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Effect of 10-valent pneumococcal conjugate vaccine on nasopharyngeal carriage of *Streptococcus pneumoniae* and *Haemophilus influenzae* among children in São Paulo, Brazil

Maria-Cristina de C. Brandileone[1], Rosemeire C. Zanella[1], Samanta C.G. Almeida[1], Angela P. Brandao[1,2], Ana F. Ribeiro[3], Telma-Regina M.P. Carvalhanas[4], Helena Sato[4], Ana-Lúcia Andrade[5], Jennifer R. Verani[6], Pneumococcal Carriage Study Group[1]

1. National Laboratory for Meningitis and Pneumococcal Infections, Center of Bacteriology, Institute Adolfo Lutz (IAL), São Paulo, Brazil

2. Oswaldo-Cruz Foundation, Rio de Janeiro, Brazil

3. Institute of Infectious Diseases Emilio Ribas, São Paulo, Brazil

4. Center of Epidemiologic Surveillance, Secretary of Health of the State of São Paulo, Brazil

5. Institute of Tropical Pathology and Public Health, Federal University of Goiás, Goiânia, Goias, Brazil

6. Respiratory Diseases Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA

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In March 2010, Brazil introduced the 10-valent pneumococcal conjugate vaccine (PCV10) in the routine infant immunization program using a 4-dose schedule and catch-up for children <23 months. We investigated PCV10 effect on nasopharyngeal carriage with vaccine-type *S. pneumoniae* (Spn) and non-typeable *H. influenzae* (NTHi) among children in São Paulo city. The baseline survey was performed in 2010, and the post-PCV10 survey in 2013. Healthy PCV-naïve children aged 12-23 months were recruited from primary health centers during immunization campaigns. We compared vaccine-type Spn and NTHi carriage prevalence pre-/post-PCV10 to estimate PCV10 effectiveness. Overall 501 children were included in the baseline and 1167 in the post-PCV10 survey. Spn was detected in 40.3% of children at baseline and 48.8% post-PCV10. PCV10 serotypes were found in 19.8% and 1.8% respectively, representing a decline of 90.9% ($p < 0.0001$). Carriage of vaccine-related serotypes increased (10.8-21.0%, $p < 0.0001$), driven primarily by a rise in serotype 6C (1.8-11.2%, $p < 0.0001$); carriage of serotypes 6A and 19A did not significantly change. PCV10 effectiveness (4 doses) against vaccine-type carriage was 97.3%. NTHi prevalence increased from 26.0 to 43.6% ($p < 0.0001$). Despite speculation that PCV10 might protect against colonization by NTHi, we observed a significant increase in NTHi carriage following PCV10 introduction and a significant association between PCV10 vaccination and carriage of NTHi. Carriage with PCV10 serotypes among toddlers declined dramatically following PCV10 introduction in São Paulo, Brazil. No protection of PCV10 against NTHi was observed. Despite these limitations, we show a clear impact of PCV10 on carriage of vaccine serotypes within 3 years after vaccine introduction. Our findings contribute to a growing body of evidence of PCV10 impact on vaccine-type carriage and highlight the importance of PCV10 as a tool to reduce the burden of pneumococcal disease in Brazil and globally.

En marzo de 2010 Brasil incorporó al calendario de inmunización infantil la vacuna antineumocócica conjugada 10-valente (PCV10), usando un esquema de 4 dosis y un *catch-up* en niños < 23 meses. Se investigó el efecto de PCV10 sobre la portación nasofaríngea de serotipos vacunales de *S. pneumoniae* (Spn) y *H. influenzae* no tipificables (NTHi) en niños de la ciudad de San Pablo. El estudio basal se realizó en 2010 y post-PCV10 en 2013. Se reclutaron niños sanos de 12 a 23 meses no vacunados con PCV que concurrían a los centros de salud primaria durante las campañas de inmunización. Se comparó la prevalencia de serotipos vacunales de Spn y portación de NTHi pre y post-PCV10, y se estimó la eficacia de la PCV10. En total, se incluyeron 501 niños en el estudio basal y 1.167 en el post-PCV10. Spn se detectó en el 40,3% de los niños en el estudio basal y 48,8% post-PCV10. Los serotipos presentes en la PCV10 se encontraron en 19,8% y 1,8% respectivamente, lo que representa un descenso del 90,9% (p <0,0001). La portación de serotipos vacunales aumentó (10,8-21,0%, p <0,0001), debido principalmente al aumento del serotipo 6C (1,8-11,2%, p <0,0001); La portación de los serotipos 6A y 19A no cambió significativamente. La eficacia de la PCV10 (4 dosis) contra la portación de serotipos vacunales fue del 97,3%.

La prevalencia de NTHi aumentó de 26,0 a 43,6% (p <0,0001). A pesar de la especulación de que PCV10 podría proteger contra la colonización por NTHi, observamos un aumento significativo en la portación de NTHi después de la introducción de PCV10 y una asociación significativa entre la vacunación con PCV10 y la portación de NTHi. La portación de serotipos PCV10 en niños pequeños disminuyó drásticamente después de la introducción de PCV10 en San Pablo, Brasil. No se observó protección contra NTHi con PCV10. Se observó un claro impacto de PCV10 en la portación de serotipos vacunales dentro de los 3 años posteriores a la introducción de la vacuna. Nuestros datos se suman a las pruebas que evidencian el impacto de PCV10 en la portación de serotipos vacunales y destacan la importancia de PCV10 como una herramienta para reducir la carga de la enfermedad neumocóccica en Brasil y en todo el mundo.

Molecular characterization of invasive *Streptococcus dysgalactiae* subsp. *equisimilis*. Multicenter study: Argentina 2011–2012.

Fernando Traverso [1,2,3], Alejandra Blanco[1], Pilar Villalón[4], Noelia Beratz[1], Juan Antonio Sáez Nieto[4], Horacio Lopardo[1], National Collaborative Group for the Study of Streptococci and Related Bacteria.

1. Servicio de Microbiología, Hospital de Pediatría Prof. Dr. Juan P Garrahan, Buenos Aires, Argentina

2. Nueva Clínica Chacabuco, Tandil, Buenos Aires, Argentina

3. Servicio de Neumotisiología, Tandil, Buenos Aires, Argentina

4. Centro Nacional de Microbiología ISCIII, Majadahonda, Madrid, Spain

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Streptococcus dysgalactiae subsp. *equisimilis* (SDSE) has virulence factors similar to those of *Streptococcus pyogenes*. Therefore, it causes pharyngitis and severe infections indistinguishable from those caused by the classic pathogen. The objectives of this study were: to know the prevalence of SDSE invasive infections in Argentina, to study the genetic diversity, to determine the presence of virulence genes, to study their antibiotic susceptibility and to detect antibiotic resistance genes. Twenty eight centers from 16 Argentinean cities participated in the study. Most of the SDSE isolates were obtained from blood (60.9%). The rest of the isolates were obtained from bone, joint fluid or soft tissue. Two adult patients died (8.7%). All isolates carried *speJ* and *ssa* genes. A total 11 different *emm* genes were identified and three types, *stG62647*, *stG840* and *stG653* were the most frequent *emm* types. Nineteen different PFGE patterns were detected. All isolates were susceptible to penicillin and levofloxacin, 6 (26.1%) showed resistance or reduced susceptibility to erythromycin [1 *mef*(A), 3 *erm*(TR), 1 *mef*(A) + *erm*(TR) and 1 *erm*(TR) + *erm*(B)] and 7 (30.4%) were resistant or exhibited reduced susceptibility to tetracycline [2 *tet*(M), 5 *tet*(M) + *tet*(O)]. The prevalence in Argentina was of at least 23 invasive infections by SDSE per year. A wide genetic diversity was observed. All isolates carried *speJ* and *ssa* genes. Similarly to other studies, macrolide resistance (26.1%) was mainly associated to the MLS_B phenotype.

Streptococcus dysgalactiae subsp. *equisimilis* (SDSE) posee factores de virulencia similares a *Streptococcus pyogenes* y, en consecuencia, produce faringitis e infecciones graves indistinguibles de las generadas por este patógeno clásico. Los objetivos del estudio fueron conocer la prevalencia de SDSE en infecciones invasivas en Argentina, estudiar su diversidad genética, determinar la presencia de genes de virulencia, ensayar su sensibilidad a los antibióticos y conocer los genes de resistencia. Participaron 28 centros de 16 ciudades argentinas. La mayoría de los aislamientos SDSE fueron obtenidos de sangre (60,9%). El resto de los aislamientos fue obtenido a partir de hueso, líquido articular o tejidos blandos. Se registraron 2 muertes en adultos (8,7%). Todos eran portadores de los genes *speJ* y *ssa*. Se identificaron 11 genes *emm* diferentes y los genotipos más frecuentes fueron *stG62647*, *stG653* y *stG840*. Por PFGE se detectaron 19 pulsotipos distintos. Todos los aislamientos fueron sensibles a penicilina y levofloxacina, 6 (26,1%) presentaron resistencia o sensibilidad disminuida a eritromicina (1 *mef*[A], 3 *erm*[TR], 1 *mef*[A] + *erm*[TR] y 1 *erm*[TR] + *erm*[B]) y 7 (30,4%) fueron resistentes o tuvieron sensibilidad disminuida a tetraciclina (2 *tet*[M], 5 *tet*[M] + *tet*[O]). La prevalencia anual en la Argentina fue de al menos 23 infecciones invasivas por SDSE y se observó una amplia diversidad genética. Todos los aislamientos presentaron los genes *ssa* y *speJ*. Como en otros estudios, la resistencia a macrólidos (26,1%) estuvo asociada, principalmente, al fenotipo MLS_B.

Multilevel population genetic analysis of VanA and VanB *Enterococcus faecium* causing nosocomial outbreaks in 27 countries (1986-2012).

Freitas AR[1,2], Tedim AP[2,3,4], Francia MV[5], Jensen LB[6], Novais C[1], Peixe L[1], Sánchez-Valenzuela A[2], Sundsfjord A[7,8,] Hegstad K[7,8], Werner G[9], Sadowy E[10], Hammerum AM[11], Garcia-Migura L[12], Willems RJ[13], Baquero F[2,3,4], Coque TM[14,3,4].

1. UCIBIO/REQUIMTE, Departamento de Ciências Biológicas, Laboratório de Microbiologia, Faculdade de Farmácia, Universidade do Porto, Porto, Portugal.

2. Servicio de Microbiología, Hospital Universitario Ramón y Cajal (IRYCIS), Madrid, Spain.

3. CIBER en Epidemiología y Salud Pública (CIBER-ESP), Madrid, Spain.

4. Unidad de Resistencia a Antibióticos y Virulencia Bacteriana (RYC-CSIC), Madrid, Spain.

5. Servicio de Microbiología, Hospital Universitario Marqués de Valdecilla (IDIVAL), Santander, Spain.

6. Division of Food Microbiology, National Food Institute, Danish Technical University, Copenhagen V, Denmark.

7. Research group for Host-microbe Interactions, Department of Medical Biology, Faculty of Health Science, UiT - The Arctic University of Norway, Tromsø, Norway.

8. Norwegian National Advisory Unit on Reference Centre for Detection of Antimicrobial Resistance, Department of Microbiology and Infection Control, University Hospital of North Norway, Tromsø, Norway.

9. Division of Nosocomial Pathogens and Antibiotic Resistance, Department of Infectious Diseases, Robert Koch Institute, Wernigerode Branch, Wernigerode, Germany.

10. National Medicines Institute, Warsaw, Poland.

11. Department of Microbiology and Infection Control, Statens Serum Institut, Copenhagen, Denmark.

12. Centre de Recerca en Sanitat Animal (CReSA), UAB-IRTA, Campus de la Universitat Autònoma de Barcelona, Barcelona, Spain.

13. Department of Medical Microbiology, University Medical Center Utrecht, Utrecht, The Netherlands.

14. Servicio de Microbiología, Hospital Universitario Ramón y Cajal (IRYCIS), Madrid, Spain mariateresa.coque@salud.madrid.org teresacoque@gmail.com.

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Vancomycin-resistant *Enterococcus faecium* (VREfm) have been increasingly reported since the 1980s. Despite the high number of published studies about VRE epidemiology, the dynamics and evolvability of these microorganisms are still not fully understood. A multilevel population genetic analysis of VREfm outbreak strains since 1986, representing the first comprehensive characterization of plasmid content in *E. faecium*, was performed to provide a detailed view of potential transmissible units. Using the medical subject heading (MeSH) terms "*Enterococcus faecium*", "diseases outbreaks" and "vancomycin resistance", the authors identified VREfm strains causing hospital outbreaks (1986-2012). In total, 53 VanA and 18 VanB isolates (27 countries, 5 continents) were analyzed and 82 vancomycin-susceptible *E. faecium* (VSEfm) were included for comparison. Clonal relatedness was established by PFGE and MLST. Characterization of *van* transposons (PCR mapping, RFLP, sequencing), plasmids (transfer, *Cla*I-RFLP, PCR typing of relaxases, replication-initiation proteins and toxin-antitoxin systems, hybridization, sequencing), bacteriocins and virulence determinants (PCR, hybridization, sequencing) was performed. The authors found that VREfm were mainly associated with major human lineages ST17, ST18 and ST78. VREfm and VSEfm harboured plasmids of different families able to yield mosaic elements. Tn*1546*-*van*A was mainly located on plasmids. The VanB2 type was predominant among chromosome and plasmids. Both, strains and plasmids, contributed to the spread and persistence of vancomycin resistance among *E. faecium*. This study showed the influence of both clonal lineages and plasmids in the spread and persistence of vancomycin resistance among *E. faecium*. Horizontal gene transfer events among genetic elements from different clonal lineages (same or different genera such as *Staphylococcus* or *Streptococcus*) result in chimeras with different stability and host range, complicating the surveillance of epidemic plasmids.

Desde la década del ´80 comenzaron a reportase aislamientos de *Enterococcus faecium* resistente a vancomicina (VREfm). A pesar del gran número de publicaciones sobre el tema, poco se conoce a cerca de la dinámica y evolución de este microorganismo. Los autores realizaron un análisis genético a nivel poblacional de los brotes de VREfm desde el año 1986 caracterizando el contenido plasmídico de las cepas. Usando el título "*Enterococcus faecium*", "diseases outbreaks" y "vancomycin resistance" para la búsqueda de bibliografía los autores identificaron cepas de VREfm que ocasionaron brotes hospitalarios en el período 1986-2012. Fueron analizados 53 aislamientos de VanA y 18 VanB provenientes de 27 países distribuidos en 5 continentes; se incluyeron como controles 82 *E. faecium* sensibles a vancomicina (VSEfm). Se estudió la relación clonal mediante PFGE y MLST. La caracterización de los transposones en los que está presente el gen *van* fue realizada por mapeo por PCR, RFLP y secuenciación. Además se caracterizaron los plásmidos (capacidad de transferencia, tipificación de las relaxasas, iniciación de la replicación, sistemas toxina-antitoxina, hibridación y secuenciación), las bacteriocinas y los genes determinantes de virulencia. Los autores encontraron que los VREfm están asociados con los linajes humanos incluidos en los secuenciotipos ST17, ST18 y ST78. Los VREfm y VSEfm poseen plásmidos de diferentes familias con estructura tipo mosaico. El transposón Tn*1546*-*van*A se encontró localizado principalmente en plásmidos, el tipo VanB2 se encontró tanto en el cromosoma como en el plásmido. De esta manera, los autores

demostraron que tanto las cepas como los plásmidos contribuyen a la diseminación y persistencia de la resistencia a vancomicina entre las cepas de *E. faecium*. La transferencia horizontal de genes entre elementos genéticos diferentes tanto de diferentes linajes como entre cepas de diferentes géneros (*Staphylococcus* o *Streptococcus*) resulta en quimeras con diferente estabilidad y rango de hospedador que complica el estudio epidemiológico de los plásmidos epidémicos.

We are reproducing here the letter sent by organizers of the next Lancefield Symposium:

SAVE THE DATE

"We are proud to announce that the 20th Lancefield International Symposium on Streptococci and Streptococcal Diseases will be held in Fiji from the 16th to 20th October 2017.

The 20th LISSSD will continue the tradition of linking laboratory excellence with high quality clinical and epidemiologic studies of streptococcal infections, but will bring a fresh and forward-looking approach with a focus on cutting-edge science, and on streptococcal disease in endemic regions. The 20th LISSSD will be held in the stunning location of the Sofitel Hotel on Denarau Island on the west coast of Fiji, providing a beautiful and relaxing setting to discuss research ideas and collaboration, and providing easy access to some of the most picturesque islands in the world.

Please visit the conference website to register your interest and be kept up-to-date with conference arrangements as they unfold.

We very much look forward to your participation in the 20th LISSSD in Fiji.

20th LISSSD Co-Chairs

Associate Professor Joseph Kado & Associate Professor Andrew Steer

20th LISSSD Vice Co-Chairs

Professor Mark Walker and Professor Pierre Smeesters

On behalf of the Organising and Scientific Committees"

Confirmed invited speakers

Emmanuelle Charpentier

Victor Nizet

Bongani Mayosi

Pre-register at http://lisssd2017.org

Sofitel Hotel, Nadi, Fiji

16-20th October, 2017

International flights direct to Nadi,
then 10 minute transfer to hotel

Pre-register at http://lisssd2017.org