Post vaccination febrile seizures: Clinical severity and outcome data is reassuring

Dr Lucy Deng

On behalf of Kristine Macartney, Nigel Crawford, Jim Buttery, Michael Gold, Peter Richmond and Nicholas Wood and the PAEDS Investigator Group
Outline

- Background on febrile seizures
- Study aims and methods
- Findings and discussions
- Conclusions and future direction
Background: Febrile seizures (FS)

- Caused by sudden change in one’s body temperature

- Most common type of seizure in childhood
  - 1 in 30 children
  - 6 months and 6 years of age
  - Peak incidence in the second year of life
  - 30% will have a second episode

- No known long term neurological effect
Background: Post-vaccination febrile seizures (PVFS)

- Associated with
  - Whole cell pertussis vaccine
  - Measles containing vaccine
  - Trivalent influenza vaccine

- Decrease parent and provider confidence on vaccine safety
Clinical question

- Child presents with FS following 12 month old MMR vaccine
  - Is this child’s FS any different to a FS due to another cause (i.e respiratory illness)?
  - Will they have another FS with subsequent vaccinations?
Aims

- Describe the epidemiological profile of children with post-vaccination FS (PVFS) and non-PVFS
- Describe the clinical severity and outcomes of PVFS and non-PVFS cases
- Describe the recurrence rates of FS
Methods: Participant recruitment

- 1 May 2013 to 30 June 2014
- Children < 6 years
- Presenting with their *first FS* at PAEDS sites
  - Children’s Hospital at Westmead, Sydney
  - Royal Children’s Hospital, Melbourne
  - Princess Margaret Hospital, Perth
  - Women’s and Children’s Hospital, Adelaide
  - Lady Cilento Children’s Hospital, Brisbane
Methods: Case definition

- PVFS
  - Seizure, associated with fever documented either by a parent and/or health provider, occurring within 14 days of any vaccine

- Non-PVFS
  - Febrile seizure outside the abovementioned period following vaccination
Methods: Data collection

- Medical and vaccination history
- Clinical features on presentation/admission
- Investigations
- Management
- Clinical outcome
Results: Study population

- FS cases: 1735
- First FS in study period: 1504
- First ever FS: 1095
  - 1011 Non-PVFS
  - 84 PVFS
- 231 cases of repeat FS
- 409 patients with history of previous FS
## Results: Participant details

<table>
<thead>
<tr>
<th></th>
<th>Non-PVFS (%)</th>
<th>PVFS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>1011</td>
<td>84</td>
</tr>
<tr>
<td>Age (months)</td>
<td>20.5 (14.2-28.9)</td>
<td>13.4 (12.4-18.3)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>549 (54.3%)</td>
<td>38 (45.2%)</td>
</tr>
<tr>
<td>Indigenous</td>
<td>29 (2.9%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Birthweight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1500g</td>
<td>16 (1.6%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>1500-2000g</td>
<td>50 (4.9%)</td>
<td>3 (3.6%)</td>
</tr>
<tr>
<td>2500-4000g</td>
<td>709 (70.1%)</td>
<td>68 (81.0%)</td>
</tr>
<tr>
<td>&gt;4000g</td>
<td>98 (9.7%)</td>
<td>9 (10.7%)</td>
</tr>
<tr>
<td>Gestation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;28 weeks</td>
<td>7 (0.7%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>28-31 weeks</td>
<td>5 (0.5%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>32-36 weeks</td>
<td>78 (7.7%)</td>
<td>4 (4.8%)</td>
</tr>
<tr>
<td>&gt;36 weeks</td>
<td>860 (85.1%)</td>
<td>78 (92.9%)</td>
</tr>
</tbody>
</table>
Results: Participant medical history

- Previous afebrile seizure: 4.5% with p=0.04
- Previous meningitis: 0.0%
- Neurological condition: 2.0%
- Chronic medical condition: 13.0%
- fHx FS: 38.1%
- fHx epilepsy: 17.0%
Results: Clinical features

- Respiratory symptoms: 60% of participants
- Abdominal pain: 20% of participants
- Diarrhoea: 10% of participants
- Vomiting: 5% of participants
- Irritability/lethargy: 3% of participants
- Rash: 2% of participants
- Headache: 1% of participants

Biological cause found:
- 14.8% Non-PVFS
- 15.5% PVFS

PAEDS Paediatric Active Enhanced Disease Surveillance
Results: Seizure severity and outcome

<table>
<thead>
<tr>
<th></th>
<th>Non-PVFS (%)</th>
<th>PVFS (%)</th>
<th>Unadjusted OR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>1011</td>
<td>84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizure duration &gt; 15 minutes</td>
<td>264 (26.1%)</td>
<td>25 (29.8%)</td>
<td>1.14 (0.70-1.86)</td>
<td>0.6</td>
</tr>
<tr>
<td>Repeat seizure within 24h admission</td>
<td>105 (10.4%)</td>
<td>8 (9.5%)</td>
<td>0.89 (0.41-1.84)</td>
<td>0.7</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During admission</td>
<td>92 (9.1%)</td>
<td>11 (13.1%)</td>
<td>1.51 (0.77-2.93)</td>
<td>0.23</td>
</tr>
<tr>
<td>On discharge</td>
<td>44 (4.4%)</td>
<td>3 (3.6%)</td>
<td>0.81 (0.25-2.68)</td>
<td>0.74</td>
</tr>
<tr>
<td>Length of stay &gt;1 day</td>
<td>146 (14.4%)</td>
<td>16 (19.0%)</td>
<td>1.40 (0.79-2.47)</td>
<td>0.25</td>
</tr>
<tr>
<td>ICU admission</td>
<td>23 (2.3%)</td>
<td>2 (2.4%)</td>
<td>1.01 (0.26-4.38)</td>
<td>0.99</td>
</tr>
<tr>
<td>Death</td>
<td>1 (0.1%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Readmission within 48h with FS</td>
<td>10 (1.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NO difference in severity or outcome
## Results: Vaccines involved

<table>
<thead>
<tr>
<th>PVFS</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>84</td>
</tr>
<tr>
<td>PVFS following inactivate vaccine only</td>
<td>12 (14.3%)</td>
</tr>
<tr>
<td>PVFS following live vaccine</td>
<td>72 (85.7%)</td>
</tr>
</tbody>
</table>

### Live vaccine involved

<table>
<thead>
<tr>
<th>Live vaccine involved</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMR</td>
<td>44 (61.1%)</td>
</tr>
<tr>
<td>MMRV</td>
<td>18 (25%)</td>
</tr>
<tr>
<td>Varicella</td>
<td>2 (2.8%)</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>8 (11.1%)</td>
</tr>
</tbody>
</table>
Results: Timing of PVFS by vaccine type

- Inactivated only
- Live only
- Combination

12 mo MMR + Hib-MenC
Results: PVFS by age and biological cause found

Children aged < 10 months (n=10)

- 6wks, 4mo, 6mo: Hep B, DTPa, HiB, IPV, 13vPCV
- 6wks, 4mo: + Rotavirus

Children > 10 months (n=74)

- 12mo: MMR + Hib-MenC
- 18mo: MMR + V / MMRV
- 4yo: DTPa-IPV

Biological cause found

Biological cause not found
Conclusions

- PVFS account for small proportion of first FS presenting to hospitals in Australia
- No difference in clinical severity or outcomes between PVFS and non-PVFS
- Majority of PVFS are simple FS requiring hospital stay 1 day or less, with no medications required
- Majority of PVFS are associated with a live-attenuated vaccine
Discussion

- **Strengths**
  - PAEDS network
    - Active surveillance
    - Prospective case ascertainment
  - Detailed clinical data

- **Challenges**
  - Short study period
    - Recurrence rates difficult to determine
  - Limited to paediatric hospitals only
Future studies

- Recurrence rates of FS following PVFS
- Genetic markers
- Developmental outcomes
PAEDS
Paediatric Active Enhanced Disease Surveillance