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Clinical utility of the beta-D-glucan assay in general medical and surgical patients.

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Background

Invasive fungal disease (IFD) is associated with significant mortality but can be difficult to diagnose in a timely fashion with culture based methods. Antifungal treatment of potential IFD can be associated with considerable toxicity, cost and development of antifungal resistance. Therefore, accurate methods of diagnosing IFD in certain populations are required. An assay for detection of (1,3) beta-D-glucan (BDG) in serum is now available, and potentially offers a timely means to achieve this[1]. To investigate the clinical utility of this test, we conducted a retrospective single centre observational study of the use of this assay in a central London teaching hospital.

Method

All BDG assays sent in the fiscal year 01/04/2017 to 31/03/2018 were identified. HIV positive, intensive care unit (ICU), and paediatric patients were excluded. Demographic, clinical, laboratory, and treatment information were extracted from electronic health records. BDG turnaround time (TAT), and antifungal initiation and cessation in relation to BDG result dates were assessed. Sensitivity and specificity of the BDG assay, against both fungal culture results and against 'clinical decision to treat', were also assessed. The culture result closest to the BDG request date was used, within 1 week either side of the BDG request date. The study site currently performs fungal culture in a centralised (off-site) laboratory, but BDG assays are sent to the national mycology reference laboratory in Bristol.

Results

83 BDG assays from 72 patients were identified with a mean patient age of 57 years [range 21-81] and 53% were female. The cohort comprised 15 oncology patients, 26 respiratory patients (17 with chronic respiratory disease) and 13 gastroenterology patients (9 gastrointestinal surgery and 4 chronic liver disease patients); all patients were deemed at risk from IFD by the treating clinician. The mean TAT was 13 days [range 1-37], with 24/83 positive results (BDG cut-off 80pg/mL). Serum galactomannan (GM) assay was performed alongside 75 of the 83 BDG assays, with only 1 positive GM result (GM cut-off 0.5 ODI).

27/72 patients received antifungals during admission. 22/27 patients were started on antifungals empirically whilst awaiting assay results. 14/22 subsequently returned a negative BDG result, with 9/14 stopping antifungal treatment before, 2/14 stopping on the day of, and 3/14 stopping after the result was received. 6/9 patients who stopped treatment before the BDG result date were discharged before the result was received. 95 patient-days of antifungals could have been saved if BDG results had been received within 24 hours. In only 5 patients was antifungal treatment initiated after return of the BDG result, suggesting that it was generally not used in the decision to initiate treatment.

The sensitivity of the BDG assay against fungal culture from invasive samples was 44%, with a specificity of 73%. Against 'clinical decision to treat with antifungals', BDG sensitivity was 37% and specificity 82%.

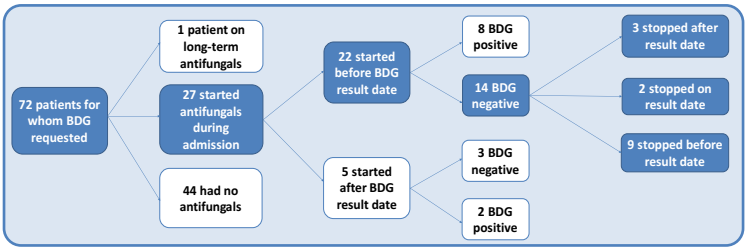
	Positive Culture	Negative Culture
Positive BDG 24/83 assays	4	20
Negative BDG 59/83 assays	5	54

	Antifungal treatment	No antifungal treatment
Positive BDG 18/71* patients	10	8
Negative BDG 53/71* patients	17	36

*1 patient out of the 72 was on long-term antifungals so excluded from decision to treat analysis

Criteria	Result [range]
Age	57 [21-81] years
BDG results	Positive: 24/83 assays Negative: 59/83 assays
Turnaround time	13 [1-37] days
Antifungals stopped due to negative BDG result	3/14
Days of antifungals that could potentially have been saved	95 [11/14* patients]

*3 patients were started on long term antifungals for ABPA



Conclusions

- Delays in obtaining BDG results mean cessation of antifungals is largely reliant on clinical parameters
- BDG sensitivity against fungal culture was poor but with a reasonable specificity
- When comparing BDG results against a clinical judgement of the likelihood of IFD, sensitivity decreased, but specificity improved
- Clinical utility of the BDG assay likely lies in its ability to aid early cessation of antifungal therapy rather than to initiate treatment
- To have any use in the diagnostic process, turnaround times must be improved

References

1.National Institute for Health and Care Excellence (NICE), *Fungitell for antifungal treatment stratification [MIB118]*. 2017. Available from: https://www.nice.org.uk/advice/mib118/chapter/Summary

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