Screening for antibiotic-resistant infection

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Antibiotic resistance is a significant and increasing problem in the UK and around the world. In 2014, UK prime minister, David Cameron said: “The world could soon be cast back into the dark ages of medicine... governments and drug firms need to act,” and he called for new antibiotics to be developed (Walsh, 2014).

The Chief Medical Officer for England, Dame Sally Davies, said: “Resistance to antibiotics now poses a significant threat to the population’s health”, and that urgent action is needed to curb their use (Ford, 2014). One area of concern is carbapenemase-producing enterobacteriaceae (CPE) infections, which are virtually untreatable with antibiotics (Box 1).

The issue of CPE in the UK was first raised by the Health Protection Agency in 2012 following an increase in reported cases, notably in Manchester and London. There is a need to improve understanding of the epidemiology of CPEs, but practical guidance for identifying and managing CPEs was needed for healthcare providers.

Public Health England published guidance and a toolkit (2013), which recommended every patient is screened on admission. Those with proven or suspected CPE colonisation or infection must be isolated, and appropriate infection prevention and control measures put in place.

However, the toolkit is costly to implement, so to provide information to support the recommendations, we carried out a point-prevalence study (PPS) across the Royal Free London Foundation Trust.

What are CPEs?

Common examples of enterobacteriaceae are *E coli* and *Klebsiella*. CPE are enterobacteriaceae that produce the enzyme carbapenemase, which makes them resistant to carbapenem antibiotics. Enterobacteriaceae usually live in the gut without causing infection or symptoms. However, if they colonise another part of the body, they can multiply and cause urinary tract infections, abdominal infections and sepsis.

The carbapenemase produced by the bacteria can break down carbapenem antibiotics, including meropenem, imipenem, ertapenem and doripenem. In fact, carbapenemase breaks down all beta-lactam antibiotics.

P. aeruginosa is carbapenem resistant
antibiotics, including penicillins, cephalosporins and carbapenems. CPEs are nearly always resistant to other families of antibiotics, including aminoglycosides, quinolones, trimethoprim and tetracycline. This makes therapeutic options extremely restricted. The reasons for the rise in antibiotic resistance is outlined in Box 2.

Resistant bacteria described above have previously been managed with standard precautions such as isolation, hand hygiene, protective clothing and standard antibiotic regimens. The main issue with their emerging ability to produce carbapenemase is that there are few, if any, treatment options with antibiotics. Therefore, preventing spread is the key to containing this infection and standard precautions must be rigorously applied.

Understanding the nature and epidemiology of CPE infections is necessary to build preventative programmes and provide evidence for infection prevention and nursing practice (Anderson, 2014). CPEs have been identified globally and the countries mainly affected include: Bangladesh, China, Greece, Ireland, Israel, Italy, Japan, Middle East, North Africa, Pakistan, south-east Asia; Taiwan and the UK (PHE, 2013).

One way to use this information is to screen patients on admission to hospital by asking if they have had any healthcare abroad in the last 12 months, recent travel abroad (especially outside northern Europe) or previous history of CPE colonisation or infection.

If the answer is yes, they can be tested for colonisation or infection. Evidence suggests the number of patients identified with CPOs each year is increasing in the UK (Figure 1). Management of CPEs must focus on identifying people coming to the UK who are already colonised to protect the UK population from further increase.

Starting point
Our critical care unit already performed admission and weekly screening for Acinetobacter baumannii, so this was adapted to include CPE screening in July 2013. Private patients in our trust are a high risk, as many are referrals from abroad to specialist teams such as haematology and renal services. CPE screening started in these services in August 2013.

As the trust is a regional renal dialysis centre, screening also began in August 2013, as a protocol for returning travellers who had received dialysis abroad. High-risk haematology patients already had stool screening on admission for resistant gram negative bacteria, so this was adapted to include CPE in September 2013.

Screening for CPE consisted of a rectal swab. Skin breaks around invasive devices and wounds were also screened.

Implementing the PHE toolkit
To implement the PHE toolkit we had to address the following questions:

- Who are our patients? How many international patients are admitted?
- Is there a similar pattern between a general hospital and a tertiary referral centre?
- Are they medical tourists?
- Are they a previously confirmed CPE case?
- What are the resource and capacity arrangements?
- What are staff training and update arrangements?
- What data is needed to provide a baseline and monitor trends?
- What are the early detection and infection prevention and control measures?
- Who should be screened: all admissions, high-risk admissions or high-risk units receiving admissions?
- Increased exposure to healthcare increases exposure to associated infection, so we need to know how many patients are medical transfers or have had significant care, such as extended hospital stay, use of devices, ventilation or parenteral nutrition, organ transplant, or dialysis.

The toolkit is costly to implement in terms of isolating, screening, testing and managing patients, so to provide information to support the recommendations, we undertook a trustwide point-prevalence study (PPS). We developed and piloted the survey tool in one general ward of 28 patients to ensure information we planned to collect would help us assess the burden of risk. The PPS was carried out on 29 January 2014, risk assessing all inpatients for: any previous medical care or admission to healthcare facility; if patients had been treated abroad, in the UK, or in our hospital.

A team of 10 infection prevention and control nurses surveyed the patients.

Survey results
Of the 551 patients surveyed, 1% had received healthcare abroad, 1% healthcare abroad and in the UK, 18% had received healthcare in a London hospital within the

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**BOX 1. DEFINITIONS**

- Carbapenem-producing organism (CPO): a bacterium that produces the enzyme carbapenemase.
- Carbapenem-producing coliform (CPC): a coliform (rod-shaped bacterium that includes E coli and Klebsiella) type of bacterium that produces the enzyme carbapenemase.
- Carbapenem-producing enterobacteriaceae (CPE): enterobacteriaceae that produce the enzyme carbapenemase.
- Carbapenem-resistant organism (CRO): a bacterium that is resistant to carbapenems – this may be by producing a carbapenemase enzyme, or by another mechanism that makes the antibiotic harmless to the bacterium.

**BOX 2. THE RISE IN ANTIBIOTIC RESISTANCE**

The rise in antibiotic resistance in enterobacteriaceae is caused by multiple factors such as:

- The overuse of antibiotics for unspecified infections that may be viral not bacterial;
- The overuse of antibiotics for minor infections that would have got better without treatment;
- The overuse of antibiotics that act on a wide range or spectrum of infections rather than antibiotics designed to treat specific infections (broad spectrum to narrow spectrum prescribing);
- Patients feeling better and stopping a course of antibiotics before the full course is completed.

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**FIG 1. TOTAL CPO CASES BY YEAR IN UK**

Source PHE, 2011

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SurvEY rESulTS

FIG 2. PR EVAlENCE SURVEY RESULTS

Showing proportion of inpatients within possible criteria groups that could be classified as high risk

last 12 months and 80% had no previous healthcare elements suspected as risk for CPO colonisation (Figure 2).

Follow-up of screening results after the survey of all the high-risk patients revealed that only 49.6% (61) of suspected cases were screened of which none were CPO colonised or infected. The high-risk areas with more than 20% of suspected cases were the stroke unit, renal unit, private patient unit, hepatobiliary and transplant wards, intensive care unit, oncology ward and infectious diseases ward (Figure 3).

This data showed there were a high number of patients from within the London area, but as a tertiary referral hospital, there were also a significant number from healthcare premises across the UK.

Positive outcomes

We proposed sharing the PPS survey tool with other London trusts, to identify trends regionally and to compare teaching trusts to district general trusts. However, because of the size of the study and the resources in time and staff, no further trusts have carried out the PPS.

We continue to encourage other trusts to carry out the PPS to add to this knowledge base over time. We plan to repeat this study in a year to measure any changes in burden over time and to assess the financial burden of this screening programme. PHE has used these results to develop the latest risk-based matrix for CPE screening (Bit.ly/CPEriskMatrix).

Lessons learned

Following the PPS, we have made the following recommendations:

- Repeat PPS after one year to identify shifts in patient population and associated risks;
- Refine the testing strategy according to national guidance and local epidemiology;
- Further carbapenemase screening studies to include perineal versus rectal swabs; and single rectal swab versus three cultures.

The yield from screening is currently low in our hospital and a cost-benefit analysis does not support universal screening of all patients. A pragmatic approach is to identify high-risk units and opt for universal screening of patients within these units, because it is less confusing to implement and is more likely to be undertaken.

In the critical care unit, routine weekly screening enabled the detection of an additional case since 2013. However, the cost effectiveness of this strategy is unknown.

Implications for patients

Carbapenem resistance is worldwide and therefore a global problem. The only way to manage CPE is to engage all healthcare staff, as there are implications for patients if they are labelled as CPE positive. As most cases are colonisation rather than infection, is it in the patients’ interest to be screened? Screening requires an invasive rectal swab, which is an unpleasant experience to explain to a patient, undertake, or have performed.

Furthermore, there is no decolonisation regime, so a positive result means isolation, without treatment. There is no agreed time period before a patient can be described as “negative” and no evidence for a clearance screening regimen, so “positive” patients are effectively “branded” indefinitely as an infection risk. This can have implications for transferring patients to another health-care facility. There are already examples of patients having difficulties accessing rehabilitation.

Conclusion

We encourage other trusts to carry out a PPS and share information with other trusts so that we can find the best way to tackle this growing problem. One thing is for certain: we must act – patients are dying today from previously treatable infections. NT

References

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