"Evaluation of Novodiag CarbaR+ for the detection of carbapenemase producing organisms from faeces – NUH prevalence study 2020"

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Introduction

Antibiotic resistant microorganisms are a major concern to public health worldwide, as they reduce effective available antibiotics. Enterobacterales can produce carbapenemases which hydrolyse carbapenems. Outbreaks of Carbapenemase Resistant Enterobacterales (CRE) occur due to the potential of these enzymes transferring between strains and species. Identifying patients CRE with colonisation is important to prevent the spread of these organisms, through screening and implementing appropriate infection control precautions.

Nottingham University hospital performs a prevalence screen for CRE in all stool samples received over a week period, once a year, as part of the CRE monitoring process.

Aim

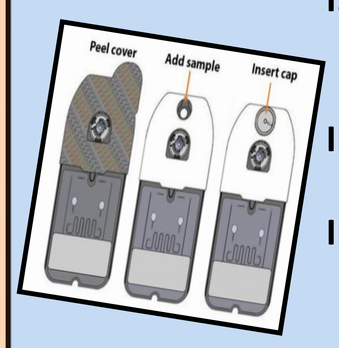
To compare a direct molecular screening system against a culture based method for effectiveness, practicality and usefulness while detecting CRE.

Methods

All stool samples received for one week (n = 417), were anonymously used to detect CRE by applying two different methods.

Stool samples used for screening

- First is molecular detection method using Novodiag CarbaR+. A swab dipped in the stool sample was used to inoculate the cartridge while using following steps .



I. Inactivation of stool samples in eNAT tubes (minimum 30 minutes).
II. Loading of sample on cartridge (600µl).
III. Cartridge run (80 minutes) on Novodiag system.

- Second is a culture based method using Colorex mSuper CARBA agar, a selective chromogenic agar plate designed for the detection of carbapenem resistance in Gram negative bacterial species.

I. The stool swab of the sample used in Novodiag CarbaR+ was used to inoculate CARBA agar plates .
II. Plates were incubated for 24 hours.
III. Putative colonies, were identified using MALDI-TOF (Bruker, USA) and underwent CRE enzyme detection on Novodiag CarbaR+.

Results

A total of 417 stool samples were tested. One sample was excluded from analysis as it wasn't available for comparative testing on the CarbaR+ assay.

Overall the Novodiag CarbaR+ detected resistance genes in six samples (1.7%) including NDM (2), IMP (1), OXA-48/181 (2), OXA-23 (1), as well as MCR-1 in another stool sample which were not identified using traditional culture methods (Table 1).

Table 2 represents the carbapenemase resistance genes detected by the CarbaR+ that were present in stool but displayed an inhibited growth phenotype by mSuperCARBA.

Table 1: Performance of both methods

	Positive	Negative
Culture method	0	416
Novodiag CarbaR+	7	409

Sample numbers	Resistance gene detected
56	MCR-1
125	NDM
156	IMP
194	NDM
233	OXA-48/181
335	OXA-48/181
402	OXA-23

Table 2: List of resistance gene detected using the Novodiag CarbaR+ that was missed by traditional culture screening methods.

In total there were 19 (4.6%) invalid tests for the CarbaR+ assay which needed to be repeated.

Note: KPC-Klebsiella pneumoniae carbapenemase, NDM-New Delhi metallo-β-lactamase, VIM-Verona integrin encoded metallo-β-lactamase ,IMP-Imipenemase metallo-β-lactamase.,OXA-Oxacillin carbapenemase , MCR-mobilized colistin resistance

Discussion

The culture based methodology did not identify any CRE isolates but the molecular methodology demonstrated improved detection by showing a 1.4% local prevalence of CRE. This is most likely due to the molecular method being more sensitive, therefore having a lower limit of detection when compared to culture methods.

It is necessary for a diagnostic assay to detect all circulating carbapenemase markers to implement early treatment and disease management, which is missed by routine culture methods.

Additionally, the molecular method is able to give a result within 2 hours, allowing earlier implementation of infection control precautions. Where as, culture method required 24 or more hours for initial CRE identification .

Novodiag CarbaR+ produced 4.6% invalid results which was likely due to PCR inhibitors present in the stool samples. This was successfully resolved by diluting the test sample. This troubleshooting steps increased the time frame for the production of a result and had cost implications associated with the process.

The culture method showed 0% prevalence of CRE in contrast to 1.4% by molecular method. In last year's study prevalence was only 0.2 % by culture method. This shows a molecular method is more sensitive but the limitation is that , it does not identify the organism which carries the resistance gene or provide antibiotic sensitivity patterns. However, early identification of colonised CRE is an important step to implement infection control strategies in hospital settings.

The molecular detection method can be implemented in active surveillance/ monitoring of CRE.

Conclusion

The molecular detection method, Novodiag® CarbaR+, has advantages over the routine culture methods as it demonstrated improved sensitivity for detection of CRE from faeces. Additionally, the molecular method is able to give a result within 2 hours, allowing earlier implementation of infection control precautions.

Limitations

- No method were identified to resolve discrepant results.
- In-depth analysis of positive results were not possible due to anonymous study.

Conflict of Interest

Novodiag system, reagents and consumables used in this study were provided free of charge by Mobidiag.

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