Antibiotic treatment of Shiga toxin-producing *Escherichia coli* related gastroenteritis and the risk of hemolytic uremic syndrome: a population based matched case-control study in Japan

Shota Myojin[1], Kyongsun Pak[1], Mayumi Sako[1], Tohru Kobayashi[1], Takuri Takahashi[2], Tomimasa Sunagawa[2], Takashi Igarashi[1], Isao Miyairi[1]

[1] National Center for Child Health and Development, Tokyo, Japan [2] National Institute of Infectious Diseases, Tokyo, Japan

Background

The role of therapeutic intervention, particularly antibiotics, for Shiga toxin-producing *Escherichia coli* (STEC) related infection is controversial.

Methods

- A population based matched case-control study to assess the association between treatment (antibiotics, antidiarrheal agents and probiotics) for STEC related infections and hemolytic uremic syndrome (HUS) development.
- We identified all STEC HUS patients as cases and matched five non-HUS patients as controls using the data from the National Epidemiological Surveillance of Infectious Diseases (NESID) between January 1, 2017, and December 31, 2018.
- Further medical information was obtained by standardized questionnaires answered by physicians who registered each patient.
- We used multivariate conditional logistic regression model to evaluate the association between exposures (use of antibiotics, use of antidiarrheal agents, use of probiotics, by matched odds ratios (OR) and 95% confidence intervals (CI).
- Covariates we used were sex, age group, area code, presence of diarrhea and other factors. We also performed subgroup analyses using age (adults and children) as a stratification factor.

Results

Figure 1. Flow chart describing the enrollment of cases and controls

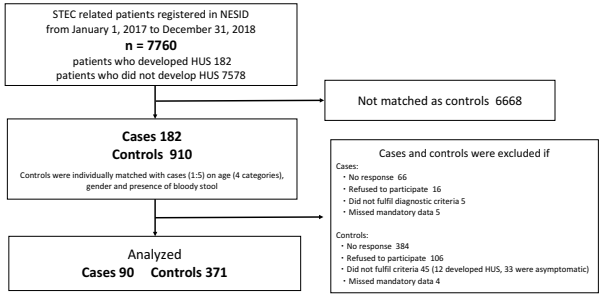

Table. Baseline characteristics of cases and controls in the analysis dataset

			Cases (n=90) No. /total No. (%)	Controls (n=371) No. /total No. (%)	p value
Symptoms					
	Vomiting		50/87 (57.5)	68/365 (18.6)	<0.001
	Diarrhea		85/89 (95.5)	355/370 (95.9)	0.772
	Abdominal pain		75/84 (89.3)	288/347 (83.0)	0.183
	Fever		69/88 (78.4)	140/365 (38.4)	<0.001
	Bloody stool		74/89 (83.1)	305/370 (82.4)	1
		Mild	12/61 (19.7)	107/278 (38.5)	0.005
		Moderate	25/61 (41.0)	134/278 (48.2)	0.325
		Severe	24/61 (39.3)	37/278 (13.3)	<0.001
STEC					
	Positivity of stool culture		54/90 (60.0)	363/367 (98.9)	<0.001
	Shiga toxin	Stx 1	23/62 (37.1)	246/367 (67.0)	<0.001
		Stx 2	44/62 (71.0)	210/367 (57.2)	0.05
		Type unknown	7/62 (11.3)	36/367 (9.8)	0.653
	Serotype	O157	65/79 (82.3)	216/365 (59.2)	<0.001
		O26	0/79 (0.0)	89/365 (24.4)	<0.001
		O103	2/79 (2.5)	13/365 (3.6)	1
		O111	1/79 (1.3)	15/365 (4.1)	0.325
		Others	11/79 (13.9)	32/365 (8.8)	0.205
	Anti-verotoxin antibody		34/36 (94.4)	23/30 (76.7)	0.068
Dialysis			27/85 (31.8)	-	-
Clinical outcome		Cured	72/85 (84.7)	354/357 (99.2)	<0.001
		Any complication	10/85 (11.8)	2/357 (0.6)	<0.001
		Encephalopathy	13/89 (14.6)	-	-
		Death	3/85 (3.5)	0/357 (0.0)	0.007

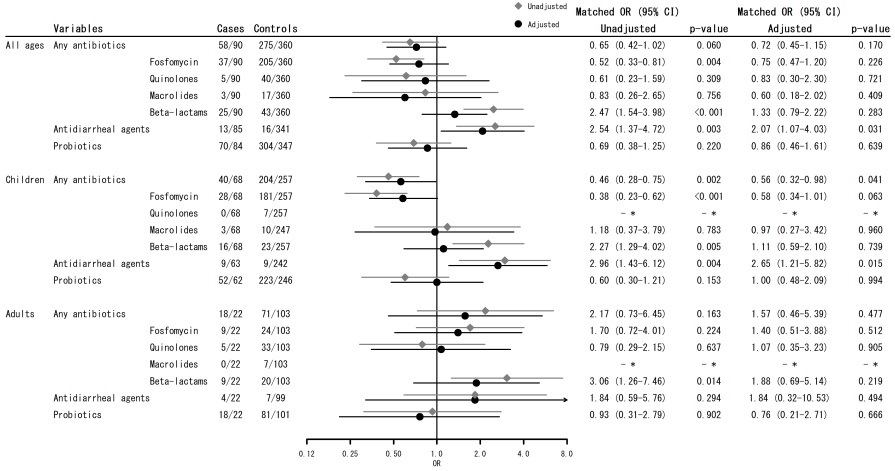

Figure 2. Conditional logistic regression analysis to evaluate the association between treatment and development of HUS

Conclusion

- Fosfomycin might decrease the risk of HUS in children younger than 15 years of age with STEC confirmed bacterial gastroenteritis.
- Antidiarrheal agents are clear risk factor of HUS regardless of ages.

Contact Address

National Center for Child Health and Development, 2-10-1,Setagaya, Tokyo 157-8535, Japan
Tel: +81-3-3416-0181,
Shota Myojin; myojin-s@ncchd.go.jp