Prevention and Control of Carbapenemase-Producing Enterobacteriaceae

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The communicable disease which will be the focus for this article is Carbapenemase–Producing Enterobacteriaceae (CPE), also referred to as Carbapenem-Resistant Enterobacteriaceae (CRE) by the World Health Organisation (WHO).[1] The focus throughout the review will be acquired CPE in an acute hospital setting in the United Kingdom(UK) and will be referred to as CPE.

BACKGROUND OF THE DISEASE

CPE are bacteria that are increasingly becoming endemic in some high, middle and low- income countries.[2] CPE can be acquired in a healthcare setting and as a result of medical treatment antibiotic use. The bacteria include Klebsiella pneumoniae, Escherichia coli and Enterobacter species.[3] The bacteria can live in the gut of humans and animals, and at times CPE are harmless and there are no signs or symptoms because a person's immune system keeps them in check (the person is colonised). However, if CPE transfers into other parts of the body for example, urine or the bloodstream, they can cause an infection and the person may need treatment. Selection of resistance in infected or colonised patients is enhanced by various patient factors, which may include immunosuppression, use of indwelling invasive devices, alteration of patient's own flora during antibiotic therapy and duration of hospital stay. Further factors include intensity and duration of exposure to broad-spectrum antibiotics, severity of illness and other associated co-morbidities.[2]

CPE have emerged globally over the last decade[4] and are a worry among scientific, medical and public health communities[5] due to the substantial cause of high morbidity and mortality rates (mortality rate of CPE bacteraemia can be as high as 57%).[6] CPE organisms spread quickly in healthcare settings and result in poor clinical outcomes due to limited therapeutic options. The increased incidence of CPE has significant financial and operational implications for healthcare providers.[7]

CPE infections can be difficult to treat due to their resistance to carbapenems, which are a powerful group of broad-spectrum beta-lactam (penicillin-related) antibiotics.[7] Carbapenemases are enzymes that destroy carbapenem antibiotics, conferring resistance. In many cases, carbapenem antibiotics are our last effective defence against infections caused by multi-resistant bacteria.[7]

There are several factors that contribute to the development of antibiotic resistant organisms such as CPE. Firstly, the inappropriate use of antibiotics where they are not indicated for example, a cough, historically this was due to patient expectation and demand for treatment.[2] Secondly, where there has been inappropriate prophylactic administration of antibiotics. Another contributing factor is if prescribers have given a patient an inadequate dose or duration of an antibiotic. The use of monotherapy can increase resistance, when treatment with combination antibiotic therapy would be clinically indicated. Resistance can develop when patients have not completed their course of antibiotics on several occasions.[2]

The driving force behind resistance has been the widespread use of antibacterial drugs, both in humans and animals. There has been a greater human demand for meat[8] and in animals who are bred for human consumption, antimicrobials are often administered prophylactically to protect whole herds from disease and for growth promotion. Antibiotics are often administered in feed at sub-therapeutic levels. Resistant bacteria such as CPE, can either be transferred to humans via the food chain, or resistant pathogens in animals can transfer resistance genes to human pathogens.[2] However, more research is being conducted into the effects of antibiotic use in animal production and its relation to the development of antibiotic resistance.[8]

PREVENTION AND CONTROL MEASURES

Control of antimicrobial resistance is improved with antimicrobial stewardship.[2] In recent years there has been the creation of antimicrobial pharmacy leads in acute hospital trusts, who work closely with health professions and advise on medication regime and length of treatment, to improve the use of antibiotics. In some countries there are a lack of control measures with over-the-counter availability of antibiotics, residents and tourists are freely able to purchase antibiotics,[2] these countries need to tighten measures to achieve a control on antibiotic use.

Furthermore, globalisation and foreign travel have resulted in new situations of people, animals and the environment merging together, altering ecosystems and providing microbes with the chance to breach species barriers.[8] People travelling to countries, having had an inpatient hospital stay, can unknowingly import back resistant organisms such as CPE to the UK, especially from countries where there is high prevalence of CPE. The European Centre for Disease Prevention and Control (ECDC)[9] argue any patient transferred from any country is at risk of carrying CPE, therefore drawing up lists of high-risk countries is discouraged.

Further factors which pose a risk for people acquiring CPE are the high bed occupancy rates in hospital and mixing of patient populations due to increase in pressures on healthcare systems for greater efficiency.[2] CPE can be spread via contaminated hands and equipment, therefore, standard and contact precautions should be used for patients suspected or known to be CPE positive.[7] Nursing and medical care is being stretched further which results in poor standards of infection control practice; staff failing to decontaminate their hands properly (using the WHO 5 moments)[10] and not changing their PPE (personal protective equipment) in between patient care.[7] In addition, patients need to be offered opportunities to clean their own hands, for example, after using a commode at a bedside. Also, visitors must be encouraged to clean their hands before and after entry to a clinical area to prevent the spread of infections such as CPE.

Patients who were previously identified as CPE positive, and patients who have multiple hospital admissions or treatments, for example patients receiving dialysis, are at an increased risk of becoming CPE positive. Patients who are admitted into augmented care or high-risk units are at an increased risk due to the various invasive devices and antibiotic use they are likely to encounter. It is important to limit unnecessary use of external devices and remove them as

soon as possible to reduce the portal of entry for an infection. Patients with recent exposure to broad-spectrum antibiotic courses, in particular carbapenems, within their last or current hospital stay are also at risk,[7] therefore prescribers need to be mindful about further antibiotic use.

WHO[1] recommends a multimodal approach should be implemented to prevent and control CPE. The strategies should consist of at least hand hygiene, surveillance, contact precautions, patient isolation (or cohorting) and environmental cleaning. The aim is to improve the quality and safety of health care and the outcome of patients accessing health services, as well as the safety of health care workers. Nevertheless, it has been recognised there will be an increased cost for trusts following these recommendations, for example the purchasing of more disposable protective equipment, cost of disposal, possibly extra equipment and a need to increase staffing levels[1], therefore, trusts may be reluctant to employ all these measures.

Hospitals in the UK have trained infection prevention professionals and microbiologists to control and prevent cases of CPE and manage outbreaks of CPE through training, auditing compliance of contact precautions, hand hygiene and environmental audits. (An outbreak of CPE would constitute of a further positive patient linked in time and place with the index case-two or more linked cases).

It has been recommended that there should be dedicated staff to look after all isolated patients who are carriers of CPE,[9] but this is not practical in an acute care setting as wards are already understaffed.[2] There are a lack of isolation facilities in UK hospitals. Isolation is a key component of good infection control.[11] Many hospitals are decades old and have had insufficient capital available for upgrades. However, creating side-rooms in existing buildings will reduce bed capacity and hospitals are already running close to full capacity all year round.[11] Alternatives are being used in hospitals to ease the lack of isolation rooms and improve isolation, some trusts in the North West of England have purchased 'Redirooms' from GAMA healthcare, to reduce harm to patients and maintain bed flow.

The hospital environment poses a risk if it has not been decontaminated effectively following discharge of an infected or colonised CPE patient, and poor maintenance of hospital buildings can make cleaning more difficult.[2] Studies have demonstrated that hospital sinks and associated drainage systems can harbour antimicrobial resistant bacteria such as CPE in biofilms.[7] There is some research to say that CPE in waste traps and drainage biofilm can transmit to patients.[7] To minimise risk, water from tap spouts should not flow directly into the drain hole; as it could cause splashing and contamination of surrounding surfaces. Taps should be cleaned before the rest of the hand wash basin to prevent any possible contamination and spread,[7] therefore cleaning should only be carried out by staff trained to do so.

Patients who have CPE may suffer discrimination in the quality of their health care unless appropriate management structures are put in place. In addition, some patients may feel socially isolated in a single room and have psychological consequences such as depression,[1] patients should be provided with support. Moreover, health care workers who frequently manage infectious patients in isolation rooms can feel a sense of stress and reduced morale, as nursing patients who require extra enhanced care can increase the healthcare worker's workload.[1] Where there is a lack of single rooms, cohorting patients with the same CPE pathogen is recommended. It has been argued however, in some cases single room and cohort isolation have been shown to be associated with a reduced standard of medical care if not well managed.[1] Patients who have had an epidemiological link in time and place with a known CPE positive patient may become 'CPE contacts', and must undergo screening and isolation for a period; epidemiological related outbreaks are increasing in the UK.[6]

SURVEILLANCE

The UK Health Security Agency (UKHSA) monitor the incidence and prevalence of CPE to track the threat at national and regional levels and to understand how well control measures are working. Since October 2020, all diagnostic laboratories in England have had a duty to notify acquired CPE in human samples. Laboratories must notify UKHSA via the Second-Generation Surveillance System (SGSS).[3] The requirement for notifying UKHSA was launched in conjunction with a national framework of actions to contain CPE, if all the measures are implemented well, they will help health and social care providers minimise the impact of CPE.

Stool samples are the gold standard for CPE testing,[6] yet it is not feasible for a routine screening programme, however rectal swabs are more practical. Different species yield differently at different anatomical sites. The addition of groin swabbing and urine sampling has been proven to increase detection and hence there is an argument for multi-site swabbing.[6] However, groin swabbing is currently not recommended by UKHSA. It is recognised that undertaking the recommended surveillance specimens could involve potential harms or unintended consequences for the patient, for example they may experience a sense of cultural offensiveness or stigma associated with obtaining stool and rectal swabs.[1]

The rate of acquired CPE incidents varies by Office for National Statistics (ONS) region. Interestingly, the highest overall rate of CPE, between January and December 2022, was recorded in the Northwest of England with 3.26 episodes per 100,000 population.[3] The lowest incidence across the same recording period was reported in the Southwest and East of England (0.27 and 0.37 episodes per 100,000 population, respectively).[3]

The most frequently isolated CPE species in the UK with a confirmed acquired carbapenemase is Klebsiella Pneumoniae, which accounts for 32.7% of all obtained specimens.[3] Aside from the species, CPE are broken down into 'carbapenemase families'. In the UK and globally, there are several families, however there are '5 big' main families which are mainly detected in UK hospital laboratories. The monitoring of the distribution of carbapenemase families has found they also vary regionally.[3] The detection of the different families is an important way to monitor surveillance and to enable rates to be compared with other countries to establish links.

Understanding the regions that have a higher incidence of CPE can enable awareness and preventative measures to be put into place to control the spread. However, such open disclosure of a country's prevalence data may be associated with some political concerns and destroy public trust and hospital reputations.[1] However, an open and honest approach should be encouraged. It is also important to understand which members of the population are most vulnerable, so healthcare workers can be made aware of the importance of strict hand hygiene, environmental and equipment decontamination and

PPE use. The rate of acquiring CPE is highest among the oldest and youngest members of the population, with the highest reported rates in those aged 75 years and over (49.9 per 100,000 population) with an overall rate of confirmed carbapenemases of 14.4 per 100,000 population in infants less than one year old.[3] There is a similar age pattern for acquiring CPE for both males and females, although it has been found the overall rate of acquisition was higher in males compared to females.[3]

When an emerging infection such as CPE is reported to WHO, epidemiologists from WHO and the reporting country (via UKHSA) assess the risk to humans. Therefore, continued surveillance is vital in order to assess the ongoing threat to the population and further measures of control may be adopted.[8]

UKHSA has published a toolkit to help acute trusts halt the spread of CPE.[7] NHS trusts can implement a local CPE policy based on the framework which is relevant to the local situation. Otter et al[4] argue there are no studies evaluating the cost-effectiveness of the prevention toolkits and guidelines that are available for CPE. According to ECDC,[9] many countries have addressed the global spread of CPE and have already adapted their local policies.

POTENTIAL SOLUTIONS

As previously mentioned, poor standards of cleanliness in hospital environments and equipment can exacerbate the spread of organisms such as CPE.[2] It has been noted that in some WHO regions environmental screening cultures for CPE was found to be worthwhile. This could potentially be tried in all acute trusts in the UK to ensure crucial environmental cleaning has been completed effectively. Information regarding a patient's CPE colonisation status does not yet constitute routine standard of care provided by health systems. Perhaps in the future, rather than just screening patients in high-risk areas, universal screening could be adopted, in a similar fashion to how MRSA screening was previously mandatory for all hospital admissions, although there will be massive cost implications.

There needs to be greater behaviour change interventions targeted at staff to embed good hygiene practices to reduce potential transmission of CPE and break the chain of infection. More investment into retaining and recruiting staff to stay within our hospitals is vital to ensure wards are not short staffed, so staff are under less pressure and therefore can perform basic infection control principles adequately. Clean care is safer care.[1] The SENIC study in the 1970s recommended one infection control nurse per 250 inpatient beds, this is not the reality, and the specialty is hugely under resourced.[2]

Even though CPE rates are relatively low in the UK compared to countries such as Greece[12] where rates have been described as epidemic, CPE presents a growing threat in the UK and investment in infection prevention and control should be an increasing priority. Unless action is taken and we learn from experiences elsewhere in the world, rapid spread of CPE will pose an ever-increasing threat to public health and medical treatment pathways in the UK.[7] America has shared a news article to the public on the rise of CRE in hospitals.[13] Awareness of CPE in the UK remains poor;[6] the UK needs to adopt a similar approach to America and improve awareness through media coverage, as has previously been done for MRSA.

There needs to be a continued multidisciplinary approach both in the UK and internationally to control the spread of CPE. Over the past decades there has been increasing recognition that the way we deal with infectious disease is often reactive and too late.

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