

Azithromycin to Prevent Sepsis or Death in Women Planning a Vaginal Birth

Alan T.N. Tita, M.D., Ph.D., et al.

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Lecture: Seminar; Comment student: Kuang-Ying Chen; Advisor: Dr. Hau-Ren Chen.
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1. 簡述論文的重大發現：

過去人們知道剖腹產時可以使用 azithromycin 抗生素降低母親感染機率。對於所有剖腹產孕婦預防性使用 azithromycin 抗生素降低整體的剖腹產成本。但是，對於自然產卻鮮少研究。

本研究發現足月自然產中使用 azithromycin 可以降低母親發生敗血症和死亡的機率，但是對於新生兒的敗血症和死亡機率沒有顯著貢獻。

2. 對論文內容的提問：

本研究的 primary outcome 數據把早產的數據排除，只算足月產。並且，這個排除條件並不在一開始的 study protocol 中，這樣是否會產生偏差？

3. 論文的缺點與評論：

每個地方的孕婦抗生素使用變化很大(Table S6)，本研究把它們合併在一起統計可能產生 ecological fallacy。¹另外，本研究未考慮預防性抗生素投藥後產生的抗藥性。

¹ Robinson, W.S. Ecological Correlations and the Behavior of Individuals. *American Sociological Review*. 1950, **15**: 351–357.

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A.T.N. Tita, W.A. Carlo, E.M. McClure, M. Mwenechanya, E. Chomba, J.J. Hemingway-Foday, A. Kavi, M.C. Metgud, S.S. Goudar, R. Derman, A. Lokangaka, A. Tshetu, M. Bauserman, C. Bose, P. Shivkumar, M. Waikar, A. Patel, P.L. Hibberd, P. Nyongesa, F. Esamai, O.A. Ekhuagere, S. Bucher, S. Jessani, S.S. Tikmani, S. Saleem, R.L. Goldenberg, S.M. Billah, R. Lennox, R. Haque, W. Petri, L. Figueroa, M. Mazariegos, N.F. Krebs, J.L. Moore, T.L. Nolen, and M. Koso-Thomas, for the A-PLUS Trial Group*

ABSTRACT

BACKGROUND

The use of azithromycin reduces maternal infection in women during unplanned cesarean delivery, but its effect on those with planned vaginal delivery is unknown. Data are needed on whether an intrapartum oral dose of azithromycin would reduce maternal and offspring sepsis or death.

METHODS

In this multicountry, placebo-controlled, randomized trial, we assigned women who were in labor at 28 weeks' gestation or more and who were planning a vaginal delivery to receive a single 2-g oral dose of azithromycin or placebo. The two primary outcomes were a composite of maternal sepsis or death and a composite of stillbirth or neonatal death or sepsis. During an interim analysis, the data and safety monitoring committee recommended stopping the trial for maternal benefit.

RESULTS

A total of 29,278 women underwent randomization. The incidence of maternal sepsis or death was lower in the azithromycin group than in the placebo group (1.6% vs. 2.4%), with a relative risk of 0.67 (95% confidence interval [CI], 0.56 to 0.79; $P < 0.001$), but the incidence of stillbirth or neonatal death or sepsis was similar (10.5% vs. 10.3%), with a relative risk of 1.02 (95% CI, 0.95 to 1.09; $P = 0.56$). The difference in the maternal primary outcome appeared to be driven mainly by the incidence of sepsis (1.5% in the azithromycin group and 2.3% in the placebo group), with a relative risk of 0.65 (95% CI, 0.55 to 0.77); the incidence of death from any cause was 0.1% in the two groups (relative risk, 1.23; 95% CI, 0.51 to 2.97). Neonatal sepsis occurred in 9.8% and 9.6% of the infants, respectively (relative risk, 1.03; 95% CI, 0.96 to 1.10). The incidence of stillbirth was 0.4% in the two groups (relative risk, 1.06; 95% CI, 0.74 to 1.53); neonatal death within 4 weeks after birth occurred in 1.5% in both groups (relative risk, 1.03; 95% CI, 0.86 to 1.24). Azithromycin was not associated with a higher incidence in adverse events.

CONCLUSIONS

Among women planning a vaginal delivery, a single oral dose of azithromycin resulted in a significantly lower risk of maternal sepsis or death than placebo but had little effect on newborn sepsis or death. (Funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development and others; A-PLUS ClinicalTrials.gov number, NCT03871491.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Tita can be contacted at atita@uab.edu or at the Center for Women's Reproductive Health, Department of Obstetrics and Gynecology, UAB Marix E. Heersink School of Medicine, University of Alabama at Birmingham, 1700 6th Ave. South, Birmingham, AL 35233.

*Members of the A-PLUS Trial Group are provided in the Supplementary Appendix, available at [NEJM.org](https://www.nejm.org).

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