IRSTI 34.27.29

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Mechanism of resistance to beta-lactam antibiotics

Abstract. *Acinetobacter baumannii* is the most commonly associated human pathogen with infections in the genus. This opportunistic pathogen causes quite serious infections, especially in fond patients, and has the ability to quickly develop resistance to new antibiotics. In the recent past, carbapenems, a. It was the first option in the treatment of Baumannii infections. But recently there have been many clinics Acinetobacter the baumannii isolate has acquired resistance to all conventional antibiotics, including carbapenems. This compilation is Acinetobacter it can refresh our knowledge about the resistance mechanisms of baumannii; however, his revolution will continue in the future.
Keywords: Acinetobacter bomannii, pathogen, knowledge.

DOI: 10.32523/2616-7034-2023-144-3-115-127

Introduction

Members of the Acinetobacter family were first identified in 1911, and in the early 1970s they took their place among nosocomial pathogens in the first in-vitro studies, it was found that many clinical isolates are sensitive to commonly used antimicrobial agents such as ampicillin, gentamicin, chloramphenicol, and nalidixic acid, but over time, an increase in the resistance of clinical isolates to the acinetobacter bauman complex was observed. Today, most of the isolates are resistant to commonly used antibacterial agents, such as aminopenicillins, ureidopenicillins, and cephalosporins of a wide spectrum of action, most of them are aminoglycosides, quinolones, chloramphenicol, and tetracyclines. The multiple drug resistance (OID) occurring in Acinetobacteria species in recent years has led to the intensive use of carbapenem (imipenem, meropenem) in the treatment of Acinetobacteria infections. However, today, high resistance to carbapenems in Acinetobacter clinical isolates is reported worldwide, and some of them are resistant to all traditional antibiotic agents(20). Some studies have shown that colistin may be useful for the treatment of infections caused by carbapenem-resistant isolates(18). In addition, the successful use of sulbactam with activity against acinetobacteria species and various combinations of antibiotics, such as ampicillin or polymyxin B, imipenem and rifampicin, has been reported(31,70). Similarly, tigecycline has been stated to be active against carbapenem-resistant isolates(5).

Recently, however, Acinetobacter resistance to colistin and polymyxin B has also begun to be reported in baumannii strains (28). These observations have clearly demonstrated the importance of understanding the resistance mechanisms of bacteria. In this review, the current situation for the molecular mechanisms of antibiotic resistance of baumannii will be tried to establish.

Mechanism of resistance to beta-lactam antibiotics

The main mechanism for resistance to beta-lactam antibiotics, including carbapenems, in Acinetobacter species, is the production of beta-lactamase, encoded either by a chromosome or a plasmid. In addition to beta-lactamases, resistance can also arise from porin replacement and modification of penicillin-binding proteins (PBPs). Beta-lactamases can be divided into natural and acquired.

Natural beta-lactamases

These enzymes are the main feature of the species and can be found in all strains of the genus or species and can be transferred vertically. Of the natural beta-lactamases belonging to the *Acinetobacter baumannii* complex- it is OXA 51-like beta-lactamases and ampC-type cephaloporinases that have been identified in almost all of the isolates.

OXA-51 like beta-lactamases

This set of enzymes, which is produced by *Acinetobacter baumannii* species and is a natural beta-lactamase, is one of the class D oxacylinases. This natural group forms a set of enzymes that, unlike other known oxacylinases, show up to 63% amino acid homology. OXA-51 gene sequence analyses show obvious differences from class D motifs when compared with other major OXA enzyme clusters. At least 18 OXA-51 variants have been detected in various geographical regions so far(7,60,62). These variants differ from each other by modification of 1-15 amino acids. But all these enzymes exhibit weak carbapenemase activity, and none of the cephalosporins, except cephaloride, a substrate weaker than ampicillin, is hydrolyzed by these enzymes. Apparently, the expression level of these genes and related enzymes is low. A. Of the members of the baumania OXA-51 enzyme cluster, only OXA-69 play an active role in resistance to all beta-lactams, including carbapenems. The genomic source of a cluster of enzymes similar to OXA-51 is still unknown. Perhaps as a mechanism of resistance to soil microorganisms producing antibiotics, or caused by unknown organisms and integrated into the chromosome. Regardless of the source, members of the OXA51 enzyme cluster are not found in other species of acinetobacteria, despite the natural structure in almost all Acinetobacter-baumanni isolates[37]. It has been suggested that these enzymes are often present in combination with acquired OXA-type enzymes belonging to other clusters, and under certain conditions may play at least a synergistic role in resistance to carbapenem[68].

AmpC-type cephalosporinases

The presence of the enzyme cephalosporinase in all species belonging to the Acinetobacter-baumannii complex is observed. Some variations in the properties of this enzyme are observed dec different types of bacteria. However, it is known that the Acinetobacter ampC gene originates from a common lineage and is more closely related to each other than the ampC genes found in other bacterial lineages. In addition, october to the similarity of the amino acid sequences of Acinetobacter ampC beta-lactamases, it can be assumed that these enzymes come from a single enzyme family. This condition, supported by phylogenetic analyzes, has been called Acinetobacter-induced cephalosporinases (50).

The enzyme quite effectively hydrolyzes first-generation cephalosporins, ureidopenicillins and aminopenicillins. It does not reduce the effects of broad-spectrum cephalosporins when they are expressed at the basal level. However, the addition of an insertion sequence (IS) to the upper part of the bla gene triggers the production of high levels of betalactamase. An increase in the level of the enzyme causes a high level of resistance to broad-spectrum compounds such as cefotaxime and ceftazidime(50).

According to IS terminology, ISAbal has a length of 1180 bases and carries reverse repeats of the terminal 16 base series belonging to the IS4 family. Its placement has been shown to be 9 bases away from the starting codon of the ampC gene. ISAbal is replaced by the main supporting sequence regulating the expression of ampC at low levels, and a new supporting sequence is

formed. The splicing event also results in nucleotide exchange of the binding sites of the ampC gene to the ribosome. However, it is known that nucleotide change in ribosome binding sites does not change ampC gene expression and that high levels of expression are associated only with the presence of ISAbel. Although it has been found as a few copies in ISAbal Acinetobacter species, it has not been shown so far in other organisms such as Enterobacter or Pseudomonas aeruginosa (24,34,51).

Acquired beta-lactamases

Broad-spectrum beta-lactamases (GSB)

Plasmid-mediated acquired betalactamases in Acinetobacter species were first raised by JUL, and then by the demonstration of SHV enzymes. Resistance to ampicillin, carboxypenicillins and ureidopenicillins has been attributed to the presence of these enzymes, but it has been emphasized that they are not active against broad-spectrum cephalosporins and carbapenems(4). It is not always easy to detect GSBLS in Acinetobacters. This can be shown if special efforts are made to detect enzymes. Thus, in the first studies, PER-1 enzymes from Turkey, VEB-1 from France, SHV-12 from China, and CTX-M enzymes from Japan were reported (26,39,40,63).

Although these genes are mostly acquired in relation to plasmids in other bacteria, it has not yet been revealed by which mechanism exactly Acinetobacter species acquire these enzymes. It has been shown that the blaVEB1 gene in *Acinetobacter baumannii* strains isolated from France is associated with the class 1 integral structure in Paeruginosa isolates(45).

Similarly, the THU-1 gene is shown to be a chromosomally localized transposon fragment, p.it is limited to ISPa12 and ISPa13 found in aeruginosa isolates and has been identified to have a 63% similarity at the amino acid level with IS4(43). Therefore, it has been hypothesized that the chromosomal location of the genes in question is caused by the transposition event following the transfer and plasmid loss. But currently, these genes are known as regions that are integrated into the chromosome and cannot be transferred.

Metallo-beta-lactamases (MBL)

Currently, there are six known groups of acquired ML (IMP, VIM, SIM, SIM, SIM, and GSM). Of these, UTIs, VIM, SIM, and GSO were registered in clinical isolations of Acinetobacter species (Chart). At least 19 variants are known in the UTI group, grouped into 7 phylogroups. Nowadays, Acinetobacter Baumanni has identified six variants of IMP (IMP-1, IMP-2, IMP-4, IMP-5, IMP-6, IMP-8, and IMP-11), of which three are different phylogenes (46,67).

While in Europe, especially in the Mediterranean countries, there is limited notification of isolates of acinetobacteria carrying genes encoding these enzymes, some Asian countries seem to be endemic to isolates carrying these genes.

So far, Acinetobacter in Baumanni, VIM enzymes are found quite rarely. Only VIM-2 came from South Korea and VIM-1 from Greece (58.69). Acinetobacter rarity in SIM, like VIM, only in Korea.It is reported in Bauman clinical isolations (29).

Table A

The mechanisms of antibiotic resistance that baumannii have (3, 21, 33, 48, 57, 71)

Antibiotic/ Resistance mechanism	**Group/ Gene**	**Antibiotic/ Resistance mechanism**	**Group/ Gene**
For beta-lactams Beta-lactamase Natural Class A/frequently seen Class A/ rare	*ampC* (ADC1-7) VEB-1,-2 PER-1,-2 TEM-92,-116 SHV-5,-12 CTX-M-2-3 SCO-1	**For aminoglycosides** Enzymatic degradation Acetyltransferase Nucleotidyltransferase Phosphotransferase Efflux pump 16srDNA metiltransferazyy	AAC-2,-3,-6 SAT-2 ANT-2,-3 APH(3′)-I, -II,-III,-IV APH(3′′)-I adeABC adeM armA
Carbapenemase	OXA-51 similar OXA-23 OXA-24	**For quinolones** DNA gyrase/ topoisomerase	 gyrA/parC adeABC adeM
Class D oxacylinase	OXA-27 OXA-37 OXA-40	Efflux pump	abeS
Metallo-beta-lactamase Class A carbapenemase Outer membrane proteins Efflux pump **For tetracyclines** Efflux pump Ribosomal target exchange	OXA-58 similari VIM IMP SIM GES-11 carO HMP-AB 33-36 kDa protein 43 kDa protein adeABC PBP2 change tetA, tetB adeABC tetM	**For chloramphenicol** Efflux pump **For trimethoprim/ sulfamethoxazole** Efflux pump Dihydrofolate synthetase Dihydrofolate reductase **For macrolides** Efflux pump **For glycylcycline** Efflux pump **For polymyxin**	adeABC adeIJK cmlA craA abeS adeM adeABC pmrAB arr-2

In Acinetobacter isolates, IMP and VIM variants have strong hydrolytic activity against carbapenem (>32 mg/L) and other betalactam antibiotics (except aztreonam) and are highly resistant. Interestingly, the isolates producing SIM-1 have a low MIC level for carbapenems (8-16 mg/L). Among beta-lactams, only cefepim and cefpir and a smaller amount of piperacillin-tazobactam have activity against decomposition strains.

Analysis of DNA sequences of MBL decoding genes showed that the Blamp blaVIM and blaSIM genes are present in the form of gene cassettes attached between the preserved regions of Class 1 integral structures. It can also be assumed that gene cassettes encoding MBL are usually associated with other antibiotic resistance cassettes, especially those encoding enzymes that modify aminoglycosides.

Oxacylinases

Class D oxacylinases are betalactamases that hydrolyze oxacylins,are not common, and are called carbapenem-hydrolyzing oxacylinases (KHO). Currently, more than 120 D-group betalactamases have been identified, of which about 45 show KHO activity(66). A.baumannii species produce natural class D oxacillinase belonging to the OXA-51-like enzyme cluster with weak carbapenemase activity. In addition, three october of acquired class D oxacylinases with activity against carbapenems have also been identified, it has been emphasized that the hydrolytic activity of these enzymes against carbapenems is quite low compared to the MBL class(68).

HO, acquired in Akinetobacter, was first shown in 1985 at the University of Edinburgh. After a genetic and biochemical study of the enzyme, it was named OXA-23(42). OXA-23, A. It has a 56% amino acid similarity with enzymes like OXA-51 naturally occurring in baumannia, and is the first representative of HO(7). Later, OCSA-27(1) was released from Singapore. It was shown that OXA-27 is separated from OXA-23 by the displacement of Thr/Ala and Asn/Lys at positions DBL95 and 247, respectively(46).

In studies, it has been shown that ISABEL belonging to the IS4 family is always located in a region close to the blaOXA-23 gene(59).

This suggested that ISABEL plays a regulatory role and plays a key role in the expression and possibly acquisition of blaOXA-23. Similarly, it has been reported that ISABA4 belonging to the IS982 family is located in a region close to blaOXA 23, such as ISAbel, and its importance has been emphasized while information about its role has not been provided(46).

The second cluster acquired includes HOXA-24, OXA-25, OXA-26 and OXA-40. These enzymes showed a 60% similarity of amino acids with OXA-23 and 62% similarity with OXA51 enzymes(46). Many of the enzymes in this cluster appear to be close variants of each other. OXA-26 was first shown in an isolation ward in Belgium(1). OXA-40 in Spain and Portugal is reported to be common in Baumannia isolation wards(13). The third potential cluster of acquired CHO is OXA-58, which was first detected in France(44). OXA-58 has a 59% similarity with the OXA-51 set of natural enzymes(46). OXA-58 type enzymes have been detected in different geographical regions all over the world(12,35,46). A of OXA-58 it has been reported that it reduces sensitivity to carbapenems when expressed in baumannii and leads to high carbapenem resistance in the case of overexpression(23).

There is not much information about the origin or possible acquisition mechanisms of KHOS. It has been shown that the genes encoding OXA-23 and OXA-58 in some species are also encoded by the plasmid and spread polyclonally(36,44). However, until now, it has been observed that the KHOS identified in Acinetobacter are chromosomally encoded. In OXA-40 sequence analyses obtained from many strains, no evidence was found regarding the mobility or transmission of the gene region. Although OXA-58 is not always surrounded by IS elements, which are usually involved in its expression(44) .The IS elements in question were not considered to be effective in acquiring the OXA-58 gene. However, in the OXA-58 gene analysis of a strain isolated in France, it was shown to have a 27-bp long repetitive DNA fragment and it was stated that this fragment may play a role in the recombination process(47).

Changes in outer membrane proteins (OMP)

Although the first reports on carbapenem resistance in Acinetobacter species reported that the permeability disorder was associated with a change in porin proteins, the details of the issue were provided through molecular information obtained in recent years(11). A 33-36 kDa OMP associated with carbapenem resistance in A baumannii was cloned in 2005 and sequence analysis

was performed. With this data, it has been shown that the amino acid sequence and content of OMP are similar to those in other Gram-negative bacteria.

As a result, as with other Gram-negative bacteria, Acinetobacter high glycine content of OMP in baumannii, lack of cysteine residues, negatively charged, absence of moderate hydrophobic residues, similarity of transmembrane, membrane and cell surface proteins shown by OMP functional protein analyses of 33-36 kDa can be counted(14). Related studies have shown that OMP loss of 20-kDa is associated with imipenem resistance in Acinetobacter clinical isolates that do not show detectable carbapenemase activity(32).

Imipenem and meropenem resistance have also been associated with a heat-exchangeable OMP loss of 25-29 kDa called CarO(54). It has been observed that carbapenem resistance occurs after degradation of CARO by recombinant genes added to the CARO protein, and CARO A. The hypothesis that it is related to the flow of carbapenem into the baumannii has been put forward. Another interesting fact is that by studying the data obtained so far, it has been determined that CARO homologues are found only in the genera Acinetobacter, Moraxella and Psychrobacter(38).

Finally, Acinetobacter at the same time, baumannii p.it has been shown to have a D2 porin homolog (OprD) of 43-kDa, which is known to be associated with carbapenem resistance in aeruginosa(15).

Penicillin-binding proteins (PBP)

In studies, it has been shown that Acinetobacter change in penicillin-binding proteins is also associated with betalactam resistance in Acinetobacter-baumannii. In the studies where carbapenem resistance was investigated; resistant mutant Acinetobacter it has been reported that baumannii strains overproduce PBP of 24-kDa, but also that the other six PBPs possessed by the bacterium, compared with susceptible strains, are expressed at lower levels by resistant mutant strains(19).

In this study, the relationship of sulbactam, clavulanic acid and tazobactam of PBPs belonging to imipenem-resistant and sensitive A baumannii isolates was investigated; it has been shown that all betalactamase inhibitors bind to PBPs of imipenem-sensitive isolates(61).

This observation is Acinetobacter it has been interpreted that invitro of betalactamase inhibitors against baumannii may help to explain its natural antimicrobial properties. However, the current formulation, which is still formulated for clinical use and shows invivo efficacy, appears to be only sulbactam.

The mechanism of resistance to aminoglycosides

Acinetobacteria species have higher resistance to aminoglycosides than many other groups of pathogens(6). Resistance to aminoglycosides in Acinetobacteria species is mainly due to the production of enzymes that modify aminoglycosides. The presence of all aminoglycoside-modifying enzymes identified as acetyltransferase, adenyltransferase, and phosphotransferase in Acinetobacteria species has been shown. It was also emphasized that Acinetobacter haemolyticus and related genomic groups are naturally resistant to aminoglycosides due to the synthesis of natural acetyltransferases.

It has been reported that other mechanisms of resistance to aminoglycosides are associated with changes in the target ribosomal protein and the transfer of aminoglycosides into the cell(21,53). Aminoglycoside resistance genes are gene cassettes that are part of the Class 1 integral structure found in Acinetobacteria species. It has been shown that the spread of aminoglycoside resistance genes in Acinetobacteria species occurs through various genetic mechanisms, including plasmid and transposon transfer. It has also been emphasized that the genes responsible for resistance and enzymes modifying aminoglycosides are also present in other gram-negative bacterial breeds, these genes and enzymes are nonspecific (41,52).

The mechanism of resistance to quinolones

Until 1990, quinolones showed fairly good activity against acinetobacteria species, but subsequently clinical isolates rapidly developed resistance to these antibiotics. As with other

gram-negative bacteria, resistance caused by a mutation in the region encoding enzymes and encoding chromosome localized genes often involves a structural change in DNA gyrase (topoisome-fold II) or topoisomerase IV. The DNA gyrase consists of two Acinetobacter subunits and two B subunits encoded by the girA and Girba genes, respectively. Similarly, topoisomer IV consists of two subunits encoded by the parC and parE genes, respectively. Acinetobacter the most common resistance to quinolone in baumannia is the 83rd GEAR of the mutational type.

This is the replacement of Leu with Ser in its codon, which leads to the fact that the MIC of ciprofloxacin is >4 mg/l. High resistance to ciprofloxacin (MIK >64 mg/L) usually requires double mutations in the gyrA and parC genes. The most frequent mutation in the PARK is 80. In the codon, this is a change of Leu, not Ser. Minor changes in resistance between isolates may also be the result of changes in the permeability of the drug and/or affecting its decomposition(30,33,64,65). With a single mutation in the Ser-83 code of the gyroscopy gene in clinical isolates, the MIC value for ciprofloxacin is up to 32 mg/l, while the MIC value for moxifloxacin remains at 1 mg/l, while in the MIC gene for clinical isolates resistant to moxifloxacin (MIC >2 mg/l) is 80. It has been shown that there is a second mutation in its codon(55).

The mechanism of resistance to tetracycline and other antibiotics

Tetracycline-resistant bacteria often express one of two different resistance mechanisms called a bubble pump or ribosomal defense system. Various genes from THETA to THETA have been identified for tetracycline resistance in gram-negative bacteria[27]. It has been stated that these genes are usually associated with plasmids or transposons, and for species of acinetobacteria this general rule is justified. Thus, Acinetobacter in clinical isolates of baumania, a transposon similar to Tn-1721 carrying the THETA gene was shown.

As is the case with other gram-negative bacteria, Acinetobacter the most common tetracycline resistance genes in baumania clinical isolates are THETA and TETB. In addition, these genes are usually present in combination with the nonspecific gene of the October pump adeB(27). A.In Acinetobacter species located outside baumannii and isolated from environmental samples, the situation seems to be different. It has been reported that these species have tetracycline resistance markers that have not yet been fully disclosed(2). The glycylcycline group is a new agent, tigecycline is broad-spectrum and has the same binding site on ribosomes as tetracyclines, but is not affected by the aforementioned resistance mechanisms for tetracyclines. However, recent publications have also begun to report resistance of up to 10% for tigecycline. There is no information about the source of the resistance in question yet.

Rifampicin is sometimes used as a member of a combination therapy for multidrug-resistant infections caused by Acinetobacter species. A high level of rifampicin resistance in Acinetobacter species occurs due to a spontaneous mutation in the rpoB gene localized in the chromosomally ribosomal polymerase subunit, similar to that observed in other Gram-negative bacteria. However, the presence of the arr-2 gene (encoding the enzyme rifampicin ADP- ribosyltransferase) in the integron-located gene cassette of Acinetobacter isolates has also been identified(25) .

The arr-2 gene cassette appears to be a major influencer of rifampicin resistance, a high MIC value for rifampicin and a decreased inhibition zone with disc diffusion was detected in arr-2 positive isolates, while the opposite was observed in arr-2 negative isolates (<14 mm)(56).

Acinetobacteria species have a low level of resistance to trimethoprim. But a high level of resistance is associated with the acquisition of a gene encoding dihydrofolate reductase. The conducted studies have raised doubts about the presence on the chromosome of the dhfr gene associated with the corresponding trans-poson or integral structure of Tn-7, providing a highly active integral system[57]. Similarly, chloramphenicol resistance genes in Acinetobacteria species are associated, in particular, with transposons of the Tn21 family integrated into the host chromosome. Bacterial plasmids, most of which are unstable in Acinetobacteria species, can be acquired by Acinetobacteria species that do not have plasmids under high pressure of antibiotics in a hospital environment, and the transfer of resistance genes from cassettes to the acinetobacteria genome can occur [9,16].

Multidrug efflux systems

In addition to specific efux pumps for special antibiotic agents found in Acinetobacteria species, a multiple efux October system was identified, chromosomally encoded in Gram-negative bacteria. The main efux systems that cause a decrease or inactivation of the action of antimicrobials are expressed in the form of a supercomputer supercomputer, a family of resistant, a family of ATP-binding cassettes, a small family of resistant to multiple drugs and a family of extrusion drugs and toxic substances[48].

When it comes to clinical resistance, a family of decompilation resistance divisions is distinguished between these main affix systems. A. In Baumania, the adeABC-efux system belonging to the family of resistant nodulation divisions was identified, and its role in aminoglycoside resistance and its relationship with reduced sensitivity to chloramphenicol, fluoroquinolones, trimethoprim and cefotaxime was clearly defined[33]. In addition, the adeA, adeB, and adeK genes are often present; they also show an association with the adeA and adeR genes (48.57). In Acinetobacter isolates, resistance nodulation division (RND) family efflux system called adeDE has been detected. The activation in the adeE gene has been stated to be associated with decreased susceptibility to amikacin, ceftazidime, chloramphenicol, ciprofloxacin, erythromycin, ethidium bromide, meropenem, rifampicin, and tetracycline (8).

A secondary active efflux system called adeXYZ has also been detected in Acinetobacter isolates. However, the potential role of this new system in antibiotic resistance has not been fully revealed. This leads to the idea that the system in question has a role in other special cell functions. A set of genes homologous to adeXYZ was also detected in Acinetobacter baylyi ADP1, but A.it has not been shown in baumannii isolates.

The role of integrons

Integrons are DNA elements containing genetic markers as a component of the region-specific recombination process that recognizes and captures mobile gene cassettes(22). Therefore, integrons contain adjacent recombination sites to which genes and gene cassettes can be attached for integrase. It has been shown that gene cassettes captured by integrons in most cases encode resistance to antibiotics and disinfectants(17). It has been shown that class 1 and class 2 integrons are also common in clinical isolates of Acinetobacter species(3). It has been stated that integrons isolated from Acinetobacter may play a role in the resistance of beta-lactam, aminoglycoside, chloramphenicol, trimethoprim and rifampicin(57).

Conclusion

In recent years, a limited number of new antibiotics have been developed and approved for the treatment of infections. Although the effectiveness of these antibiotics is considered to be different, they have fundamentally the same mechanisms of action. In addition, of these new agents, only colistin, sulbactam, ertapenem, and tigecycline are effective for Gram-negative bacteria. Acinetobacter given that baumannium has a natural resistance to ertapenem, colistin, sulbactam, and tigecycline seems to be an alternative. Often found in intensive care units of hospitals as an infectious disease specialist. In the fight against strains of baumania, new antibiotics are needed, as well as the correct and rational use of existing antibiotics. In the first hours after admission of patients to such units, it is necessary to determine whether the patient hospitalized in the department was colonized by resistant strains, and colonized patients should be isolated as much as possible from the safety of other patients.

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Бета-лактамды антибиотиктерге төзімділік механизмі

Аңдатпа. *Acinetobacter baumannii* инфекциясы осы ауру түрінің ең жиі адам қоздырғышы болып табылады. Бұл шартты-патогенді қоздырғыш өте ауыр инфекцияларды, әсіресе ерекше күтімді қажет ететін науқастарда тудырады және жаңа антибиотиктерге төзімділікті тез дамыту мүмкіндігіне ие. Соңғы уақытта *A. baumannii* инфекцияларын емдеуге бірінші болып карбапенемдерге таңдау жасалды. Бірақ соңғы уақытта клиникаларда *A. baumannii* изоляттары барлық дәстүрлі антибиотиктерге, соның ішінде карбапенемдерге төзімділікті көрсететін жағдайлар көп болуда. *A. baumannii* қарсылық механизмдері туралы бұл мақала біліміміздің жаңартуы мүмкін, бірақ оның эволюциясы болашақта жалғасын табады.

Түйін сөздер: *Acinetobacter baumannii*, қоздырғыш, микробқа қарсы препараттар, антибиотиктер, штамм.

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Механизм резистентности к бета-лактамным антибиотикам

Аннотация. *Acinetobacter baumannii* является наиболее часто ассоциированным человеческим патогеном с инфекциями подобного рода. Этот условно-патогенный возбудитель вызывает довольно серьезные инфекции, особенно у больных, нуждающихся в особом уходе, и обладает способностью быстро вырабатывать устойчивость к новым антибиотикам. В недавнем прошлом карбапенемы были первым выбором в лечении инфекций, вызванных A. baumannii. Но в последнее время в клиниках наблюдается множество случаев, когда изоляты *A. baumannii* приобретают устойчивость ко всем традиционным антибиотикам, включая карбапенемы. Эта компиляция о механизмах устойчивости *A. baumannii* может обновить наши знания, однако его эволюция будет продолжаться в будущем.

Ключевые слова: *Acinetobacter baumannii*, возбудитель, противомикробные препараты, антибиотики, штамм.

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