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Post vaccination febrile seizures: clinical severity and long-term developmental outcome data

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Introduction

- Febrile seizures (FS) are the most common type of childhood seizures.
- FS occurs in 3-5% children aged between 6 months and 6 years.¹
- Most children with a history of FS have normal behaviour, intelligence and academic achievement, and do not later develop epilepsy.^{2,3}
- FS associated with a vaccination can decrease parent and provider confidence in vaccine safety.
- There is little data comparing seizure severity of FS following vaccination to FS due to other causes.
- There is no data on developmental outcomes of children following vaccine proximate FS.

Aims

- To determine whether seizure severity of vaccine-proximate FS (VP-FS) differ from non-vaccine-proximate FS (NVP-FS).
- To determine whether long-term developmental outcomes differ between VP-FS, NVP-FS or healthy controls with no history of seizures.

Methods

- Prospective recruitment of children aged 6 years and under with first FS presentation to an Australian paediatric hospital (n = 5) from May 2013 – June 2014.
- Clinical features, management and outcome data obtained from parent interview and medical record reviews.
- Clinical outcomes compared between:
 - Vaccine proximate FS (VP-FS)
 - 0-2 days post inactivated vaccine
 - 5-14 days post live vaccine
 - 0-14 days post live and inactivated
 - Non-vaccine proximate FS (NVP-FS)
 - FS outside of abovementioned period
- Bayley-III developmental assessment performed on subset of children 12-24 months post initial FS.
- Developmental outcomes of NVP-FS and VP-FS cases was compared to healthy controls of similar ages with no history of seizures.

Figure 1: Patient enrolment

Results

- Of FS cases, 6.6% (68/1095) were VP-FS.
- VP-FS cases were younger than NVP-FS cases (13 vs 20 months, $p < 0.001$).
- 82% (56/68) of VP-FS cases were associated with measles containing vaccine.
- Developmental assessments were conducted on average 14.7 months (SD 2.1) for VP-FS and 16.7 months (SD 2.6) for NVP-FS post initial FS.

Figure 2: Timing of first FS following vaccination by type of vaccine

Table 1: Bayley-III assessment mean (SD) scores for VP-FS, NVP-FS and control groups

Bayley-III	Control (n = 85) Mean (SD)	NVP-FS (n = 70) Mean (SD)	VP-FS (n = 62) Mean (SD)	p
Cognitive	105.18 (8.32)	101.21 (11.62)	101.72 (9.95)	0.12
Language	107.31 (10.93)	104.56 (17.32)	104.25 (14.41)	0.82
Motor	109.14 (12.19)	102.86 (15.61)	104.16 (13.05)	0.05
Social-emotional ^a	108.17 (14.20)	108.17 (18.12)	104.25 (16.5)	0.45
General-adaptive ^a	101.11 (15.12)	99.51 (17.38)	100.96 (14.57)	0.44

Differences analysed by ANCOVA with maternal years of education as covariate. Composite scale score and standard score mean (SD) = 100(15) with lower scores indicating impairment.

^an = 82 controls, n = 63 NVP-FS, n = 52 VP-FS

Table 2: Seizure severity and risk estimates for each severity indicator comparing those with VP-FS versus NVP-FS.

	NVP-FS (n = 1027) n (%)	VP-FS (n = 68) n (%)	aOR* (95% CI)	p
Admission details				
Length of stay > 1 day	149 (14.5%)	13 (19.1%)	1.37 (0.72-2.63)	0.34
ICU admission	24 (2.3%)	1 (1.5%)	0.64 (0.08-4.90)	0.67
Death	1 (0.1%)	0 (0.0%)	NA	0.98
Seizure details				
Duration > 15 min	121 (11.8%)	11 (16.2%)	1.40 (0.70-2.79)	0.34
Repeat seizures within 24h	107 (10.4%)	6 (8.8%)	0.71 (0.30-1.70)	0.44
Antiepileptic use				
On presentation	92 (9.0%)	10 (14.7%)	1.92 (0.93-3.96)	0.08
On discharge	44 (4.3%)	3 (4.4%)	1.63 (1.47-5.64)	0.44
Readmission with FS				
Within 7 days	11 (0.1%)	0 (0.0%)	NA	0.99

ICU = intensive care unit

*Multivariate analysis adjusted for age group (<12, 12-24, 24-36, ≥36 months), gender, history of previous afebrile seizure

Conclusion

- No difference in clinical outcomes of VP-FS compared to NVP-FS.
- Most VP-FS were < 15 minutes duration, no antiepileptics required, with length of stay less than 1 day.
- VP-FS cases had comparable developmental outcomes at follow up to NVP-FS and healthy controls.

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