APORTES A LA EPIDEMIOLOGÍA DE ENTEROPATÓGENOS DE CERDOS JÓVENES EN CUBA

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RESUMEN

La diarrea de los cerdos jóvenes es una enfermedad multifactorial que impacta negativamente la eficiencia productiva de carne de cerdo a nivel mundial. El presente trabajo fue conducido para actualizar el conocimiento epidemiológico de la etiología infecciosa de la diarrea en los cerdos jóvenes criados en Cuba. *E. coli* enterotoxigénica fue el patógeno más frecuente (25.6%). La ocurrencia de otros patógenos fue del 10% para el virus de la gastroenteritis trasmisible y *Cryptosporidium parvum*, 6.7% para rotavirus A e *Isospora suis*, 5.6% para *Clostridium perfringens* α-toxigénico, 3.3% para *E. coli* verocitotoxigénica, y 2.2% para *Salmonella entérica* subespecie *enterica* serotipo Newport. *E. coli* mostró alta tasa de resistencia frente a antibióticos administrados tradicionalmente: tetraciclina (69%), ampicilina (54%), sulfonamidas (50%), y kanamicina (50%), pero fue muy susceptible al ácido nalidíxico, ciprofloxacina, gentamicina, amikacina, cloranfenicol, cefalosporinas, amoxicilina-ácido clavulánico y trimetoprim. El análisis de diversidad genética demostró alto polimorfismo en las secuencias de ADN y relación del clonal entre aislados de *E. coli* que portaban los mismos factores de virulencia y similares patrones de antibioresistencia. Se encontraron niveles bajos, moderados, y altos de anticuerpos específicos contra la fimbria F4 en el 67.6%, 26.8%, y 5.6% de los cerdos, respectivamente, mientras que un 66.4% y 33.6% de ellos mostraron niveles bajos y altos de anticuerpos F18-específicos, respectivamente. Finalmente se determinó la frecuencia de genotipos y alelos que codifican susceptibilidad o resistencia de los cerdos a infecciones por *E. coli*. El genotipo de cerdos resistentes a *E. coli* F18+ no fue encontrado frecuentemente (0.13), mientras los genotipos heterocigoto u homocigoto susceptibles fueron frecuentes (0.27 y 0.60, respectivamente). En Cuba puede mejorarse la eficiencia en la producción de carne de cerdo si se mejoran los programas de vigilancia, prevención, y el control de la diarrea infecciosa en los cerdos jóvenes, particularmente el de colibacilosis. En el a corto plazo, la vacunación contra *E. coli*, la introducción de antibióticos eficaces y la mejora de prácticas de manejo parecen ventajosos para controlar la diarrea porcina en Cuba. En el largo plazo, la selección y cría de cerdos resistentes a infecciones por *E. coli* e inversiones en instalaciones serán necesarios.

COMUNICACIÓN CORTA

La diarrea pre- y post-destete de los cerdos son enfermedades multifactoriales que afectan negativamente la eficiencia de la producción en granjas porcinas a nivel mundial. A menudo los veterinarios del sector porcino de Cuba se quejan de la escasa información sobre la epidemiología de la diarrea y las limitaciones para la identificación específica de enteropatógenos. Por lo tanto, se llevan a cabo medidas de control insuficientes que resultan en un aumento de la incidencia de la diarrea porcina.

Primeramente se procedió a una revisión bibliográfica dedicada a la producción porcina en el contexto cubano y a la epidemiología de los principales

enteropatógenos causantes de diarrea en cerdos jóvenes en todo el mundo. También se discutió sobre la identificación diferencial de enteropatógenos y se introdujo el término epidemiológico ¨tipos mixtos¨ que se refiere a la etiología infecciosa combinada que la diarrea porcina puede presentar.

Posteriormente se condujo una actualización del conocimiento epidemiológico sobre la etiología infecciosa de la diarrea en cerdos jóvenes de Cuba a través de la identificación diferencial de enteropatógenos en cerdos recién nacidos, lactantes, y recién destetados. Este estudio epidemiológico identificó a *Escherichia coli* como un enteropatógeno común por lo que las investigaciones se enfocaron más en las infecciones por *E. coli*. En primer lugar se determinó la resistencia a los antibióticos y la relación genética de cepas cubanas de *E. coli* enteropatógenas. Posteriormente se evaluó la seroprevalencia de anticuerpos contra las fimbrias F4 y F18 de *E. coli*. Por último se analizó la susceptibilidad genética de los cerdos de Cuba para la colonización entérica por *E. coli* F4+ y F18+. A continuación se resumen más detalladamente los resultados de cada tarea científica:

1- Identificación diferencial de enteropatógenos porcinos.

Se llevó a cabo para obtener información sobre la etiología infecciosa de la diarrea porcina pre- y post-destete en la provincia de Villa Clara, Cuba. Fueron analizados contenidos intestinales de cerdos diarreicos por medio de cultivo, microscopía, y técnicas inmunológicas o basadas en el ADN. Por lo menos un enteropatógeno s e detectó en el 64.4% y en el 42.2% de los lechones lactantes y destetados, respectivamente. *E. coli* enterotoxigénica (ETEC) fue significativamente el patógeno más frecuente, y la mayoría de los virotipos fueron STa+/STb+ o F4+/STa+/STb+. La ocurrencia global del resto de los patógenos fue del 10% para el virus de la gastroenteritis transmisible y *Cryptosporidium parvum*, 6.7% para rotavirus A e *Isospora suis*, 5.6% para *Clostridium perfringens* α-toxigénico, 3.3% para *E. coli* verotoxigénica (VTEC), y 2.2% para *Salmonella enterica* subespecie *enterica* serovar Newport. El virus de la diarrea epidémica porcina, *C. perfringens* β-toxigénico, *Eimeria* spp., y helmintos no fueron identificados. Doce de los 48 lechones positivos a enteropatógenos (25%) estaban infectados con más de un patógeno y ETEC estuvo presente en 10 de las 12 infecciones mixtas. Estos resultados demuestran que varios enteropatógenos, solos o como parte de una infección mixta, están asociados con la diarrea porcina pre- y post-destete en la provincia de Villa Clara, Cuba. Dado que *E. coli* fue el enteropatógeno más frecuente, se estudió más detalladamente.

2- Resistencia a antibióticos y relatividad genética de E. coli enteropatogénicas.

Se determinó el perfil de resistencia a los antibióticos y la relación genética de *E. coli* patógenas aisladas de lechones que sufrían diarrea. Las mayores tasas de resistencia se mostraron ante antibióticos tradicionalmente administrados en granjas porcinas cubanas: tetraciclina (69%), ampicilina (54%), compuestos de la

sulfonamida (50%), y kanamicina (50%); además el 65% de los aislados fueron resistentes a múltiples antibióticos. El ERIC-PCR reveló un alto grado de polimorfismo en las secuencias de ADN de *E. coli* así como relación entre los aislados F4+/STa+/STb+ o F18+/LT+/STb+ detectados en granjas porcinas diferentes, y entre aislados STb+, STa+/STb+, F4+/STa+/STb+ o F18+/Stx2e+ procedentes de una misma cochiquera. *E. coli* patogénicas, genéticamente diversas o genéticamente relacionadas, así como altamente susceptibles al ácido nalidíxico, ciprofloxacina, gentamicina, amikacina, cloranfenicol, cefalosporinas, amoxicilina-ácido clavulánico y trimetoprim están asociadas con la diarrea de los lechones en la provincia de Villa Clara, Cuba. El análisis de la diversidad genética por medio de ERIC-PCR demostró relación clonal entre *E. coli* patógenas que portaban los mismos factores de virulencia y similar perfil de resistencia a los antibióticos. La implementación de los resultados de esta investigación epidemiológica en toda Cuba puede contribuir a la vigilancia, prevención y control de la colibacilosis porcina.

Teniendo en cuenta que los anticuerpos séricos específicos para F4 o F18 en los cerdos cubanos podrían reflejar la presencia y propagación de ETEC F4+ o ETEC/VTEC F18+, se procedió a la siguiente tarea científica.

***3- Seroprevalencia de anticuerpos contra las fimbrias F4 y F18 de* E. coli.**

Se determinó la prevalencia de anticuerpos específicos contra F4 y F18 en el suero de 1044 cerdas jóvenes. Para el análisis de datos se emplearon modelos de efectos aleatorios así como modelos de mezcla en R (paquete "mixAK"; Komárek, 2009). Niveles bajos, moderados y altos de anticuerpos específicos contra F4 se encontraron en el 67,6%, 26,8% y 5,6% de las cerdas, mientras que el 66,4% y 33,6% presentaron niveles bajos y altos de anticuerpos específicos contra F18, respectivamente. En este estudio se ha mostrado que *E. coli* F4+ y F18+ son muy frecuentes como enteropatógenos potenciales en cochiqueras cubanas.

4- Susceptibilidad genética de cerdos criados en Cuba a infecciones entéricas por* E. coli *fimbriada.

Dicha tarea se llevó a cabo para conocer en primer lugar la frecuencia de los genotipos y los alelos que determinan la susceptibilidad o resistencia a las infecciones por *E coli* F18+. Para investigar la susceptibilidad a infecciones por *E. coli* F4+ se determinó el polimorfismo *Xba*I del gen porcino *mucin 4* en cerdos criados en la provincia Villa Clara, Cuba. El genotipo resistente a la digestión por *Xba*I fue detectado frecuentemente (0,66), y los genotipos susceptibles heterocigoto u homocigoto fueron menos frecuentes (0,31 y 0,03, respectivamente). Dado que hemos encontrado una alta seroprevalencia de anticuerpos específicos contra F4 en suero de cerdas jóvenes en Cuba, el polimorfismo *Xba*I en el gen *mucin 4* no puede ser utilizado como marcador fiable para determinar la resistencia genética a infecciones por *E. coli* F4+. Los cerdos portadores del genotipo resistente a F18 no fueron encontrados con frecuencia

(0,13), mientras que los genotipos susceptibles homocigoto o heterocigoto ocurrieron con mayor frecuencia (0,27 y 0,60, respectivamente), coincidiendo con informes anteriores de una alta prevalencia de *E. coli* F18+ y de anticuerpos específicos contra F18 en el rebaño porcino de Cuba. Para el control de *E.coli* F18+ se podría considerar un mejoramiento genético de los cerdos teniendo en cuenta el genotipo resistente. Esta estrategia no se recomienda para F4.

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