 2. Monthly number of 1,3-β-D-glucan tests performed in the pre-intervention period (Group1) and 1,3-β-D-glucan test requests in the post-intervention period (Group 2)

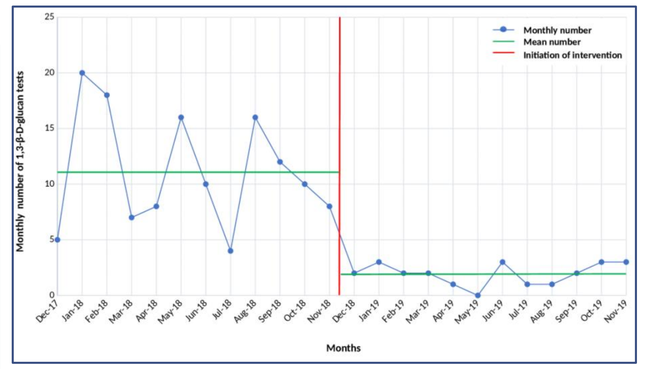

Figure 3. Monthly numbers of 1,3-β-D-glucan test performed in the pre-intervention period (Group 1) and approved 1,3-β-D-glucan tests in the post-intervention period (Group 2a)

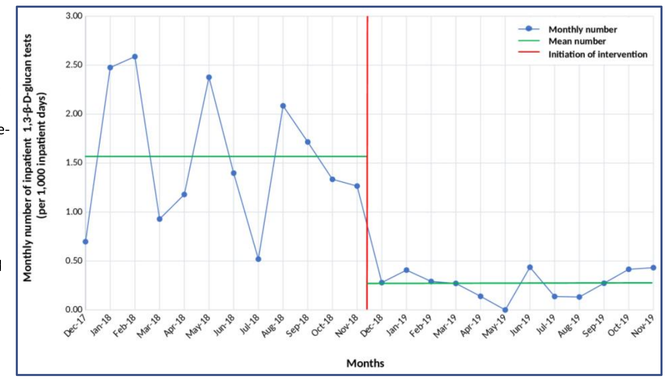

Figure 4. Monthly number of inpatient 1,3-β-D-glucan tests performed in the pre-intervention period (Group 1) and approved inpatient 1,3-β-D-glucan tests in the post-intervention period (Group 2a), adjusted by 1,000 inpatient days

Table 1. Comparison of order characteristics between 1,3-β-D-glucan tests in the pre-intervention group (Group 1) and all test requests in the post-intervention group (Group 2)

	Pre-intervention 1,3-β-D-Glucan Test Orders N = 156	Post-intervention 1,3-β-D-Glucan Test Requests N= 65	p-value
Patient characteristics			
Age, mean [SD] years	52.5 [14.0]	52.3 [13.8]	.964
Male, n (%)	**106 (67.9)**	**33 (50.8)**	**.016**
Immunocompromised condition [a], n (%)	52 (33.3)	26 (40.0)	.348
Neutropenia	6 (3.8)	4 (6.2)	.485
HIV	29 (18.6)	12 (18.5)	.982
Hematologic malignancy	8 (5.1)	5 (7.7)	.478
Organ transplant	2 (1.3)	1 (1.5)	1.0
Immunosuppression for autoimmune disease	6 (3.8)	3 (4.6)	.677
Chemotherapy for malignancy	14 (9.0)	9 (13.8)	.280
Primary immunodeficiency	1 (0.6)	0 (0)	1.0
Clinical and laboratory findings [a], n (%)			
Fever within 48 hours, n (%)	41 (26.3)	24 (36.9)	.114
CBC within 48 hours, n (%)	**140 (89.7)**	**45 (69.2)**	**.001**
Leukocytosis (WBC >12 x 10^3 cells/mcL)	50 (32.1)	27 (41.5)	.177
Leukopenia (WBC <4 x 10^3 cells/mcL)	20 (12.8)	12 (18.5)	.278
Chest imaging, n (%)			
Chest x-ray within 30 days	130 (83.3)	49 (75.4)	.170
CT chest within 30 days	123 (78.8)	47 (72.3)	.293
Normal radiographs	4 (25.6)	3 (4.6)	.422
No radiographs meeting criteria	**0 (0)**	**4 (6.2)**	**.007**
ID consult within 24h before/after order, n (%)	63 (40.4)	33 (50.8)	.156
Recommend/agree with testing	11 (7.1)	7 (10.8)	.357
Empiric antifungal	35 (22.4)	16 (24.6)	.726
Duration of antifungal, n [SD] days	3.9 [2.3]	3.5 [2.2]	.611
Mortality and readmission, n (%)			
All-cause 30-day death	22 (14.1)	6 (9.2)	.321
All-cause 30-day readmission	13 (8.3)	11 (16.9)	.062
Location, n (%)			
Outpatient	21 (13.5)	13 (20.0)	.220
Hospital floor	**82 (52.6)**	**24 (36.9)**	**.034**
ICU	53 (34.0)	28 (43.1)	.201
Specimen type, n (%)			
Serum	111 (71.2)	50 (76.9)	.380
Bronchoalveolar lavage	45 (28.8)	15 (23.1)	.380

Table 2. Comparison of order characteristics between approved (Group 2a) and rejected (Group 2b) 1,3-β-D-glucan test requests in the post-intervention group

	1,3-β-D-Glucan Test Requests Approved N= 24	1,3-β-D-Glucan Test Requests Rejected N=41	p-value
Patient characteristics			
Age, mean [SD] years	54.2 [14.4]	51.2 [13.6]	.416
Male, n (%)	**17 (70.8)**	**16 (39.0)**	**.013**
Immunocompromised condition [a], n (%)	12 (50.0)	14 (34.1)	.208
Neutropenia	2 (8.3)	2 (4.9)	.622
HIV	6 (25.0)	6 (14.6)	.299
Hematologic malignancy	3 (12.5)	2 (4.9)	.350
Organ transplant	1 (4.2)	0 (0)	.369
Immunosuppression for autoimmune disease	1 (4.2)	2 (4.9)	1.0
Chemotherapy for malignancy	3 (12.5)	6 (14.6)	1.0
Clinical and laboratory findings [a], n (%)			
Fever within 48 hours, n (%)	**15 (62.5)**	**9 (22.0)**	**.001**
CBC within 48 hours, n (%)	19 (79.2)	26 (63.4)	.184
Leukocytosis (WBC >12 x 10^3 cells/mcL)	12 (50.0)	15 (36.6)	.290
Leukopenia (WBC <4 x 10^3 cells/mcL)	3 (12.5)	9 (22.0)	.511
Chest imaging, n (%)			
Chest x-ray within 30 days	21 (87.5)	28 (68.3)	.083
CT chest within 30 days	16 (66.7)	31 (75.6)	.437
Normal radiographs	1 (4.2)	2 (4.9)	1.0
No radiographs meeting criteria	1 (4.2)	3 (7.3)	1.0
ID consult within 24 h before/after order, n (%)	15 (62.5)	18 (43.9)	.148
Recommend/agree with testing	**7 (29.2)**	**2 (4.9)**	**.001**
Empiric antifungal	**12 (50.0)**	**4 (9.8)**	**.001**
Duration of antifungal, n [SD] days	3.7 [1.8]	3.0 [3.7]	.596
Mortality and readmission, n (%)			
All-cause 30-day mortality	2 (8.3)	4 (9.8)	1.0
All-cause 30-day readmission	7 (29.2)	5 (12.2)	.089
Location, n (%)			
Outpatient	**1 (4.2)**	**12 (29.3)**	**.022**
Hospital floor	8 (33.3)	16 (39.0)	.646
ICU	**15 (62.5)**	**13 (31.7)**	**.016**
Specimen type, n (%)			
Serum	22 (91.7)	28 (68.3)	.036
Bronchoalveolar lavage	**2 (8.3)**	**13 (31.7)**	**.036**

Table 3. Comparison of 1,3-β-D-glucan test results in pre-intervention period (Group 1) and approved tests post-intervention period (Group 2a)

	Pre-intervention Fungitell, N=154 [b] (serum 110, BAL 44)	Post-intervention Approved Fungitell, N=24 (serum 22, BAL 2)	p-value
Positive (serum≥80, BAL>500), n (%)	**39 (25.3)**	**11 (45.8)**	**0.038**
Turnaround Time, mean [SD] hours	49.4 [31.1]	46.9 [30.0]	0.729

Conclusions

- We successfully and safely implemented a diagnostic stewardship intervention for BDG testing and improved test utilization.
- The intervention did not delay diagnosis of invasive fungal infections or increase empiric antifungal use.

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Internal Citations

[a] Not mutually exclusive
[b] Two of the tests were not performed due to inadequate lab specimen

References

1. Wright WF, Overman SB, Ribes JA. (1–3)-β-D-Glucan Assay: A Review of its Laboratory and Clinical Application. *Lab Med Am Soc Clin Pathol*. 2011. 42: 679–85.
2. Koo. S. Et al. Diagnostic performance of the (1->3)-bet-D-glucan assay for invasive fungal disease. *Clin Infect Dis*. 2009 Dec 1;49(11):1650-9.
3. Kritikos, A. Et al. Impact of the beta-glucan test on management of intensive care unit patients at risk of invasive candidiasis. *J. Clin. Microbiol*. April 2020.
4. Obayashi, T. Et al. Plasma (1-> 3)- β-D-glucan measurement in diagnosis of invasive deep mycosis and fungal febrile episodes. *Lancet* 1995; 345: 17-20.
5. Morgan DJ. Et al. Diagnostic Stewardship—Leveraging the Laboratory to Improve Antimicrobial Use. *JAMA*. 2017;318(7):607-608
6. Posteraro B. Et al. Early diagnosis of candidemia in intensive care unit patients with sepsis: a prospective comparison of (1→3)-β-D-glucan assay, Candida score, and colonization index. *Crit Care*. 2011.15 (5):R249.
7. Nucci, M. Et al. Discontinuation of empirical antifungal therapy in ICU patients using 1,3-β-d-glucan. *J Antimicrob Chemother*. 2016 Sep;71(9):2628-33.
8. Giacobbe DR. Et al. Combined use of serum (1,3)-β-D-glucan and procalcitonin for the early differential diagnosis between candidaemia and bacteraemia in intensive care units. *Crit Care*. 2017. 21 (1):176.
9. Singh, S. Et al. Evaluation of biomarkers: Galactomannan and 1,3-beta-D-glucan assay for the diagnosis of invasive fungal infections in immunocompromised patients from a tertiary care centre. *Indian J Med Microbiol*. 2018. 36 (4):557-563.
10. Lahmer T. Et al. Comparison of 1,3-β-d-glucan with galactomannan in serum and bronchoalveolar fluid for the detection of Aspergillus species in immunosuppressed mechanical ventilated critically ill patients. *J Crit Care*. 2016 Dec;36:259-264.
11. Hammarstrom, H. Et al. Serum-based diagnosis of Pneumocystis pneumonia by detection of Pneumocystis jirovecii DNA and 1,3-β-D-glucan in HIV-infected patients: a retrospective case control study. *BMC Infect Dis*. 2019. 19(1):658.