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Comparison of Vitek 2 YS08 with Sensititre YeastOne for *Candida* susceptibility testing

Sir,

An early and accurate antifungal susceptibility result is important for the treatment of invasive candidiasis. Sensititre YeastOne (Thermo Scientific, USA) has good concordance with the standard Clinical and Laboratory Standards Institute (CLSI) reference method for *Candida* susceptibility testing,[1] and therefore is a widely utilised commercial method of determining *Candida* susceptibility. The automated Vitek 2 AST YS08 (bioMérieux, France) has advantages in decreased turnaround time, reduced costs and ease of use; however, there are limited data regarding its performance for resistant isolates.

A total of 68 clinical isolates of *Candida* species, many known to have antifungal resistance, were tested by Vitek 2 AST YS08 and the Sensititre YeastOne method according to the manufacturer's instructions. They were comprised of *Candida albicans* (*n*=20), *Candida glabrata* (*n*=21), *Candida tropicalis* (*n*=9), *Candida parapsilosis* (*n*=10) and *Candida krusei* (*n*=8). *Candida* species were identified with a log score >2.0 using the MALDI Biotyper (Bruker, USA).

Essential agreement was defined as ≤2 minimum inhibitory concentration (MIC) dilution difference and categorical agreement was obtained when the MIC result fell within the same interpretive categories according to CLSI breakpoints for azoles and echinocandins,[2] and according to the epidemiological cutoff values for amphotericin B.[3] Very major errors, major errors and minor errors were defined according to a prior study, with Sensititre YeastOne as the reference method.[4] Very major errors occurred where the reference method categorised the isolate as resistant and Vitek 2 categorised it as susceptible. Major errors occurred where the reference method categorised the isolate as susceptible and Vitek 2 categorised it as resistant. Minor errors occurred where one of the methods categorised the isolate as susceptible or resistant and the other method categorised the isolate as intermediate or susceptible dose dependent.

Table 1 demonstrates that essential agreement and categorical agreement were suboptimal for fluconazole and voriconazole with some very major errors, while there was good agreement for the other antifungals tested, acknowledging the lack of isolates which were non-susceptible to micafungin and amphotericin. Poor agreement for fluconazole was largely found in *C. albicans* where essential agreement occurred in 14/20 isolates and categorical agreement in 17/20 isolates. Poor agreement for voriconazole was predominantly found in *C. krusei* where essential agreement occurred in 2/8 isolates and categorical agreement occurred in only 2/8 isolates, mostly classified as minor errors. Caspofungin non-susceptibility occurred predominantly in *C. glabrata* complex and it was in this species complex that poor categorical agreement for caspofungin occurred with essential agreement in 15/15 isolates and categorical agreement in 5/15 isolates, mostly classified as minor errors.

Many previous studies of Vitek 2 *Candida* susceptibility testing had a low percentage of resistant isolates,[5–7] hampering the comparison to our study; however, some studies which were enriched for resistant isolates like ours have shown better performance. Cuenca-Estrella *et al.* tested a set of 154 *Candida* isolates, approximately half with elevated azole MICs.[8] They found essential agreement between Vitek 2 and the formal CLSI method of >96% for fluconazole and voriconazole. Using old CLSI breakpoints for fluconazole, minor errors occurred for 25 isolates, and major or very major errors in three isolates. For voriconazole, minor errors occurred for two isolates, and major or very major errors for four isolates. Posteraro *et al.* found good essential agreement and categorical agreement for their set which included 11 azole resistant *C. albicans* and 48 azole resistant *C. glabrata*.[4] The better essential agreement seen in these two studies compared to our study may have been influenced by the *Candida* species which were tested. Both studies included an assessment of fluconazole and

Table 1 Comparison of Vitek 2 AST YS08 to reference method Sensititre YeastOne *Candida* susceptibility testing

Antifungal agents	Isolates[a] (*n*)	Resistant[b] (*n*)	I/SDD[b] (*n*)	EA (%)	CA (%)	Misclassified isolates (*n*)		
						VME	ME	mE
Fluconazole	39	18	1	77	90	2	0	2
Voriconazole	47	14	11	79	66	2	1	13
Caspofungin	62	3	7	100	82	0	2	9
Micafungin	54	1	0	100	100	0	0	0
Amphotericin	67	0	0	100	100	0	0	0
Flucytosine[c]	68	NA	NA	99	NA	NA	NA	NA

CA, categorical agreement; EA, essential agreement; mE, minor errors; ME, major errors; VME, very major errors.
[a] Vitek 2 AST YS08 does not provide results for *Candida glabrata* against fluconazole and voriconazole, nor for *Candida krusei* against fluconazole. Six isolates for caspofungin and one isolate for amphotericin terminated by Vitek AST YS08 so did not allow comparison. Fourteen isolates were not tested for micafungin by YeastOne so did not allow comparison.
[b] Resistant or intermediate/susceptible dose dependent according to Sensititre YeastOne results with CLSI interpretative criteria.
[c] There is no CLSI breakpoint or epidemiological cutoff value for flucystosine, therefore no CA was calculated.

voriconazole for *C. glabrata* complex, which we could not assess as the current Vitek 2 system issues no result for fluconazole or voriconazole for this species complex. Additionally, Posteraro *et al.* did not test *C. krusei* which in our study had poor essential agreement for voriconazole. Categorical agreement between Vitek 2 and Sensititre YeastOne for caspofungin was noted to be suboptimal in our study, congruent with Astvad *et al.* who found 6/31 *fks* mutant *Candida* isolates were misclassified as susceptible by the Vitek 2 system, while the reference CLSI and European Committee on Antimicrobial Susceptibility Testing (EUCAST) methods misclassified <4% of these isolates.[9]

In our study skewed for resistant *Candida* isolates, essential agreement and categorical agreement between Vitek 2 AST YS08 and Sensititre YeastOne were suboptimal. More validation data with resistant isolates needs to be obtained for the Vitek 2 AST YS08 system.

Conflicts of interest and sources of funding: BioMerieux supplied Vitek 2 AST YS08 cards free of charge. The authors state that there are no conflicts of interest to disclose.

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A descriptive account of sequential nailfold capillaroscopy in scleroderma

Sir,

Microvasculopathy is an early and prominent pathological feature of systemic sclerosis (SSc), or scleroderma, and is most easily recognised in the capillaries of the nailfold using the simple technique of nailfold capillaroscopy (NFC).[1] Many studies have confirmed that NFC has proven utility in the early diagnosis of SSc and it has been included in the classification criteria for this disease since 1988.[1] However, to date there is little information concerning sequential NFC in scleroderma and whether documentation of nailfold capillary morphology and density over time may assist in disease management and prognosis.

In this current study we have compared and contrasted sequential nailfold capillary density and morphological characteristics in both healthy subjects and scleroderma patients for periods of up to 12 months.

There were nine patients in the scleroderma study group, three with diffuse cutaneous scleroderma, five with limited cutaneous scleroderma and one with overlap scleroderma. All patients were recruited from the South Australian Scleroderma Register and all patients fulfilled the diagnosis of scleroderma according to the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) 2013 classification criteria and stratified as limited cutaneous, diffuse cutaneous or overlap scleroderma according to LeRoy's criteria.[2–4] The demographics, clinical and serological features and medications of the scleroderma study group (at entry to the study) are shown in Table 1.

There were four healthy control subjects, three females and one male with an age span of 28–66 years. None were smokers and none had Raynaud's phenomenon. NFC was performed on both patients and controls at regular intervals over the year study period.

NFC was performed on the fourth finger nailfold of each hand using a Capiscope (supplied by KK Technology, United Kingdom). Paraffin oil or KY jelly was applied to the nailbed to reduce the skin/air refractive barrier. The Capiscope technique allows visualisation of the nailfold capillaries at magnifications of 100× and 300× and has the capability of digitalisation of the nailfold images or video capillaroscopy. The procedure was done exactly as described in the Capiscope user's manual enabling the capture of multiple digitalised images.[5] Overlapping images were then aligned and electronically spliced to form a composite mosaic of the nailfold and its capillary arcades. The microvasculature was then assessed from the digitalised images. In particular, we assessed either quantitatively or qualitatively the symmetry or otherwise of the capillary arcades, the morphology and dimensions [normal size dilated or grossly dilated (giant) of the capillary loops, nailfold capillary density, the presence and appearances of capillary microbleeds and the appearance of the cuticle (widened, roughened, discoloured)].

Capillary density was measured from the digitalised nailfold images of each nailfold by the direct observation method