OPEN ACCESS

ISSN: 2835-9496

Ken-ichi H, et al. (2024): 670
DOI: 10.47991/2835-9496/AJCMR-165

Short Communication

American Journal of Clinical and Medical Research

Newborn *Bifidobacterium* And Other Gut Microbiota Species Remain After 5-Day Oral Amoxicillin Administration

(**Running title:** Newborn *Bifidobacterium* post-amoxicillin)

Ken-ichi Honda, MD, PhD[1†*], Yasushi Kurihara, MD, PhD [2†], Takuma Wada, MD, PhD[2†], Ikushi Shimazaki, MD[3†], Yuko Hotta, MD, PhD[4‡], Makoto Enomoto, MD[5‡], Yuri Momose, MD[6], Takuji Imamura, MD, PhD[4], Kunihiko Doh, MD, PhD[1], Koji Kajitani, MD, PhD[7]

[1]Department of Obstetrics and Gynecology, PL Hospital, Tondabayashi, Japan
[2]Department of Obstetrics and Gynecology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan
[3]Department of Obstetrics and Gynecology, Kishiwada City Hospital, Kishiwada, Japan
[4]Department of Pediatrics, PL Hospital, Tondabayashi, Japan
[5]Enomoto Infant Clinic, Habikino, Japan
[6]Department of Pediatrics, Kashiwara Municipal Hospital, Kashiwara, Japan
[7]Department of Obstetrics and Gynecology, Kashiwara Municipal Hospital, Kashiwara, Japan
[†] Previous affiliation: Department of Obstetrics and Gynecology, Kashiwara Municipal Hospital
[‡] previous affiliation: Department of Pediatrics, Kashiwara Municipal Hospital

[*]**Corresponding author:** Ken-ichi Honda, MD, PhD, Department of Obstetrics and Gynecology, PL Hospital, Tondabayashi, Japan. Email: j21206v@omu.ac.jp

Citation: Ken-ichi H, Yasushi K, Takuma W, Ikushi S, Yuko H, et al. (2024) Newborn *Bifidobacterium* And Other Gut Microbiota Species Remain After 5-Day Oral Amoxicillin Administration. Ameri J Clin Med Re: AJCMR-165.

Received Date: 05 November, 2024; **Accepted Date:** 14 November, 2024; **Published Date:** 21 November, 2024

Abstract

Antibiotic infusion for mothers with a positive vaginal–rectal swab culture is essential to prohibit neonatal early-onset group B Streptococcus (GBS) infection. Antibiotics are also administered to the newborn if GBS is detected in newborn specimens. In our hospital, the oral antibiotic amoxicillin is routinely administered for newborns delivered from mothers with a positive result for GBS in a vaginal–rectal swab culture. Early-onset GBS disease has not been found in the past 15 years in our hospital, but there is concern that the development of newborn gut flora may be disturbed by oral amoxicillin administration. Therefore, in this study, we examined bacterial DNA in newborn feces. We found that the percentages of Bifidobacterium and other bacterial species in the gut microbiota were not decreased in the feces of newborns treated with oral amoxicillin administration for 5 days.

Keywords: *amoxicillin, Bifidobacterium, group B Streptococcus (GBS), gut microbiota.*

Introduction

The prevention of neonatal group B *Streptococcus* (GBS) infection in newborns is important in obstetric facilities [1]. In the neonatal gut, *Bifidobacterium* species play a role in development of the microbiome in an anaerobic status [2]. Species of bacteria in the newborn gut flora are considered to be mainly transferred from the mother's vaginal flora during vaginal delivery. A study of the effect of intrapartum antibiotic infusion in mothers with GBS showed that the percentage of *Bifidobacterium* species in newborn feces was lower than that in those without intrapartum antibiotic infusion at 7 days of age. However, this difference was not present when the newborns were 40 days of age [3]. Another study showed that some *Bifidobacterium* species have resistance to amoxicillin–clavulanic acid and proliferate again after a temporary decrease in their numbers [4]. One report on common bacterial species in the vagina and intestinal microbiome suggested that the rectum is a reservoir of the vaginal microbiota [5]. The current study aimed to evaluate the effects of 5-day oral amoxicillin administration to newborns delivered from mothers who were positive for vaginal GBS and received intrapartum cefazolin infusion,

Methods

From June to July 2018 and from June to July 2019, the newborns' mothers were admitted to Hospital K for full-term vaginal delivery. Seven mothers whose vaginal–rectal swab culture was positive for GBS at 35 weeks' gestation were administered intrapartum cefazolin infusion and their newborns were treated with oral amoxicillin (30 mg every 8 h) administration for 5 days. Eight mothers whose vaginal–rectal swab culture was negative for GBS did not receive intrapartum ampicillin infusion and their newborns were not treated with oral amoxicillin administration.

We isolated bacterial DNA using enzymatic digestion of the bacterial membrane [6]. Approximately 20 mg of newborn feces on a diaper was collected and treated with 100 mg of lysozyme in 285 µL of 10 mM Tris–1 mM EDTA buffer (pH 8.0) (TE buffer) at 37 C for 1 h. A total of 1000 units of achromopeptidase in 33 µL of TE buffer was then added and incubated for 30 min. DNA was isolated and analyzed using the Illumina Miseq platform (Illumina, Inc., San Diego, CA, USA) as described previously [7]. The composition of bacterial DNA in the feces of newborns who were not treated and those who were treated with oral amoxicillin administration for 5 days was compared by nonparametric methods using PASW statistics

software version (SPSS, Chicago, IL, USA). Furthermore, we examined the number of episodes of allergy or asthma in the medical records of the children who were treated with amoxicillin administration after birth and visited Hospital K at an age older than 2 years.

Results

There was broad individual diversity of bacterial DNA in newborn feces and no significance difference in the percentages of bacterial spieces between newborns treated with oral amoxicillin and untreated newborns. However, there appeared to be larger percentages of DNA from *Bifidobacterium*, *Bacteroides*, *Blautia*, *Coprococcus*, *Ruminococcus*, *Faecalibacterium*, and *Gemmiger* in feces from newborns treated with oral amoxicillin than in feces from newborns who were not treated with oral amoxicillin (Figure 1).

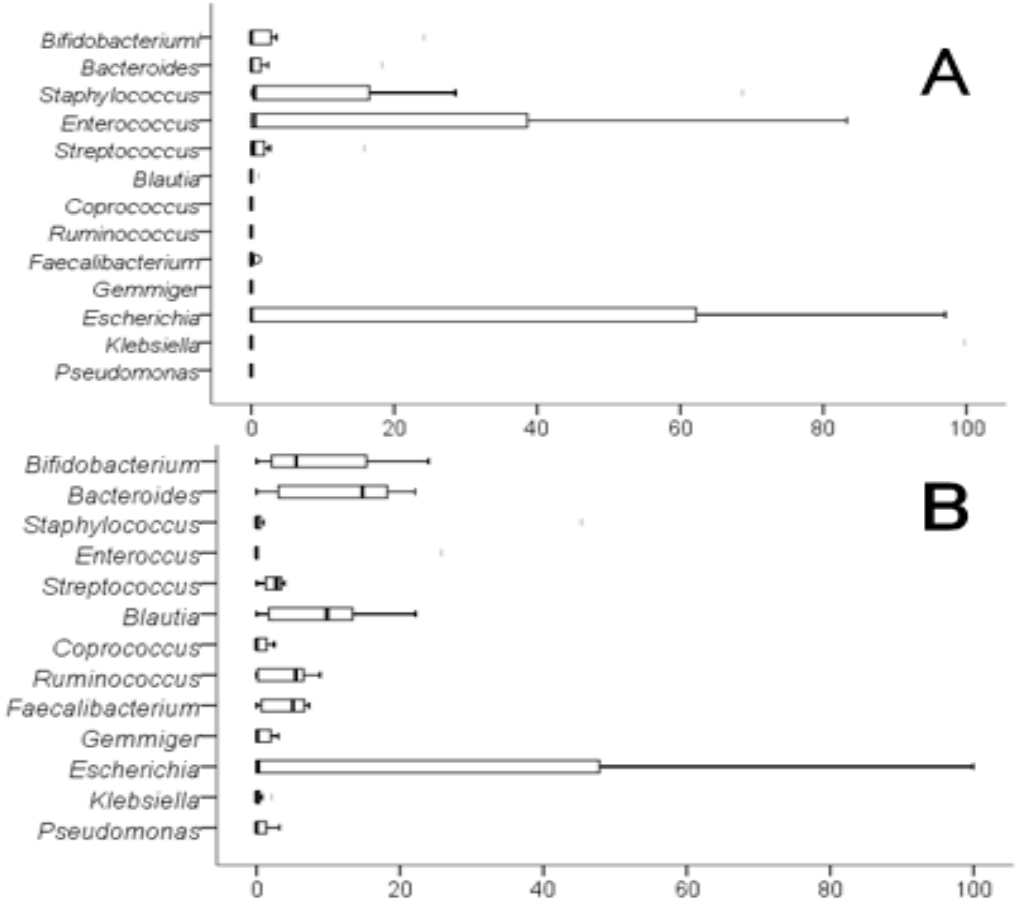

Figure 1: (A) Percentages of bacteria in feces of newborns who were not treated with oral amoxicillin for 5 days. (B) Percentages of bacteria in feces of newborns who were treated with oral amoxicillin for 5 days.

The mean (±standard deviation) percentages of some bacterial species in feces from treated newborns versus untreated newborns were as follows: *Bifidobacterium*, 10.96%±10.95% vs 3.71%±5.10%; *Bacteroides*, 11.36%±7.99% vs 2.63%±3.91%; *Blautia*, 8.89%±6.63% vs 0.14%±0.23%; *Coprococcus*, 0.92%±1.22% vs 0.00%±0.00%; *Ruminococcus*, 3.97%±3.31% vs 0.01%±0.02%; *Faecalibacterium*, 3.88%±2.93% vs 0.13%±0.17%; and *Gemmiger*, 1.03%±1.14% vs 0.03%±0.05%).

In contrast, the percentages of DNA from *Staphylococcus* and *Enterococcus* in feces from newborns treated with oral amoxicillin were lower than those from untreated newborns. The mean (±standard deviation) percentages of these bacterial species in feces from treated newborns versus untreated newborns were as follows: 6.62%±11.04% vs 12.93%±17.83% for *Staphylococcus* and 3.71%±6.23% vs 20.19%±26.33% for *Enterococcus*. The mean (±standard deviation) percentages of *Streptococcus*, *Escherichia*, and *Pseudomonas* in feces were similar in treated newborns versus untreated newborns as follows: *Streptococcus*, 2.82%±1.69% vs 2.54%±3.35%; *Escherichia*, 27.96%±39.824% vs 27.69%±34.59%; and *Pseudomonas*, 0.85%±0.97% vs 0.00%±0.00%.

From 2009 to 2014, 17,640 newborns were delivered in Hospital K. Among them, 302 newborns were treated with oral amoxicillin for 5 days because the mother had a positive result for GBS in a vaginal–rectal swab culture at 35 weeks' gestation. In these newborns, 156 attended the outpatient clinic of the hospital after 2 years of age. Among these, 10 children had an episode recorded as an allergic reaction or asthma in their medical record.

Discussion

In Hospital K, amoxicillin was routinely administered for 5 days in newborns who were delivered from mothers with a vaginal–rectal swab that was positive for GBS, because a timely examination by a pediatrician was not possible, and no early onset of GBS infection had occurred since 2009. In another Hospital P, only newborns whose mothers were not received ampicillin infusion more than two times because of a delivery time shorter than 4 h were treated with oral amoxicillin administration for 5 days. In Hospital P, one early-onset GBS infection occurred after a rapid delivery with no preparation time for antibiotic infusion for a positive vaginal–rectal cultured, but pediatricians observed the signs of infection of the newborn and early antibiotic infusion therapy resulted in a good prognosis.

Our finding that the percentages of *Bifidobacterium* and other species appeared to be higher in newborns who were treated with oral amoxicillin than in untreated newborns is considered to reflect a reduction in the percentage of bacterial species that are sensitive to amoxicillin. Additionally, other bacterial species in the gut microbiota, such as *Bacteroides*, *Blautia*, *Coprococcus*, *Ruminococcus*, *Faecalibacterium*, and *Gemmiger*, might have been insensitive to amoxicillin and showed a relative increase in their percentages.

Bifidobacterium has important roles in the intestines in newborns and infants. *Bifidobacteria longum*, which is an abundant species, metabolizes carbohydrates to short-chain fatty acids, acetate, and lactate, and the low pH caused by these metabolites protects the intestines [8]. Researchers showed *Bifidobacterium* have also important roles in the development of immune tolerance and allergic responses are protected by *Bifidobacterium breve* in intestinal microbiota well developed in breast-fed babies [9]. If *Bifidobacterium* species remain after 5 days of oral amoxicillin administration, allergic reactions may not be induced in the future.

Acknowledgements

We are grateful to Toshitaka Odamaki and Eri Mituyama of Next Generation Science institute, Morinaga Milk Industry Co., Ltd. for guidance and analysis of bacterial genes using the Illumina Miseq platform. We thank Ellen Knapp, PhD, from Edanz (https://jp.edanz.com/ac) for editing a draft of this manuscript.

Source of funding: This research was not supported by any grant.

References

1. Verani JR, McGee L, Schrag SJ Prevention of perinatal group B streptococcal disease: revised guidelines from CDC, 2010. MMWR Recomm Rep 2010; 59:1-36.
2. Faden H. Development of the anaerobic microbiome in the infant gut. Pediatr Infect Dis J 2023; 42: 620-5.
3. Corvaglia L, Tonti G, Martini S, Aceti A, Mazzola G, Aloisio I, *et al.* Influence of intrapartum antibiotic profilaxis for group B streptococcus on gut microbiota in the first month of life.J Pediatr Gastroenterol Nutr 2016; 62: 304-8.
4. Mancabell L, Mancino W, Lugli GA, Argentini C, Longhi G, Milani C *et al.* Amoxicillin-clavulanic acid resistance in the genus *Bifidobacterium*. Appl Environ Microbiol 2021; 87: e03137-20.
5. Fudaba M, Kamiya T, Tachibana D, Koyama M, Ohtani N. Bioinformatics analysis of oral, vaginal, and rectal microbial proifiles during pregnancy: A pilot study co-residence in pregnant women. Microorganisms 2021; 9: 1027.
6. Kim SW, Suda W, Kim S, Oshima K, Fukuda S, Ohno H *et al*. Robustness of gut microbiota of healthy adults in response to probiotic intervention revealed by high-throughput pyrosequencing. DNA Res 2013; 20: 2411-53.
7. Kato K, Ishida S, Tanaka M, Mitsuyama E, Xia J-Z, Odamaki T. Association between functional lactase variants and a high abundance of *Bifidobacterium* in the gut of healthy Japanese people. Plos One 2018; 13: e0206189.
8. Mills S, Yang B, Smith GJ, Stanton C, Ross RP. Efficiency of *Bifidobacterium longum* alone or in multi-strain probiotic formulations during early life and beyond. Gut Microbes 2023; 15: 218609.
9. Cukrowska B, Bieria JB, Zakrzewska M, Klukowski M, Maciorkowska E. The relationship between the infant gut microbiota and allergy. The role of *Bifidobacterium breve* and prebiotic oligosaccharides in the activation of anti-allergy mechanisms in early life. Nutrients 2020; 12: 946.