P0742
Poster Session III
Diagnosis of Clostridium difficile and other gastrointestinal infections

CAN A HUMAN GUT MODEL OF CLOSTRIDIUM DIFFICILE INFECTION (CDI) BE USED TO EXPLAIN GDH-POSITIVE/TOXIN-NEGATIVE FAECAL SAMPLES SEEN IN CLINICAL PRACTICE?

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Objectives: The optimal diagnosis of C. difficile infection (CDI) has recently been reported as glutamate dehydrogenase (GDH) or nucleic acid amplification tests (NAAT) followed by *C. difficile* toxin detection on those samples positive by the first test. This has led to the identification of a new category of patient: GDH-positive/toxin-negative individuals. The clinical relevance of such patients is unclear, as is the relationship between GDH and toxin expression/detection. We aimed to use a human gut model to measure GDH expression during simulated CDI in relation to bacterial growth and toxin production.

Methods: A triple-stage weir cascade continuous culture model was loaded with human faecal slurry and allowed to reach steady state. *C. difficile* spores were added, the model allowed to stabilise again and then a CDI inducing antibiotic was added. Culture for *C. difficile* spores and total viable counts, cell cytotoxicity assay and GDH enzyme immunoassay (EIA) (*C. DIFF CHEK-60*®, Techlab, US) were performed daily on samples. Once germination had occurred (increase in total viable counts and toxin titre) a CDI treatment antibiotic was added. Again, samples were monitored using culture, cell cytotoxicity and GDH EIA. Two models (A and B) were run in parallel.

Results: The GDH assay was able to detect the enzyme in vessels two and three of both models. During steady state there was a rise in the level of GDH detected; in model B only this coincided with a small peak in toxin production. However, there was no increase in *C. difficile* total viable counts in either model. After 4-5 days the level of GDH decreased and remained undetectable until after induction of germination via an antibiotic. During germination the rise of GDH mirrored that of the total viable counts and toxin production in vessels two and three of both models; however, once the level of toxin and total viable count began to decrease, the level of GDH remained at the maximum detectable for an additional 2-4 days. Once the level of GDH began to decrease, it was cleared from the gut model at the same rate as toxin.

Conclusions:GDH levels in the gut model can rise without a concurrent rise in toxin or cell proliferation. Additionally, a high level of GDH can remain in the system whilst toxin and viable cell counts decrease. GDH-positive/toxin-negative clinical sample results could be explained by this model. Potentially, patients who have primary *C. difficile* colonisation, or who have cleared/are resolving CDI may have raised levels of GDH in the absence of detectable toxin. Prospective studies in patients are needed to validate whether these data on alterations in the results of *C. difficile* diagnostics are seen *in vivo*.