4. CONCLUSIONS

Caracterització de les β-lactamases implicades en la disminució de la sensibilitat a les cefalosporines de tercera generació (C3G) en enterobacteris sense β-lactamasa cromosòmica induïble (articles I, II i IV)

1. Els mecanismes implicats en la disminució de la sensibilitat o la resistència a les C3G en *E. coli* durant el trienni 1994-1996, van ser: hiperproducció de la β-lactamasa cromosòmica AmpC (0,78%), hiperproducció de la β-lactamasa plasmídica SHV-1 (0,39%), producció d'oxacil·linases (0,03%) i producció de β-lactamases d'espectre ampliat (BLEA) (0,14%).
2. En *K. pneumoniae* els mecanismes implicats en la disminució de la sensibilitat o la resistència a les C3G van ser: la hiperproducció de la β-lactamasa SHV-1 (1,03%) i la producció de la β-lactamasa d'espectre ampliat SHV-2 (0,17%).
3. En *K. oxytoca* els mecanismes van ser la hiperproducció de la β-lactamasa cromosòmica K_{OXY}, amb una incidència del 4,81% en el subtipus OXY-1 i 9,03% en el subtipus OXY-2.
4. La β-lactamasa cromosòmica AmpC d'*E. coli* va presentar una gran variabilitat de punts isoelèctrics, entre 8,9 i 9,9, la qual cosa va permetre especular sobre la possible variabilitat genètica d'aquest gen en una mateixa espècie, així com la seva implicació en la resistència i la seva correlació amb l'evolució de l'espècie.
5. En el trienni 1994-1996, de totes les soques aïllades en clínica amb freqüència significativa, únicament les espècies pertanyents a *E. coli* (0,14%) i *K. pneumoniae* (0,17%) expressaven una BLEA. En el període posterior 1997-2000, van presentar BLEA *E. coli* (0,46%), *K. pneumoniae* (1,07%) i *Salmonella enterica* serovar Enteritidis (0,09%). També es van detectar soques productores de CMY-2 (0,07%), que és una cefamicinasa plasmídica, en les espècies d'*E. coli* (0,07%), *K. pneumoniae* (0,11%), *Proteus mirabilis* (0,08%) i *S. enterica* serovar Mikawasima (0,09%).
6. A la nostra àrea, la incidència de BLEA en enterobacteris durant el període 1994-1996 és baixa: el 0,14%. En el període 1997-2000 es va observar un lleuger increment (0,44%). En tots dos períodes es va apreciar una gran variabilitat: SHV-2 (27,54%), TEM-12 (4,35%), CTX-M-9 (65,21%), SHV-4 (1,45%) i TEM-10 (1,45%). Les dues darreres classes de β-lactamases únicament es van detectar en el període 1997-2000.

Caracterització d'una nova β-lactamasa d'espectre ampliat (article III)

7. Es descriu una nova β-lactamasa d'espectre ampliat, que pertany a la família de les CTX-M, anomenada CTX-M-9. Aquesta és la primera β-lactamasa d'aquesta família descrita a Espanya. La seva incidència representa el 65,22% de les BLEA detectades al nostre laboratori.

Estudi de l'entorn genètic del gen codificador de la β-lactamasa CTX-M-9 (article V)

8. Caracterització del nou integró compost anomenat In60, portador de la β-lactamasa CTX-M-9. Aquest integró consta de les regions conservades 5'-CS i 3'-CS entre les quals es troben els gens casset: *aadA2* i *dfrA16*; a continuació hi ha una regió que conté l'*orf513*, $bla_{\text{CTX-M-9}}$ i una nova seqüència d'inserció IS*3000*. Finalment hi ha una repetició de la regió conservada 3'-CS.
9. L'alt grau d'identitat entre la regió que inclou $bla_{\text{CTX-M-9}}$ i una seqüència a 3' d'aquest gen amb $bla_{\text{KLUA-1}}$ i l'*orf3* de *K. ascorbata*, suggereix que aquesta regió pot procedir del genoma de *K. ascorbata*.
10. In60 comparteix una organització genètica similar a la dels altres tres integrons compostos descrits, la qual cosa podria indicar un origen comú.
11. Les 34 soques estudiades, portadores de la β-lactamasa CTX-M-9, no presentaven cap relació epidemiològica. En totes excepte en una, l'entorn genètic de $bla_{\text{CTX-M-9}}$ era compatible amb In60. Això indica una gran difusibilitat del vector portador d'aquesta β-lactamasa.

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6. ARTICLES