

Monitoramento de bactérias de alto risco de infecção nosocomial em equinos do HOVET FMVZ-USP

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Objetivos

Realizar uma análise retrospectiva de amostras coletadas de animais envolvidos em surtos de infecção por enterobactérias resistentes, descrevendo os principais gêneros envolvidos e o perfil de resistência para as classes de antimicrobianos de uso crítico e compartilhada com a medicina humana (Beta-lactâmicos, Quinolonas e Aminoglicosídeos).

Métodos e Procedimentos

Para a análise retrospectiva foram analisados os registros do Laboratório de Medicina Aviária das culturas microbiológicas solicitadas por demanda do HOVET-FMVZ-USP no período de janeiro de 2016 a novembro de 2018. Estes registros incluíam animais hospitalizados que foram submetidos a procedimentos cirúrgicos e aqueles que evoluíram para óbito, com coleta durante a necropsia.

Foram incluídos nesta pesquisa um total de 207 isolados, que foram então agrupados de acordo com as 3 principais classes de antimicrobianos pesquisadas em: "Resistente aos aminoglicosídeos" (resistente a amicacina ou gentamicina ou, se não testado em nenhuma, resistente a outro aminoglicosídeo), "Resistente às cefalosporinas (resistente a cefoxitina ou cefotaxima ou, se não testado em nenhuma, resistente a outra cefalosporina) e "Resistente às quinolonas (resistente à ciprofloxacina, enrofloxacin ou levofloxacina). As informações a respeito do tipo do material, data da coleta, bactéria isolada e perfil de

resistência foram coletadas e inseridas em uma planilha de Excel, para posterior análise dos dados no software R.

Resultados

Foram isoladas 207 estirpes resistentes de equinos pacientes do hospital, sendo 18 (8,7%) de 2016, 166 (80,19%) de 2017 e 23 (11,11%) de 2018. Estes dados foram obtidos por demanda espontânea, então não representam um aumento no número de infecções resistentes de um ano para outro. Dos isolados identificados, 104/207 (50,24%) eram da espécie *E. coli*, 26/207 (12,56%) *Klebsiella pneumoniae* e 22/207 (10,63%) *Salmonella* spp. Outros gêneros encontrados incluíam *Pseudomonas* spp., *Enterobacter* spp e outros. Vinte e quatro isolados não foram identificados pela técnica de MaldiTof.

A análise da resistência bacteriana às 3 classes de antimicrobianos demonstrou que 140 foram considerados resistentes a aminoglicosídeos, 145 a cefalosporinas e 32 a fluorquinolonas. O perfil de resistência foi o seguinte:

- Aminoglicosídeos: 140 resistentes, 13 sensíveis, e 54 não testados;
- Cefalosporinas: 148 resistentes, 5 sensíveis, 54 não testados e 1 indefinido;
- Quinolonas: 32 resistentes, 38 sensíveis e 138 não testados.

Os isolados multirresistentes foram 66, em oposição a 4 não-multirresistentes. Desses

isolados multirresistentes, 28 eram *E. coli*, 16 *Salmonella* spp., 10 *K. pneumoniae*, 3 *P. aeruginosa*, 1 *C. freundii*, 1 *E. cloacae*, 1 *K. oxytoca* e 6 não foram identificados.

Conclusões

Constatou-se a presença majoritária de enterobactérias, especialmente *E. coli* - pertencendo à microbiota, estão constantemente expostas a eventuais tratamentos com antimicrobianos, sendo potenciais reservatórios de genes de resistência, o que poderia explicar essa alta prevalência. Percebe-se altas taxas de resistência a aminoglicosídeos e a cefalosporinas. Nestas, se destaca a resistência à cefotaxima. As ESBL do tipo CTX-M estão aumentando sua prevalência em enterobactérias nos últimos anos e consolidando sua presença como a ESBL mais comum em algumas áreas, o que condiz com o que foi encontrado neste levantamento. Embora haja mais sensibilidade do que resistência às quinolonas, diversas amostras não foram analisadas para esta classe, tornando o número de análises inferior às outras, o que pode ter prejudicado o resultado da análise retrospectiva. Entre os isolados multirresistentes, embora sejam muitos em relação aos não multirresistentes, é importante ressaltar que a escolha das amostras a serem submetidas ao antibiograma estava atrelada à gravidade do caso que originou a amostra, o que pode distorcer essa relação. Entretanto, a mera presença desses isolados no ambiente hospitalar pode trazer graves danos às tentativas de tratamento no HOVET, que já são dificultadas devido à maioria dos animais estarem imunossuprimidos e com quadros graves quando chegam ao hospital. Assim, a constatação de sua presença é certamente preocupante.

Referências Bibliográficas

CLINICAL AND LABORATORY STANDARDS INSTITUTE (CLSI). Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals; approved standard. VET01-A4., 4th Ed. Wayne, PA, USA, 2013
CLINICAL AND LABORATORY STANDARDS INSTITUTE (CLSI). Performance Standards for

Antimicrobial Susceptibility Testing—Twenty-Ninth Edition: M100. 2019.

D'AGATA, E. M. C. et al. Efficacy of infection control interventions in reducing the spread of multidrug-resistant organisms in the hospital setting. PLoS ONE, v. 7, n. 2, p. 1–11, 2012.

FAO; WHO; OIE. Joint FAO/OIE/WHO Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance: Scientific assessment, 2003.

MADDOX, T. W. et al. Longitudinal study of antimicrobial-resistant commensal *Escherichia coli* in the faeces of horses in an equine hospital. Preventive Veterinary Medicine, v. 100, n. 2, p. 134–145, 2011.

MADDOX, T. W. et al. Antimicrobial resistance in bacteria from horses: Epidemiology of antimicrobial resistance. Equine Veterinary Journal, v. 47, p. 756–765, 2015.

MAGIORAKOS, A. P. et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clinical Microbiology and Infection, v. 18, n. 3, p. 268–281, 2012.

MILTON, A. A. P. et al. Nosocomial Infections and their Surveillance in Veterinary Hospitals. Advances in Animal and Veterinary Sciences, v. 3, n. 2, p. 1–24, 2015.

R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, 2021. Vienna, Austria. URL <https://www.R-project.org/>.

ROSSOLINI, G. M.; D'ANDREA, M. M.; MUGNAIOLI, C. The spread of CTX-M-type extended-spectrum β -lactamases. Clinical Microbiology and Infection, v. 14, n. 1, p. 33–41, 2008.

WALTHER, B.; TEDIN, K.; LÜBKE-BECKER, A. Multidrug-resistant opportunistic pathogens challenging veterinary infection control. Veterinary Microbiology, v. 200, p. 71–78, 2017.

WEESE, J. S. et al. Methicillin-Resistant *Staphylococcus aureus* in Horses at a Veterinary Teaching Hospital: Frequency, Characterization, and Association with Clinical Disease. Journal of Veterinary Internal Medicine, v. 20, p. 182–186, 2006.

WHO. The burden of health care-associated infection worldwide, 2018. Disponível em: https://www.who.int/infection-prevention/publications/burden_hcai/en/

WHO. Critically Important Antimicrobials for Human Medicine, 6th revision, 2019.

Monitoring high-risk bacteria of nosocomial infection in horses at the Veterinary Hospital from FMVZ-USP

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Objectives

To make a retrospective analysis of samples collected from animals involved in resistant enterobacteria infection outbreaks, describing the main genera involved and the resistance profile for antimicrobial classes that are of critical use and shared with human medicine (Beta-lactams, Quinolones and Aminoglycosides).

Materials and Methods

For the retrospective analysis, records from microbiological cultures of Laboratório de Medicina Aviária, requested by HOVET-FMVZ-USP from January 2016 to November 2018, were analysed. These records included hospitalized animals that were submitted to surgical procedures and also those that evolved to death, with samples collected in necropsy.

207 isolates were included in this research, which then were grouped according to the 3 main antimicrobial classes: "Resistant to aminoglycosides" (resistant to amikacin or gentamicin or, if not any, another aminoglycoside), "Resistant to cephalosporins" (resistant to cefoxitin or cefotaxime or, if not any, to another cephalosporin) and "Resistant to quinolones" (resistant to ciprofloxacin, enrofloxacin or levofloxacin).

Information on the type of material, date of collection, isolated bacterium and resistance profile were collected and inserted into an Excel

sheet, to posterior data analysis in the R software.

Results

207 resistant strains were isolated from horses in the hospital, of which 18 (8,7%) were from 2016, 166 (80,19%) from 2017 and 23 (11,11%) from 2018. This data was obtained from spontaneous demand, so it does not represent an increase in resistant infection from a year to another. Of the identified isolates, 204/207 (50,24%) were from *E. coli*, 26/207 (12,56%) *Klebsiella pneumoniae* and 22/207 (10,63%) *Salmonella* spp. Other identified genera included *Pseudomonas* spp., *Enterobacter* spp. and others. Twenty four isolated were not identified by the MaldiTof technique.

The analysis of resistance to the 3 classes revealed that 140 isolated were considered resistant to aminoglycosides, 145 to cephalosporins and 32 to fluoroquinolones. The resistance profile was the following:

- Aminoglycosides: 140 resistant, 13 sensitive, and 54 not tested;
- Cephalosporins: 148 resistant, 5 sensitive, 54 not tested and 1 undefined;
- Quinolones: 32 resistant, 38 sensitive and 138 not tested.

Multiresistant isolated were 66, as opposed to 4 not multiresistant. 28/66 were *E. coli*, 16/66 *Salmonella* spp., 10/66 *K. pneumoniae*, 3/66 *P. aeruginosa*, 1/66 *C. freundii*, 1/66 *E. cloacae*, 1/66 *K. oxytoca* and 6/66 were not identified.

Conclusions

The majority of the isolates were enterobacteria, especially *E. coli* - as it belongs to the microbiota, it is constantly exposed to eventual treatments with antimicrobials, being potential reservoirs of resistance genes, which could explain this high prevalence. High resistance rates to aminoglycosides and cephalosporins were noted. From the latter, resistance to cefotaxime was especially high. ESBL of the CTX-M type are becoming more prevalent in enterobacteria in the last years and consolidating their presence as the most common ESBL in some places, which is in accordance with what we found. Although there is more sensitivity than resistance to quinolones, several samples were not analysed for this class, which may have altered the result of this retrospective analysis.

Although many multiresistant isolated were found, it is important to highlight that the choice of which samples to submit to antibiogram was due to the severity of the case that originated the sample, which can distort this multiresistant: not-multiresistant ratio.

However, the mere presence of these isolated in the hospital environment may reduce treatment options in the hospital, which are already difficult due to the fact that most animals are immunosuppressed and are already gravely sick when entering the hospital. Therefore, finding these isolated is certainly worrying.

References

CLINICAL AND LABORATORY STANDARDS INSTITUTE (CLSI). Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals; approved standard. VET01-A4., 4th Ed. Wayne, PA, USA, 2013

CLINICAL AND LABORATORY STANDARDS INSTITUTE (CLSI). Performance Standards for Antimicrobial Susceptibility Testing—Twenty-Ninth Edition: M100. 2019.

D'AGATA, E. M. C. et al. Efficacy of infection control interventions in reducing the spread of

multidrug-resistant organisms in the hospital setting. PLoS ONE, v. 7, n. 2, p. 1–11, 2012.

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MADDOX, T. W. et al. Longitudinal study of antimicrobial-resistant commensal *Escherichia coli* in the faeces of horses in an equine hospital. Preventive Veterinary Medicine, v. 100, n. 2, p. 134–145, 2011.

MADDOX, T. W. et al. Antimicrobial resistance in bacteria from horses: Epidemiology of antimicrobial resistance. Equine Veterinary Journal, v. 47, p. 756–765, 2015.

MAGIORAKOS, A. P. et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clinical Microbiology and Infection, v. 18, n. 3, p. 268–281, 2012.

MILTON, A. A. P. et al. Nosocomial Infections and their Surveillance in Veterinary Hospitals. Advances in Animal and Veterinary Sciences, v. 3, n. 2, p. 1–24, 2015.

R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, 2021. Vienna, Austria. URL <https://www.R-project.org/>.

ROSSOLINI, G. M.; D'ANDREA, M. M.; MUGNAIOLI, C. The spread of CTX-M-type extended-spectrum β -lactamases. Clinical Microbiology and Infection, v. 14, n. 1, p. 33–41, 2008.

WALTHER, B.; TEDIN, K.; LÜBKE-BECKER, A. Multidrug-resistant opportunistic pathogens challenging veterinary infection control. Veterinary Microbiology, v. 200, p. 71–78, 2017.

WEESE, J. S. et al. Methicillin-Resistant *Staphylococcus aureus* in Horses at a Veterinary Teaching Hospital: Frequency, Characterization, and Association with Clinical Disease. Journal of Veterinary Internal Medicine, v. 20, p. 182–186, 2006.

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WHO. Critically Important Antimicrobials for Human Medicine, 6th revision, 2019.