Update on Antifungal Stewardship

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Safeguarding antibiotics for Scotland, now and for the future
Antifungal Steering Group

Chaired by Prof Brian Jones
Representatives from SAPG, Haemato-oncology, Critical Care and Respiratory medicine

Key aim is to produce national best practice recommendations to optimise use of antifungals

This is expected to:
- Reduce unnecessary use
- Standardise practice to reduce unwarranted variation
- Reduce resistance at individual and population level
Antifungal use in critical care – key issues

Data on antifungal use from ICUs in GGC, Lothian and Fife

• Significant variation in volume of antifungals used (DDD/1000 OBD)
• Variation in azoles versus echinocandins
• Many caveats to data and difficult to compare boards/units

Main indication for antifungal use is potential/suspected candidaemia

• Guidelines give weak support for prophylaxis in specific patient groups and empirical use in patients failing to respond to antibacterial therapy
• Risk-based predictive algorithms are available
• Diagnostics - β-D-glucan assay may have a role – based on NPV
Survey of Antifungal use in Critical Care

An on-line survey was disseminated via the Scottish Intensive Care Society Audit Group (SICSAG) team in ISD to gather info on:

• Local guidelines
• Use of antifungal prophylaxis & empirical treatment
• First and second line choices
• Criteria used to start and stop antifungal therapy

RESULTS
15 responses across 6 board areas, variation in practice, some boards have guidelines, fluconazole is main first line choice but a few units use caspofungin, low use of biomarker diagnostics

I'd fully support this initiative as treatment of possible fungal infection feels like guesswork at present. Although there isn't much evidence to inform guideline contents at least uniformity in practice will allow future evidence to be gathered and keep costs down
Use of biomarker diagnostics in adult critical care

Clinical and cost effectiveness of Beta-D-glucan (BDG) tests in invasive Candida infection assessed by Scottish Health Technologies Group (SHTG)

- Clinical evidence and economic modelling suggests potential for the Fungitell® Beta-D glucan (BDG) test to reduce empirical antifungal overuse with minimal direct cost impact
- Evidence indicates that BDG tests can be used as part of strategies to increase the rate of early discontinuation of empirical antifungal therapies
- Optimum cost-effectiveness of BDG testing is only seen in units with very high antifungal use and high lab throughput. Good clinical microbiology liaison remains pivotal.

The gold standard for the diagnosis of candidaemia is a **positive blood culture** but overall sensitivity of blood cultures in diagnosing invasive candidiasis is approximately 50%. May be negative in cases of low-level level candidaemia, intermittent candidaemia or deep-seated *Candida* infection.
Good practice recommendations - treatment

**Initial antifungal therapy: positive culture but no sensitivities**

First Line therapy: **IV fluconazole**

Alternative therapy: **Echinocandin e.g. IV Caspofungin**

Or

**AmBisome® IV lipid formulation amphotericin B**

May be considered in patients who are critically ill; on vasopressors for resuscitation of septic shock and evidence of sepsis-associated organ dysfunction. Note that echinocandins have higher cost than azoles

*No single trial to date has demonstrated clear superiority of an echinocandin over fluconazole in the management of candidaemia.*
<table>
<thead>
<tr>
<th>Drug</th>
<th>Standard Dose</th>
<th>Extremes of body weight</th>
<th>Hepatic Impairment</th>
<th>Renal Impairment</th>
<th>CRRT$</th>
</tr>
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<tbody>
<tr>
<td>Fluconazole</td>
<td>IV 800mg stat then 400mg daily</td>
<td>12mg/kg stat then 6mg/kg daily</td>
<td>No change</td>
<td>200mg daily if creatinine clearance (CrCL) &lt; 50ml/min</td>
<td>400mg twice daily</td>
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<tr>
<td></td>
<td></td>
<td>Dose according to total body weight</td>
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<tr>
<td>Caspofungin</td>
<td>IV 70mg stat then 50mg daily (70mg daily if &gt; 80kg)</td>
<td>If weight &gt; 110kg give 105mg daily</td>
<td>If Child-Pugh B or C, maintenance dose 35mg daily*</td>
<td>No change</td>
<td>No change</td>
</tr>
<tr>
<td>Liposomal Amphotericin B</td>
<td>IV 3mg/kg</td>
<td>Dose on lean body weight</td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
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*The choice of antifungal agent and dose should always be discussed with a Microbiologist (or an infection specialist) and Pharmacist.*
Good practice recommendations – prophylaxis and empirical use of antifungals

There are no current multicentre randomised controlled clinical trials in adult patients to support the use of prophylactic, empirical or pre-emptive antifungal therapy in non-neutropenic patients

The role of antifungal prophylaxis in high-risk patients may be considered, in consultation with a Microbiologist or an Infection Specialist, in ICU settings with a high rate (>5%) of invasive candidiasis. The use of empirical antifungal therapy in high risk patients (in the absence of proven/confirmed invasive candidiasis) may be justified and should be discussed with a Microbiologist or an Infection Specialist. Note that endotracheal colonisation alone is not an indication for empirical antifungal therapy.
Good practice recommendations – other *Candida* infection

<table>
<thead>
<tr>
<th><strong>Candida species isolated from sputum/respiratory tract specimen</strong></th>
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<tbody>
<tr>
<td>Growth of <em>Candida</em> from sputum/respiratory tract secretions without clinical signs of oral thrush commonly indicates colonisation and does not warrant treatment.</td>
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<tr>
<td><em>Candida</em> in the sputum/respiratory tract secretions is not an indicator of <em>Candida</em> pneumonia, which is considered an extremely rare infection.</td>
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<thead>
<tr>
<th><strong>Candida species isolated from throat swab/sputum/upper respiratory tract specimen indicative of oropharyngeal candidiasis</strong></th>
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</thead>
<tbody>
<tr>
<td>HIV testing should be considered in all patients with unexplained oropharyngeal candidiasis.</td>
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<tr>
<td>For mild <em>Candida</em> infection, nystatin oral suspension is a reasonable empirical agent. For moderate to severe disease, oral fluconazole for 7–14 days is recommended. For denture-related candidiasis, appropriate disinfection of the denture, in addition to antifungal therapy is advised.</td>
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<tr>
<th><strong>Candida species isolated from urinary tract specimen (mid-stream urine, catheter specimen)</strong></th>
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<tr>
<td>Growth of <em>Candida</em> is commonly encountered, particularly in patients with an indwelling urinary catheter. Elimination of predisposing factors, such as removal/change of urinary catheters when feasible and repeat sampling is advised. Antifungal treatment is not recommended in asymptomatic patients who are not high risk for dissemination. High-risk patients include neutropenic patients, very low-birth-weight infants (&lt;1500 g), and patients undergoing urologic manipulation or instrumentation.</td>
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<tr>
<th><strong>Candida species isolated from genital tract specimens indicative of vulvo-vaginal candidiasis</strong></th>
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<tr>
<td>For the treatment of uncomplicated candida vulvo-vaginitis, topical antifungal therapy is recommended. No one agent has been shown have superiority to another.</td>
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Next steps for AF stewardship work

- Publish candidaemia guidance on SAPG website
- Draft good practice recommendations for antifungal use in Haemato-oncology incorporating biomarker diagnostic advice from SHTG
- Review results of chronic respiratory fungal infection survey – current practice to inform good practice recommendations
What is happening in England

• CQUIN 2019-20 includes antifungal stewardship within the Specialised Services Scheme Prevention of ill health section

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<tr>
<th>Highlighted action / method</th>
<th>Benefit delivered</th>
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<tr>
<td>PSS1: Medicines Optimisation and Stewardship</td>
<td>• The medicines optimisation programme that this indicator supports is delivering cost savings of hundreds of millions.</td>
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<td></td>
<td>• Using these techniques also to address over-use of antifungals will enable the NHS to play its part in stemming the worldwide build-up of resistance to antifungals (a WHO priority). This will protect neutropenic patients and others at risk of invasive fungal infections.</td>
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- Audits involve collecting data on treatments, diagnostics and clinical reviews
What next?

- GUIDANCE - Good Practice Recommendations
- SURVEILLANCE OF USE & RESISTANCE - national and local data plus Point Prevalence Surveys
- ANTIMICROBIAL REVIEW AUDIT – include in day 3 review work
THANK YOU

ANY QUESTIONS?