Antimicrobial resistance in non-O157 Shiga-toxin producing E. coli

Amy Gentle, Martin Day, Claire Jenkins
Gastrointestinal Bacteria Reference Unit, Public Health England, Colindale

INTRODUCTION

Shiga-toxin producing E. coli (STEC) is defined by Shiga toxin genes; stx1 and/or stx2
- stx1 has 3 subtypes – stx1A, stx1B, stx1C and stx2 has 7 – stx2A, stx2B, stx2C, stx2D, stx2E, stx2F, stx2G
- There are over 400 STEC serotypes → O157:H7 causes majority of human disease, but non-O157 serotypes can cause significant illness in humans eg. O26, O45, O103, O111, O113, O145
- They are zoonotic pathogens (the major reservoir being ruminants) that cause severe symptoms of gastrointestinal disease in humans and cause a wide spectrum of illness, ranging from mild to bloody diarrhoea to Haemolytic Uremic Syndrome (1,2)

Antimicrobial resistance (AMR) has been demonstrated in STEC O157 isolates from humans, animals and food over the past 20 years (3,4,5,6)
- But this is known about the AMR in non-O157 isolates as it causes disease less frequently
- AMR in STEC doesn’t impact treatment and management of patients as antimicrobial treatment is generally not recommended - it results in worse clinical outcomes (7)
- But surveillance is important for other Public Health reasons including:
  - Monitoring transmission of resistant isolates and resistance genes from ruminants to humans, which then have potential to transfer genes to other bacteria in the gut – which may have implications for treatment of other infections
  - Monitoring global transmission of antimicrobial resistant association with travel
  - Detecting novel and emerging antimicrobial resistance

The aims of this project were focused on non-O157 to increase understanding on the full extent of the AMR spectrum in these isolates
- To assess the AMR of non-O157 STEC in England and Wales, in order to understand the diversity of antimicrobial-resistant E. coli that are introduced into the food chain, and subsequently the extent that resistance genes are transferred to commensal bacteria in the human gut
- To compare and evaluate phenotypic antimicrobial susceptibility testing (AST) and genotypic AST for the detection of AMR in non-O157 STEC in England & Wales

RESULTS

Overall of the 457 isolates, 332 were fully susceptible to all 11 antibiotics tested and 125 were found to carry 1 or more AMR genes.
- 46 different genes were detected in total and these conferred resistance to 8 different antibiotic classes
- Table 1 shows the genes that were detected for each antibiotic class and how many isolates carried each of them
- 83 isolates were multi-drug resistant
  - (defined as resistance to 3 or more antibiotic classes)
  - The most common MDR profiles were:
    1. Ampicillin/Streptomycin/Tetracycline/Sulphonamide
    2. 8x Streptomycin/Tetracycline/Sulphonamide
  - (These are also the most commonly used antibiotics in farm animals)

The phenotypic and genotypic AST was compared for the 100 isolates that were tested by both methods.
- 76 isolates showed concordant results across their complete susceptibility profile of 11 antibiotics
- 23 isolates had one discrepant result
- 1 isolate had 2 discrepant results
- So a total of 25 discrepant results out of 1010 isolate/antimicrobial combinations
- So an overall concordance of 97.5% between the 2 methods

CONCLUSIONS

I was able to assess the antimicrobial resistance in non-O157 STEC and defined the diversity of resistance genes they may introduce into the human gut

I was also able to compare phenotypic and genotypic methods for antimicrobial resistance detection and show a concordance of 97.5%, which adds to the growing evidence base to support the use of the genotypic method as a replacement for phenotypic testing – both for surveillance and clinical decision making in the future

Possible areas of future work:
- Phenotypic AMR testing on the full dataset to detect potential novel mechanisms of resistance, and allow the AMR gene database to be updated
- Mechanisms of acquisition of antimicrobial resistance could be determined
- Phenotypic/genotypic discrepancies could be explored further to find explanations for these and discover potential novel mechanisms of resistance

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REFERENCES


DISCUSSION

- The most commonly detected resistance was to: Sulphonamide, Streptomycin, Tetracycline and Ampicillin
  - These are also the most common antibiotics in farm animals
  - Worrying as indicates-transfer of resistant isolates from livestock to humans, with potential to spread genes to other bacteria once in the human gut
  - So ongoing surveillance is important - to know the diversity of resistance genes being introduced via the food chain

Genotypic methods as an alternative to phenotypic methods?
- Just because an isolate carries a particular AMR gene it doesn’t necessarily mean it will be phenotypically resistant – so can make analysis of data quite complex
- Genotypic method will not detect all mechanisms of resistance – bacteria acquire new mechanisms continuously so need to be vigilant and continuously update the database
- The implementation of routine WGS for all STEC isolates for public health surveillance also allows surveillance of AMR genotypically at no extra cost – this will save time and money as phenotypic methods are laborious

The dataset was divided into clonal complexes (CCs).
Figure 1 shows the number of isolates in each of these CCs, as well as the number of antimicrobial resistant isolates per CC

The 25 discrepancies were divided into major or very major errors
- 8 major errors (Isolates predicted resistant genotypically, but were resistant phenotypically)
- 17 very major errors (Isolates predicted susceptible genotypically, but were resistant phenotypically)
- Possible explanations include:
  - Mixed with a resistant organism when phenotypic testing performed retrospectively - contamination during storage
  - Novel antimicrobial resistance genes or mechanisms that have not been identified previously