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EXTENDED SPECTRUM BETA LACTAMASES: PRESENT AND FUTURE PERSPECTIVES

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ABSTRACT

Beta lactam antibiotics are a broad class of antibiotics which consists of all antibiotic agents that contains β-lactam ring in their molecular structures. Most beta lactam antibiotics work by inhibiting cell wall biosynthesis in bacterial species and are most widely applicable group of antibiotics. Extended-spectrum β-lactamases are the mutant, plasmid mediated enzymes which hydrolyse the beta lactam ring of the antibiotics. The present communication deals with past, present and future perspectives of ESBLs.

KEY WORDS

β- lactam, ESBLs, Plasmid mediated β-lactamases.

INTRODUCTION

Extended-spectrum β-lactamases (ESBLs) are enzymes that can hydrolyze oxyimino- β -lactams (e.g., cefotaxime, ceftazidime,and ceftriaxone) and the monobactam, aztreonam, resulting in resistance to these drugs. ESBLs, predominantly derivatives of plasmid-mediated TEM or SHV β-lactamases, arise through mutations that result in one or more amino acid substitutions that alter the configuration or binding properties of the active site, thereby expanding the hydrolytic spectrum of the enzyme (Asma et al 2006). First β-lactamase identified were Amp C beta – lactamase in two species in year 1940, Escherichia coli and penicillinase, Staphylococcus aureus. The First plasmid- mediated β- lactamase containing TEM-1 gene was reported in 1965, in E.coli, in Greece (David et al 2005).

ESBLs are mutant enzymes with broader range of activity than the β-lactamase enzymes. They hydrolyze 3rd and 4th generation cephalosporins and aztreonam but donot affect cephamycins which is second generation cephalosporin or carbapenems and remain susceptible to beta- lactamase inhibitors (Varsha et al 2007). There are so many types of ESBLs like TEM, SHV, CTX, OXA, AmpC, etc. but majority of the ESBLs are derivatives of TEM or SHV enzymes and these enzymes are most often found in E. coli and K. pneumoniae. “Classical” ESBLs are derived from TEM and SHV enzymes whereas “Non Classical” ESBLs are derived from enzymes other than TEM or SHV. Upto 90% of ampicillin resistance in E.coli is due to production of TEM-1(Sohei et al 2008)

The first plasmid-mediated β-lactamase in gram-negative bacteria, TEM-1, was described in the early 1960s. (Datta et al 1965) Carried by transposons on plasmids, the TEM-1 genes have spread to several bacterial species and are now distributed around the world. SHV-1 is another frequently encountered plasmid- mediated β-lactamase among gram-negative bacteria.The first plasmid-mediated β-lactamase capable of hydrolyzing extended-spectrum cephalosporins, now known as SHV-2, was reported in 1983 (Knothe et al) and a number of other groups of β-lactamases with expanded hydrolytic activity were reported thereafter .The term ‘extended-spectrum β-lactamases (ESBLs)’was applied to denote these enzymes with activity against extended-spectrum cephalosporin(Bush et al 2013). All ESBLs have serine at their active sites except for a small (but rapidly growing) group of metallo b-lactamases belonging to

class B(They share several highly conserved amino acid sequences with penicillin binding proteins (PBPs).b-lactamases attack the amide bond in the b lactam ring of penicillins and cephalosporins, with subsequent production of pencilinoic acid and cephalosporic acid, respectively, ultimately rendering the compounds antibacterially inactive. Plasmids responsible for ESBL production tend to be large (80Kb or more in size) and carry resistance to several agents, an important limitation in the design of treatment alternatives(David et al 2005).The most frequent coresistances found in ESBL producing organisms are aminoglycosides, fluoroquinolones, tetracyclines, chloramphenicol and sulfamethoxazole-trimethoprim.
Since, ESBL production is usually plasmid mediated it is possible for one specimen to contain both ESBL producing and non ESBL producing cells of the same species. This suggests that for optimal detection, several colonies must be tested from a primary culture plate.

CONCLUSION

Today more than 200 types of ESBL genes have been characterized. Due to high use of antibiotics their environmental release should be the matter of concern. Possibly the genes have been transferred from species to species. Several appropriate prevention and treatment guidelines may be applied to fight against ESBLsproducing organisms. These may include public awareness programs especially in rural areas, combination therapy, drug cycling by making a policy, identification of new pharmacophores and good clinical practice.

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