Evaluation of remote triazole capillary blood testing to facilitate remote therapeutic drug monitoring (TDM) - A validation study

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Background: The advent of COVID-19 has meant that patients with chronic diseases needed to shield, however, investigations were needed to guide continual management of their disease. Remote monitoring options were evaluated to ensure the standard of care is not compromised.

Purpose and Hypothesis: The aim was to validate remote (finger-prick) capillary triazole blood testing and evaluate the potential role of remote TDM in chronic antifungal therapy.

Methods: A single-center prospective cross-sectional study of tenosan finger prick capillary blood testing compared with gold standard venous sampling was performed. Remote finger prick capillary blood testing was validated compared to local standard venous using comparative statistical analysis. Comparative statistical analysis: Paired t-test, correlation and Bland-Altman were used to determine if there was agreement or association between the sampling methods.

Results: A total of 66 patients receiving triazole therapy were recruited and 17 pooled pairs of remote capillary and venous triazole concentrations and metabolites were prospectively analysed, with the rest of the blood samples not being analysed due to insufficient sample, hemolysis, or undetectable triazole level (<0.2 mg/L). There was a significant difference in the comparison of the two methods of sampling with paired t-test: P < 0.001. Bland-Altman analysis yielded wide bias (-49.07%) and wide limits of agreement (-85.5% to +32.4%). On average capillary triazole concentrations were 37% lower than venous concentrations (Fig. 1). There was however a very strong correlation between capillary and venous tests (Pearson's correlation coefficient r = 0.9219, P < 0.001, Fig. 2).

Conclusions: Remote capillary triazole sampling does not appear interchangeable with venous sampling, but being strongly correlated and on average 27% of the venous value, could be a predictor of venous triazole level, or be useful for intra-patient longitudinal monitoring. When incorporated into an outpatient clinical pathway it can improve shared decision-making and patient experience. Further research is required to determine appropriate target reference ranges if the new lower capillary levels can be used routinely, especially in the climate of COVID-19 where social distancing measures limit patient access to hospitals and clinics for routine investigations.
Paired t test - pooledazole

Paired T comparison for capillary and venous samples
A study to compare detection of *Aspergillus* galactomanan in patients with clinically suspected invasive Aspergillosis using the Lateral Flow Assay (LFA) in comparison with Enzyme Linked Immunoassorbent Assay (ELISA) and identification of new risk factors as per BM-AspICU criteria

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Objectives

1) To compare
   a) performance characteristics of lateral flow assay (*Aspergillus* galactomanan LFA, Inter, USA) in comparison with ELISA (PlateliaTM *Aspergillus* antigen, Bio-Rad, France) for detection of *Aspergillus* antigen in blood and BAL samples from suspected cases of invasive Aspergillus (IA)
   b) turn-around time for reporting and the cost per test for both the methods
2) To identify new host factors for categorization of IA as per BM-AspICU (Hamans et al. Ann. Intensive Care, 2021) guidelines

Methods: A total of 50 consecutive leftover samples (30 blood and 20 BAL) received for testing by Galactomanan assay by ELISA method were included. LFA and ELISA were performed as per manufacturers’ instructions. Results were recorded using the Digital Reader provided which gives readings as Positive (>0.5 and ≥0.0 Negative). Additionally, results were rated visually by two different people and graded as 0 (negative), 1+ (very faint band), 2+ (faint band), and 3+ (strong band). The values obtained by ELISA were reported as Galactomanan Index. Results of LFA and ELISA were compared. Patient profiles were studied to identify the possible and probable cases of IA as per BM-AspICU guidelines.

Results: Overall, 92% samples (n = 46) were positive with ELISA. Results of LFA and ELISA were comparable in 68% samples (n = 34). For all except two samples, visual readings of LFA (1 with 3+ and 2+ with 1+ readings) correlated with digital readings. Sensitivity of LFA was 73.6% (95% CI). Applying BM-AspICU criteria, 26% (n = 14) were categorized as probable, 64% (n = 32) as possible cases of IA and 9% (n = 4) as NO IA. A total of 12 patients had clinical host factors, 42% (n = 21) had other risk factors and we were able to identify 14% (n = 8) cases with new risk factors which were CNS involvement/treatment injury/hemorrhage on mechanical ventilation. Clinical features were present in all of these 58% (n = 29) cases whereas radiological imaging was done in only 25 cases out of which 28% (n = 14) were positive. BM-AspICU criteria require ≥2 radiological criteria, but only two of the BAL samples were culture positive for *Aspergillus* species. These criteria could not be strictly applied to most patients in our study since invasive procedure such as BAL was not done, instead blood was sent for galactomannan detection.

The average turn-around time was 5–7 days for ELISA since the test was run once a week whereas it was 5–24 h for the LFA. The pre-processing of samples and time required to perform the procedure for both the assays are similar. The cost per test for ELISA was Rs.1875/- as against LFA for Rs.750/-.

Conclusion: LFA for galactomannan detection is an easier to perform, cost-effective method for diagnosis of IA as compared with ELISA. LFA overcomes the difficulty of insufficient volume of calibrators and controls provided with the ELISA kit. Useful especially for patients admitted in ICU where reports can be issued on the same day instead of batch testing. Identification of new risk factors and inclusion of the same under guidelines is essential to outper and send samples for testing for early initiation of treatment.