Antifungal Stewardship in Critical Care: Implementing a diagnostics-driven care pathway in the management of invasive candidiasis

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Introduction

- Invasive candidiasis (IC) is the most common invasive fungal disease in patients admitted to critical care (CrCU)[1]
- Early diagnosis of IC has remained challenging due to the low sensitivity of culture-based techniques and the lack of internationally agreed case definitions
- St James's Hospital (SJH) is the largest tertiary referral centre in Ireland and has a multi-specialty 28 bed CrCU, with *Candida* spp. being the third most common aetiology of nosocomial bloodstream infection
- Based on national data, SJH has high antifungal consumption rates[3] and an audit carried out in 2016 showed a median duration of 8-10 days of empiric antifungal therapy (AFT) for suspected IC in our CrCU[2]
- The fungal biomarker (1-3)-β-d-glucan (BDG) has been shown to aid in the diagnosis of IC in critical care and has been studied as an antifungal stewardship tool due its high negative predictive value[4, 5]
- A prospective study on invasive fungal disease in our CrCU in 2015 indicated that on-site BDG testing may be useful as part of an antifungal stewardship program[6]

Objectives

- To analyse the impact of a diagnostics-driven care pathway incorporating an in-house serum BDG assay on the management of IC in CrCU in SJH

Methods

- A prospective audit of BDG testing and antifungal stewardship in accordance with a proposed care pathway was performed (Figure 1)
- Patients started antifungal therapy for suspected IC in CrCU between 1st December 2017 and July 31st 2018 were included
- A treatment episode was defined as a patient receiving ≥1 treatment dose of a systemic antifungal agent for suspected IC in CrCU, having not been on AFT in the previous 24 hours
- Patients on AFT prior to admission to ICU, or those on AFT for reasons other than IC were excluded
- Data regarding adherence to the clinical pathway, antifungal consumption in CrCU, BDG and microbiology results, patient outcome and demographics were prospectively collected and tabulated using Microsoft Excel™
- Data were obtained during daily Clinical Microbiology ICU rounds, as well as through electronic patient records and laboratory information systems.
- BDG testing was performed once weekly using the Fungitell™ (Associates of Cape Cod inc.) assay
- A negative serum BDG was <60 pg/ml, a positive result was >80 pg/ml, whereas 60 – 80 pg/ml was classified as indeterminate

Care Pathway for suspected IC

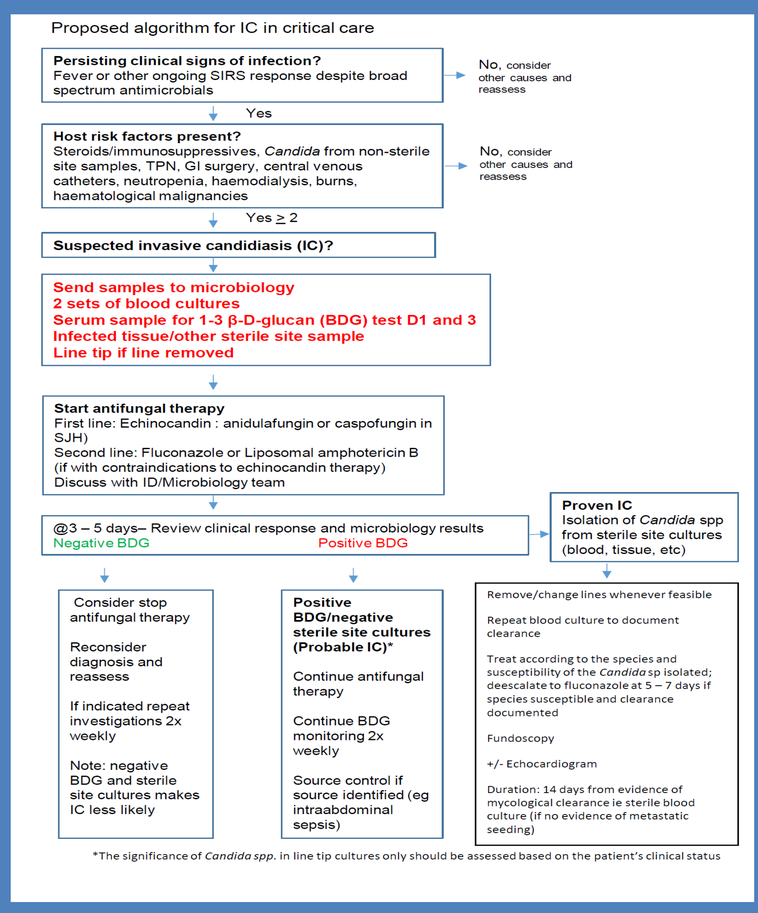

Figure 1. Care Pathway

Results

- During the 7 months there were 116 antifungal treatment episodes commenced in CrCU for suspected IC, in 98 different patients
- At least one serum BDG sample was sent in accordance with the Clinical Pathway in 103 (89%) of these treatment episodes
- Indications for starting AFT were recorded, and episodes were subsequently classified as proven, probable, colonised or having no microbiological evidence of IC, in accordance with the care pathway (Table 1)

Treatment Episodes	N= 116 (%)
With BDG sent	103 (89%)
Individual patients	**98**
Indications for starting AFT (pre-BDG result)	**N=103 (%)**
Targeted	4 (4%)
Pre-emptive	20 (19%)
Empirical	71 (69%)
Prophylactic	8 (8%)
Diagnostic Category (incorporating BDG result)	**N = 103 (%)**
Proven IC	10 (10%)
Probable IFD	35 (34%)
Colonised	42 (41%)
No microbiological evidence	16 (15%)

Table 1.

AFT commenced Empirically

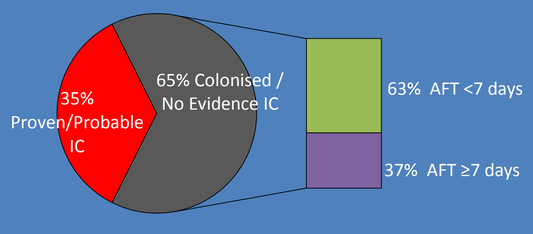

Figure 2.

- 46/71 (65%) of empiric episodes were deemed to be either colonised or have no evidence of IC
- Of this group 29/46 (63%) stopped AFT after < 7 days of treatment, in accordance with the care pathway
- Median duration of AFT for patients treated empirically was 5 days (range 1-47 days)
- Antifungal consumption data was analysed for the period of the audit, as well as the preceding 6 months (Figure 3)

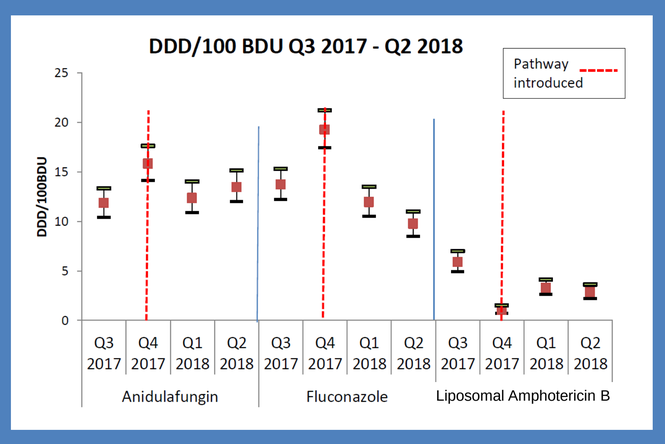

Figure 3. AFT consumption

Diagnostic Performance of BDG

Sensitivity	64%
Specificity	70%
NPV	88%
PPV	36%
NLR	0.53
PLR	2.06

- Positive result = ≥ 1 BDG ≥ 80 pg/L

Sensitivity	55%
Specificity	82%
NPV	84%
PPV	52%
NLR	0.55
PLR	3.08

- Positive result = ≥ 2 BDG ≥ 80 pg/L

Table 2

Patient Safety

- 42/58 (72%) of episodes classified as colonised or having no evidence of IC stopped AFT in CrCU
- Only 1 patient in this group was diagnosed with proven or probable IC within 7 days of discontinuation

Conclusion

- Our results indicate that access to an in-house BDG assay can assist clinicians to adopt a diagnostic-driven approach in the management of IC in critical care
- Median duration of empirical AFT was reduced in the cohort of patients with negative BDG who were managed according to the algorithm, although further analysis is needed to assess the impact on antifungal consumption

References

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