Serostatus Following Polio-containing Vaccination Before and After Liver Transplantation

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Introduction

Polio is one of the most catastrophic infectious diseases in the world. Therefore, the strategy to eradicate polio is based on preventing infection by immunizing all children until the world is polio-free. However, data regarding effectiveness of polio-containing vaccination in immunocompromised patients, especially in those who received liver transplantation (LT) is limited.

Objective

The aims of this study are 1) to investigate the seropositivity rate after the completion of polio-containing vaccines in pediatric LT recipients,
2) to investigate the difference of seropositivity rate based on vaccination Schedule (OPV*2, OPV*1 + IPV or DPT-IPV*3, IPV or DPT-IPV*4) and timing of vaccination (pre-LT or post-LT)

Methods

- Design: an prospective cohort study (observational)
- Setting: the National Center for Child Health and Development (with the largest pediatric LT center in Japan)
- Study duration: from January 2011 to January 2015
- Inclusion criteria:
  1) Patients who received LT and completed the Japanese polio vaccination program
  2) Age <20 years old at the time of LT
- Exclusion criteria: 1) incomplete follow-up data
- Definitions
  - Completion of polio vaccination program:
    1) OPV ×2, 2) OPV ×1, (IPV or DPT-IPV) ×3
    3) (IPV or DPT-IPV) ×4
  - Antibody test: neutralizing test (NT): ≥4 (positive)

【National Immunization Program (Polio-containing vaccines) 】
- ～2012, August: OPV【twice】
- 2012, Septemb:er ～: IPV or DPT-IPV 【four times】

【Vaccine strain】
- OPV: trivalent (Sabin strain)
- IPV: trivalent (Salk strain) / DPT-IPV: trivalent (Sabin strain)

【statistical analysis】SPSS ver.21.0 (IBM inc., IL)
Fisher's exact test for categorical variables and Mann-Whitney's U test for continuous variables → logistic regression analysis

Results

- Sixty seven patients were enrolled in this study.
- Polio seropositivity of the LT recipients were as follows: 94% for type1, 91% type2, and 55% for type3.
- Serostatus pre and post LT was evaluated in 19 patients.
  【Type1: 100% (pre) → 84% (post), Type2: 100% (pre) → 89% (post), Type3: 79% (pre) → 53% (post)】
- Mean (±SD) follow-up period after LT was 46 ± 29.6 months.

Table 1. Patients' characteristics according to the poliovirus strain and the seropositivity (n=67)

Variables		Polio 1 (+) n=63	Polio 1 (−) n=4	P-value	Polio 2 (+) n=61	Polio 2 (−) n=6	P-value	Polio 3 (+) n=37	Polio 3 (−) n=30	P-value
Gender (female, %)		42 (67%)	2 (50%)	0.603	40 (66%)	4 (67%)	>0.999	23 (62%)	21 (70%)	0.608
Age (month) at sampling blood	median±SD, IQR	74±50.8, 70	74±7.6,14	0.909	75±51.5, 74	73±13.1, 26	0.906	52±43.9, 52	85±48.8, 57	*<0.001
Body weight (kg)	median±SD, IQR	18.4±11.0, 10.3	17.4±4.0, 7.6	0.390	18.4±11,1, 10.4	17.3±3.8, 7.8	0.189	16.5±7.8, 7.7	22.8±12.7, 10.0	*0.001
Underlying diseases (n)	Cholestatic disease	40 (63%)	2 (50%)	0.304	41 (67%)	1 (17%)	*0.010	28 (76%)	14 (46%)	*0.040
	Metabolic disease	10 (16%)	2 (50%)		4 (7%)	3 (50%)		4 (11%)	8 (27%)	
	Fulminant hepatic failure	6 (10%)	0 (0%)		9 (15%)	2 (33%)		1 (2%)	5 (17%)	
	others	7 (11%)	0 (0%)		7 (11%)	0 (0%)		4 (11%)	3 (10%)	
Type of vaccine	OPV only	33 (52%)	2 (50%)	>0.999	30 (49%)	5 (83%)	0.380	10 (27%)	25 (83%)	*<0.001
	OPV+IPV	8 (13%)	0 (0%)		8 (13%)	0 (0%)		6 (16%)	2 (7%)	
	IPV only	22 (35%)	2 (50%)		23 (38%)	1 (17%)		21 (57%)	3 (10%)	
Timing of vaccination	Pre-LT	34 (54%)	2 (50%)	0.636	32 (52%)	4 (67%)	0.853	13 (35%)	23 (77%)	*0.002
	Pre and Post LT	12 (19%)	0 (0%)		11 (18%)	1 (16%)		8 (22%)	4 (13%)	
	Post-LT	17 (27%)	2 (50%)		18 (30%)	1 (16%)		16 (43%)	3 (10%)	
Age at LT (month)	median±SD, IQR	19±43.2, 38	27±15.5, 28	0.769	21±43.6, 44	15±7.1, 13	0.485	10±45.5, 61	40±32.4, 14	*<0.001
Follow-up period after LT (month)	median±SD, IQR	43±30.6, 40	43±13.4, 25	0.808	41±30.9, 40	60±14.7, 25	0.189	41±31.6, 44	44±27.9, 32	0.835
Period after the latest polio containing vaccination (month)	median±SD, IQR	31±55.1, 75	13±26.0, 47	0.333	25±55.9, 79	31±32.5, 70	0.851	10±51.9, 65	69±46.2, 23	*<0.001
Number of IS	one	54 (86%)	4 (100%)	>0.999	53 (87%)	5 (83%)	0.365	32 (86%)	26 (86%)	>0.999
	two	4 (6%)	0 (0%)		3 (5%)	1 (17%)		2 (5%)	2 (7%)	
	three	5 (8%)	0 (0%)		5 (8%)	0 (0%)		3 (9%)	2 (7%)	
Tacrolimus trough level (ng/mL) (n=64)	<1.5	19 (30%)	3 (75%)	0.270	17 (29%)	5 (83%)	*0.038	13 (36%)	9 (32%)	0.502
	1.5-5.0	36 (57%)	1 (25%)		36 (62%)	1 (17%)		19 (53%)	18 (64%)	
	5.0<	5 (13%)	0 (0%)		5 (9%)	0 (0%)		4 (11%)	1 (4%)	
ALC (<1,000/μl [≥6y.o], <1,500/μl [<6y.o.]) (n=66)		2 (3%)	1 (25%)	0.174	2 (3%)	1 (17%)	0.252	1 (3%)	2 (7%)	0.587
Serum albumin(Alb)	<3.5g/dL	0 (0%)	1 (25%)	0.060	1 (2%)	0 (0%)	1.000	0 (0%)	1 (3%)	0.448
SEROPOSITIVITY		**94%**			**91%**			**55%**		

Table 2. Logistic regression analysis for investigating factors associated with polio seropositivity

* statistically significant (p <0.05)

Covariates	Polio 2 positivity			Polio 3 positivity		
	Coefficient ± SE	P-value	OR (95%CI)	Coefficient ± SE	P-value	OR (95%CI)
ALC (<1,000/μl [≥6y.o], <1,500/μl [<6y.o.])	2.384 ± 2.184	0.262	10.8 (0.2-696.5)	1.226 ± 1.363	0.368	3.4 (0.2-49.2)
Underlying diseases (category)	-0.686 ± 0.584	0.240	0.5 (0.2-1.6)	-0.134 ± 0.316	0.672	0.9 (0.5-1.6)
Tacrolimus trough level	3.039 ± 1.434	*0.034	20.9 (1.3-346.9)	-	-	-
Body weight (kg)	0.367 ± 0.174	*0.035	0.9 (0.9-1.0)	-0.023 ± 0.061	0.699	1.0 (0.9-1.1)
Follow-up period after LT (month)	-0.053 ± 0.036	0.148	1.4 (1.0-2.0)	-	-	-
Period after the latest vaccination (month)	-	-	-	-0.005 ± 0.015	0.735	1.0 (1.0-1.0)
Timing of vaccination (pre, post, combined)	-	-	-	-0.297 ± 0.636	0.640	0.7 (0.2-2.6)
Type of vaccination (live, inactivated, mixed)	-	-	-	1.307 ± 0.788	0.097	3.7 (0.8-17.3)
Age at LT (month)	-	-	-	-0.010 ± 0.013	0.446	1.0 (1.0-1.0)

- In LT recipients, antibody titers against poliovirus appeared to wane within a relatively short period of time.
- Higher body weight was independently associated with seropositivity. Unexpectedly, high trough level was also associated with seropositivity, although not biologically plausible.
- Patients who received oral polio vaccination tended to have lower type3 seropositivity compared with IPV.

Conclusions

Seropositivity against poliovirus 3 was particularly low compared to other serotypes after LT. Additional inactivated polio-containing vaccination may be needed after LT.