International Journal of Advanced Research and Review

www.ijarr.in

OUTBREAK OF ESBL-PRODUCING ENTEROBACTER CLOACAE IN NEONATAL UNITS: ABOUT 7 CASES.

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ABSTRACT

Background: Enterobacter cloacae species is responsible for nosocomial outbreaks in vulnerable patients in neonatal intensive care units (NICU). The environment can constitute the reservoir and source of infection in NICUs.

The aim of the present study was to describe the epidemiological and bacteriological aspects of an outbreak of ESBL-producing Enterobacter cloacae in the neonatology unit of the Mohammed VI University Hospital of Marrakech.

Materials and Methods: We reported seven cases of ESBL-producing Enterobacter cloacae infections in neonates hospitalized in a neonatal unit over a period of two weeks, diagnosed by microbiological study of the different cultural, morphological and biochemical characteristics, as well as by the study of the germ's sensitivity to antibiotics

Results: The presence of ESBL was retained in front of an antibiogram showing a resistance to all the betalactamins except carbapenems, as well as a synergy between the disks of C3G, C4G and clavulanic acid, the resistance to the betalactamins was associated with that of the tested fluoroquinolones in particular Ciprofloxacin and Norfloxacin and to the aminoglycosides except amikacin as well as the resistance to the co-trimoxazole.

Conclusion: The emergence of multi-resistant bacteria with a high epidemic risk in our hospital implies, Hence the interest in developing rapid and efficient means of identification in order to limit their spread.

Keywords: Enterobacter cloacae, neonatology, antibiogram, prevention

INTRODUCTION

ESBL-producing strains are constantly increasing and frequently cause therapeutic impasses associated with prolonged hospitalizations and additional costs of care, especially in intensive care units. Interest in implementing corrective measures to limit their spread.

The rise of Gram-negative bacteria involved in neonatal infection is a major issue both because of the associated morbidity but also because of theemergence of multidrug resistant (MDR) strains [1]. Inparticular, the Enterobacter cloacae species is a Gram negative bacteria responsible for nosocomial outbreaks invulnerable patients in neonatal intensive care units(NICU) [2, 3].

The aim of the present study was to describe the epidemiological and bacteriological aspects of an outbreak of ESBL-producing Enterobacter cloacae in the neonatology unit of the Mohammed VI University Hospital of Marrakech.

MATERIALS AND METHODS

We reported seven cases of ESBL-producing Enterobacter cloacae infections in neonates hospitalized in a neonatal unit over a period of two weeks. The diagnosis was made by microbiological study of the different cultural, morphological and biochemical characteristics, as well as by studying the sensitivity of the germ to antibiotics.

The biochemical identification by using the Api 20NE gallery (BioMérieux),
The presence of ESBL was detected by Antibiogram by the agar diffusion technique according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations.

RESULTS

These were 7 cases hospitalized in the neonatology unit, the average age was around 10.2 days with extremes ranging from 4 to 19 years, the average term was 36 weeks of amenorrhea with extremes ranging from 32 weeks to 39 weeks, 3 cases were male (57%) of all cases, and 4 cases were female (43%) and sex ratio was M/F=1,33 the reason for hospitalization was prematurity in 3 cases (57%), foetal distress in 2 cases (28,5), and respiratory infection in 2 cases (28,5).

The clinical characteristics of the 30 infected patients are summarized in Table1, indeed all cases presented a signs of systemic infection with the predominance of hemodynamic signs with a rate of 90%.

The average birth weight was 2.13 kg with extremes ranging from 0.9 kg to 3.1 kg, delivery was by vaginal route in 5 cases (71,5%) and by caesarean section in 2 cases (28,5%).

Table 1: Epidemiological and clinical Characteristics.

	Rate (%)
Basic data	
Sexeratio (M/F)	1,33
average of age (days)	10,2
gestational age of birth (weeks	36,3
birth weight (Kg)	2,13
caesarean	28,5%
Vaginal route delivery	71,5%
reason for hospitalisation	
prematurity	57%
foetal distress	28,5%
respiratory infection	28,5%
Sepsis data	
Fever (%)	71%
Respiratory signs (%)	85,5%
Hemodynamic signs (%)	90%
Gastrointestinal signs (%)	43%

Bacteriological examination isolated ESBL-producing Enterobacter cloacae strains from blood culture and urine samples in neonatology.

The presence of ESBL was retained in front of an antibiogram showing a resistance to all beta-lactam antibiotics except carbapenems, as well as a synergy between C3G, C4G and

clavulanic acid disks, the resistance to beta-lactam antibiotics was associated with that of the fluoroquinolones tested, in particular Ciprofloxacin and Norfloxacin, and to aminoglycosides except amikacin, as well as resistance to cotrimoxazole. The strainwas sensitive to Colistin and Tigecycline.

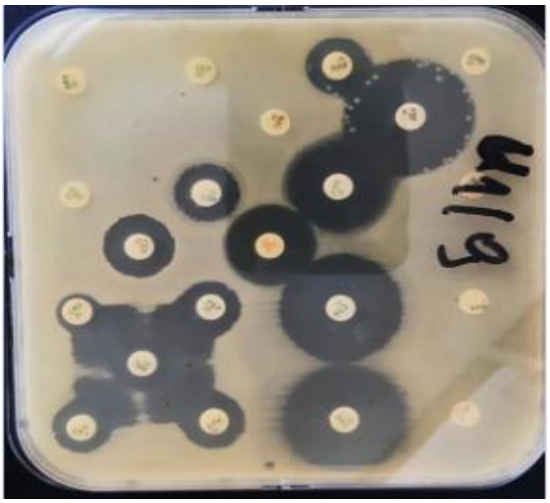

Figure 1: Antibiogram of the ESBL producing Enterobacter cloacae strain

Figure 3: Synergy between C3G, C4G and clavulanic acid discs ("champagne cork" appearance)

DISCUSSION

Extended-spectrum-lactamases (ESBLs) are plasmid-mediated bacterial enzymes that confer resistance to a broad range of extended-spectrum-lactam antibiotics (4). The most commonly encountered plasmid-mediated ESBLs are derived from the TEM and SHV enzyme families (5). Large nosocomial outbreaks caused by ESBL-producing gram-negative bacilli have been reported, with Escherichia coli and Klebsiella pneumoniae being the most frequently involved pathogens (6, 7, 8, 9, 10). Selective antibiotic pressure, particularly that caused by the intensive use of expanded spectrum cephalosporins and cross-transmission, has been associated with the emergence and dissemination of ESBL producing members of the family Enterobacteriaceae(11,12).

In E. cloacae, ESBL production needs to be distinguished from a constitutive Amp Chyper production phenotype, the most frequent mechanism of broad-spectrum cephalosporin

resistance in this species. As screening methods recommended for E. coli and K. pneumoniae that are based on resistance to ceftazidime or cefotaxime may not be adequate for Enterobacter spp., an increased cefepime MIC may be a reliable marker for the presence of an ESBL in these species (13). This can be confirmed by the DDST. This distinction has only limitedclinical impact because therapeutic options are similarly limited, but there is evident epidemiological significance.

It has been suggested that ESBLs are related to the acquisitionof plasmids encoding resistance to non-lactam antibiotics, including amino glycosides and trimethoprim-sulfamethoxazole,and recently described qnrA determinants that confer resistance to quinolones (14, 15, 16, 17).

According to the literature, K. pneumoniae, E. coli and E. cloacae are the 3 most frequently described species of enterobacteria in the digestive flora of neonatal patients (18,19), with a more marked epidemic potential for Klebsiella spp. and Enterobacter spp.

A study conducted in 2001 in a neonatal intensive care unit of a Cleveland hospital (USA) showed that E. cloacae was the most frequently isolated antibiotic-resistant enterobacteria, with 5 clones having generated epidemics out of 42 different clones characterized (20). As E. cloacae is naturally resistant to ampicillin and first and third generation cephalosporins (antibiotics usually prescribed in neonatal wards, especially in case of suspected maternal-fetal infection), this could partly explain the epidemic episodes found in neonatal wards involving E. cloacae.

The latest data from the "Neocat" network (21) for surveillance of central line bacteremia in neonatology show an increase in the incidence of E. cloacae bacteremia between 2013 and 2016.

The investigation of these clustered case episodes has allowed us to study the possible role of several sources of contamination or reservoirs that may have played a role in their occurrence. In the literature, the following sources are mentioned in particular: vials and multidose solutions, blood gas analyzers (22), saline or parenteral solutions, distilled water (23). However, it is not uncommon that no source is identified (24).

Neonatal sepsis involving Enterobacter spp. may be associatedwith a high rate of mortality. Grouped cases of infection inside one setting are not necessarily related to a single-clone outbreak and could reveal other environmental and organisational problematics. The fight against establishment and transmission of Enterobacter spp. and especially MDR strains inside a setting is amajor challenge involving respect of standard hygiene, reinforcement of disinfection procedures and restriction of large spectrum antibiotic use (25).

CONCLUSION

The emergence of multi-resistant bacteria with a high epidemic risk in our hospital implies. Hence the interest in developing rapid and efficient means of identification in order to limit their spread. Transmission is believed to be person-to-person, either via contaminated hands of health care providers or through shared equipment. Control measures focus on optimizing infection control practices.

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