Challenges of carbapenemase-producing Enterobacteriaceae (CPE) in Haemodialysis Patients

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Introduction

CPE is a global threat to both individual and public health. Asymptomatic colonisation of gastrointestinal tract by CPE is an important reservoir for transmission that may precede infection[1]. Infection occurs in about 10% of colonised patients resulting in higher mortality compared to other infection[2]. Colonisation pressure is a major risk factor associated with transmission. Prior antibiotic use, hospital length of stay, intensive care admission, being in contact with health-care abroad and renal dialysis- dependence has been found to be the risk for colonisation. However there is paucity of data regarding managing CPE patients in specialist areas like dialysis units who are in regular contact with health-care.

The PHE Acute Trust CPE toolkit (2013) states that patients who have within the last 12 months been an inpatient in a hospital abroad or an inpatient in a UK hospital which has problems with the spread of CPE are to be screened, consisting of 3 consecutive screens 48 hours apart with pre-emptive isolation of patients.

Aims & Objectives

The Heartlands, Good Hope & Solihull (HGS site) has 4 haemodialysis units serving approximately 425 patients. Dialysis patients are encouraged to maintain a normal life-style and go on holiday where their dialysis is undertaken by the holiday unit.

Following the national CPE toolkit, a hospital- wide CPE policy was introduced in patients who have had health-care abroad in the last 12 months. This was extended to include holiday screening programme on the haemodialysis units in 2014.

We aim to share our experience of

- CPE management in haemodialysis patients and discuss challenges posed in terms of infection prevention and control (IPC) resources and outcomes.
- There is limited evidence for duration of carriage and we attempted to do serial CPE screens to risk assess 2 of our patients regarding need for isolation.

Methods

A holiday database with destination is maintained. Pre-holiday screening is performed as required.

A blood borne viruses (BBV) policy already existed for dialysis patients returning from 'high risk' areas for BBV, to be isolated (cohorted in a satellite unit) (Figure1) for 3 months whilst having BBV screens[3] but not for patients returning from non BBV 'high risk' areas (continue to dialyse in base units) with no follow-on screening.

CPE screening and Isolation

With CPE policy anyone returning from outside UK is deemed 'high risk' and this creates discrepancy and two tier system in the management of patients.

Thirty- forty patients go on holiday in a year and isolation of all (for BBV and CPE) would prove impossible. We follow pre-emptive isolation of BBV policy whilst undertaking 3 serial CPE screens and the Dialysis unit follow strict IPC and cleaning. If CPE screen is positive contact screening is done.

Confirmed CPE patients are isolated for future dialysis sessions and hydrogen peroxide vapour (HPV) clean is done post-dialysis (Figure 2).

Figure 1

Figure 2

Clearance

We attempted serial screening in 2 patients to check for clearance and make risk assessment for removal from isolation.

Laboratory diagnosis

CPE chromogenic media is used without enrichment broth for culture. Confirmation is done by PCR to detect 4 main CPE genes; KPC, NDM, OXA-48 & VIM. Negative result is referred to the reference lab for further tests.

Results

130 patients had holiday- dialysis since January 2015 to June 2018. The epidemiology is illustrated in Table 1 showing no positive in 2015 and only 1 in 2016.

7 patients have screened CPE positive; 5 returned from holiday abroad, 1 case transferred from a unit in London and 1 patient was detected on pre-holiday screening samples with no travel history for a few years prior and first time CPE screened. This led to extended contact tracing but no other positives were found.

Table 1- Epidemiology of CPE patients

Patient	Site	Year	Organism	Gene	Clinical or screening sample	Travel destination
1	A	2016	Klebsiella Pnuemoniae	OXA-48	Rectal & clinical	Tanzania and India
2	A	2017	Escherichia coli	OXA-48	Rectal	Pakistan
3	B	2017	Enterobactor cloacae	IMI	Rectal	none
4	A	2017	Klebsiella pneumoniae	OXA-48	Rectal	Turkey
5	B	2018	Escherichia coli	OXA-48	Rectal	London
6	B	2018	Escherichia coli	NDM & OXA-48	Rectal	Pakistan
7	B	2018	Escherichia coli	NDM	Rectal	Pakistan

Our current CPE prevalence is 1.6%. One patient had CPE infection.
Majority (5 out 7) are OXA-48s.There were no KPC-producing CPE detected. There has been no transmission of CPE on any of the dialysis units.

Clearance screening- Table 2 a & b

Date	Specimen	Result
04.08.16	Rectal	Positive
08.08.16	Clinical	Positive
02.02.17	Rectal	Negative
09.02.17	Rectal	Negative
11.02.17	Rectal	Negative
04.04.17	Rectal	Negative
06.04.17	Rectal	Negative
08.04.17	Rectal	Negative
02.08.17	Rectal	Positive
15.03.18	Rectal	Negative
22.03.18	Rectal	Negative
29.03.18	Rectal	Negative

Date	Specimen	Result
15.08.17	Rectal	Negative
17.08.17	Rectal	Negative
19.08.17	Rectal	Positive
22.08.18	Rectal	Negative
29.08.18	Rectal	Negative
05.09.18	Rectal	Negative

Patient 1 screening history OXA-48 CPE (Table 2a)

Patient was admitted into acute hospital in June 2017 and had non- carbapenem antibiotics. Her repeat screening in August 2017 was similar organism and CPE type. She remains in isolation.

Patient 3 screening history IMI CPE (Table 2b)

Patient was admitted twice on acute hospital ward in April and June18 and had non-carbapenem antibiotics accompanied by amputation surgery.

Patient has been moved out of isolation following 3 negative screens and plan to re-screen on a 3- monthly regime.

Discussion

Prompt detection and maintaining effective IPC is paramount in preventing the spread of CPE.

The key challenges in this specific specialist group of dialysis patients are

1. Patient factors- high risk with multiple co-morbidities, frequent hospital admissions, antibiotics, increased hospital length of stay, sometimes intensive care which are risk factors for CPE colonisation
2. Regular Health care contact with three times a week haemodialysis
3. Part of holidays need health- care at different hospitals which risk acquiring CPEs.

Haemodialysis units with limited isolation and high quality cleaning facilities

We have limited number of side-rooms and patients are booked in to accommodate the demands for isolation and it is challenging to incorporate HPV cleaning in the schedule. Using HPV machine takes 3 hours and as we have it in our acute hospital policy we believe we should provide similar standards in satellite areas. Ultraviolet light cleaning is being considered.

The limited isolation facilities have led us not to pre-emptive isolate all holiday- returners and to match with the BBV risk assessment to prevent operational confusion.

Cohorting and Universal screening of high risk specialities

There is a case for speciality- based screening. This would add further to the burden on isolation facilities as cases will be expected to increase.

Cohorting with dedicated health- care workers for CPE carriers[4] has been used however it is expensive and difficult to implement. Moreover with heterogeneity in CPE genes and their impact on antibiotics available for treatment its use in routine has risks.

Duration of CPE Carriage and Clearance

There is no robust evidence on re-screening positive patients and guidelines do not recommend repeat screening[5]. The duration of carriage is variable and we performed serial re-screens to check for duration. One patient relapsed after being admitted to acute hospital and receiving antibiotics proving the antibiotic consumption as risk factor however the second patient remained negative in spite of repeated admissions and antibiotics. The different CPE gene involved could be the explanation (OXA versus IMI) as the evidence [4&6] suggests variability.

Psychological impact

To place dialysis patients in isolation forever can have significant psychological impact both on them and their families[7]. Our 2nd patient in whom we re-screened we had repeated meetings with the patient and the family and realising the distressing situation we decided to remove isolation after 3 negative screens one year after diagnosis. We agreed to continue 3 monthly re-screening. This brings to the forefront the issue of balancing individual patient's situation with wider remit of prevention of spread of CPE.

Conclusion

With the rise in CPE prevalence worldwide the number of patients with CPE is going to increase in haemodialysis units. This will have a significant impact on the operational management and pose significant challenges especially if we continue to have limited isolation facilities and constraints of cleaning schedules.
In the future we will have to increasingly do risk assessments and balance the evidence with practical solutions, including financial implications and psychological impact.

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