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Adverse Events Following Live Immunization in Patients with DiGeorge Syndrome: A Retrospective, Single Center Study in Korea

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Background

- ✓ DiGeorge syndrome (DGS) is a syndrome accompanied by congenital heart defect, hypoparathyroidism and varying degree of immunodeficiency.
- ✓ Live vaccination is generally contraindicated in patients with DGS.
- ✓ However, in real clinical practice, there are cases in which live vaccines are immunized before the diagnosis of DGS or are incidentally immunized.

Objectives

- ✓ We aim to investigate adverse events following live immunizations (AEFLI), especially infections caused by the vaccine strains in DGS.

Methods

- ✓ Study period: November 2005 – July 2021
- ✓ Study subjects : DGS patients (extracted using International Classification of Disease-10 code from the Severance Clinical Research Analysis Portal)
- ✓ Exclusion: patents without genetic confirmation of 22q11.2 deletion
- ✓ Medical data and laboratory findings: chart review.
- ✓ The subjects were categorized into three groups:
  (1) group A [CD3 < 500 or CD8 < 200 T cells/mm3] contraindicated for live vaccination
  (2) group B [CD3 ≥ 500 and CD8 ≥ 200 T cells/mm3] recommended for MMR and VAR vaccinations
  (3) group C for unknown immunity status
- ✓ Five live vaccines were included (BCG, rotavirus, MMR, VAR and LJEV).
- ✓ For investigating AEFLI, we reviewed the outpatient department and emergency room visits, hospitalizations, and medical records within 60 days (12 months for BCG) from the date of live vaccination.
- ✓ For causality assessment, AEFLI cases were analyzed. (1999 WHO classification and 2018 WHO causality classification)

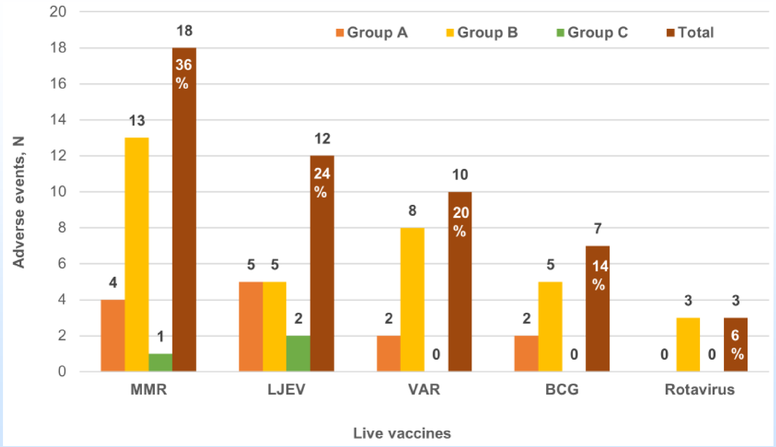
Results

Live immunization coverage in the study subjects

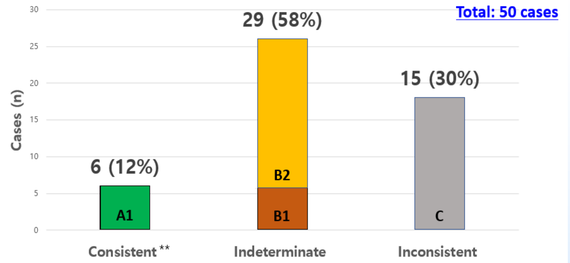
	Group A (n = 8)[a]		Group B (n = 30)[b]		Group C (n = 56)[c]		Total (n = 94)	
	N (%)	Vaccine doses (N)	N (%)	Vaccine doses (N)	N (%)	Vaccine doses (N)	N (%)	Vaccine doses (N)
BCG	4 (50)	4	18 (60)	18	23 (41)	23	45 (48)	45
Rotavirus	1 (13)	2	11 (37)	25	11 (20)	26	23 (24)	53
MMR	5 (63)	10	22 (73)	32	39 (70)	59	66 (70)	101
VAR	5 (63)	7	19 (63)	20	23 (41)	26	47 (50)	53
LJEV	3 (38)	6	9 (30)	17	6 (11)	11	18 (19)	34
Total[d]	6 (75)	29	24 (80)	112	43 (77)	145	73 (78)	286

Abbreviations: BCG, Bacillus Calmette–Guérin; MMR, measles-mumps-rubella; VAR, live attenuated varicella; LJEV, live attenuated Japanese encephalitis virus
[a]Patients with moderated T cell deficiency, CD3 < 500 or CD8 < 200 cells/mm3.
[b]Patients with mild to normal T cell deficiency, CD3 ≥ 500 and CD8 ≥ 200 cells/mm3.
[c]Patients without lymphocyte subset results.
[d]The number of patients who received at least one live immunization in each group.

Adverse events following live immunization (AEFLI)



Causality assessment using WHO 2018 algorithm



**Consistent: Fever 5 (LJEV 3, MMR1, varicella 1), injection site pus: 1 (BCG)

- ✓ A1: vaccine product-related reaction
- ✓ B1: temporal relationship is consistent but there is insufficient definitive evidence for vaccine causing event
- ✓ B2: qualifying factors result in conflicting trends of consistency and inconsistency with causal association to immunization
- ✓ C: coincidental

Summary of Results

- ✓ 146 were identified and among them, 94 patients with confirmed 22q11.2 deletion were selected as the study subjects.
- ✓ CD3 and CD8 T cell counts were available for approximately 40% (38/94) patients (8 [21%] and 30 [69%] belonged to group A and B, respectively).
- ✓ Of the 94 subjects, approximately 80% (73/94) received at least one live vaccination; MMR (70%, 66/94), VAR (50%, 47/94), BCG (48%, 45/94), rotavirus (24%, 23/94), and LJEV (19%, 18/94).
- ✓ Among 73 live vaccine recipients, 17 showed a total of 50 AEFLI.
- ✓ 50 AEFLI: fever (n = 29), upper respiratory infection (n = 9), diarrhea (n = 4), rash (n = 3), thrombocytopenia (n = 3), injection site pus (n = 1), and febrile convulsion (n = 1).
- ✓ In groups A and B, 13 (LJEV, 5; MMR, 4; VAR, 2; BCG, 2) and 34 (MMR, 13; VAR, 8; BCG, 5; LJEV, 5; rotavirus, 3) AEFLIs occurred after 29 and 112 live vaccine doses, respectively, with no significant difference in the incidence of AEs between groups A and B (45% vs. 30%, P = 0.14).

Conclusion

- ✓ Our data indicated that live immunizations are well-tolerated by patients with partial DGS in Korea.
- ✓ We emphasized that immune screening test should be encouraged before all live vaccinations in patients with DGS.
- ✓ Furthermore, this study of the safety of live vaccine immunization may contribute to alleviating vaccine hesitation and facilitating greater coverage among patients with immunodeficiency.
- ✓ Multicenter, prospective, large-scale studies are required to validate our findings and provide guidance for live immunizations in patients with DGS.