Background

- Neonatal enteroviral (EV) necrotising encephalopathy (NES) is a severe enterovirus (EV) infection in the neonate that may manifest with serious complications such as hepatic necrosis, coagulopathy, and myocarditis. Among neonates with EV-infection, and hepatic necrosis, coagulopathy and/or myocardial involvement, case-fatality rates between 0 to 83% have been reported. 1-3
- Currently no U.S. Food and Drug Administration (FDA) approved drug product exists for the treatment of NES, although reports on investigational new drugs for NES treatment.
- Limited data are available regarding the epidemiology of NES. FDA required observational data on NES prevalence and mortality rates to inform the design of future clinical trials to evaluate investigational new drugs for NES treatment.

Objective

To describe NES prevalence and mortality rates among hospitalized neonates in the U.S. FDA Sentinel System.

Methods

Population

- Potential NES cases were identified using Sentinel inpatient EHR data from 7/1/2012 – 3/31/2016
- Patients aged <60 days on admission were considered eligible for inclusion. This included neonates aged 0-30 days and older infants aged 31-60 days

NES case definition criteria

- Laboratory confirmation of EV infection was not available
- Potential NES cases were identified using a combination of diagnostic code-based cases denoting sepsis and EV-infection, as well as hepatic necrosis, coagulopathy and myocarditis
- Case definition criteria were constructed based on combinations codes for EV-infection, sepsis, and one or more of the organ dysfunctions to satisfy the NES case definition criteria (Table 1 & 2).

Exclusion criterion

- Potential NES cases with greater than 2 administration dates of antibacterial, antiviral, or antifungal therapy allowing a gap of 1 day after the first administration date, identified from the inpatient pharmacy table, were excluded
- Neonates hospitalized with suspected sepsis typically receive broad antimicrobial treatments such as the aforementioned therapies. Once bacterial, fungal or herpetic infection are excluded, or if EV-infection is diagnosed, these agents are normally discontinued

Patient characteristics

- Patient demographics: age in days, sex
- Hospitalization characteristics: admission year, length of stay, discharge disposition, receipt of therapy (IVIG)

Results

- Among all eligible hospitalizations of neonates in 119 facilities during the study period (n=842,260), 10 patients with EV-infection and sepsis were identified and of these, 7 met the stricter NES case definition criteria. Of the 7, 3 presented with EV-infection, sepsis, and coagulopathy, and 2 had EV-infection sepsis, coagulopathy, and myocarditis (Table 1 & 2).
- NES prevalence was 0.83 per 100,000 neonate inpatient stays.
- At admission, the majority (86%) of the patients with NES were <30 days old (Table 2).
- EV-infected patients with organ dysfunction had longer length of stay (LOS) (median LOS 91 days, range 46-347 days, depending on specific organ dysfunction) compared to those without organ dysfunction (median LOS 3 days, range 3-11 days).
- One NES patient received IVIG therapy (Table 2).
- No in-hospital deaths were observed among NES cases.

Table 1. Number of cases that meet each case definition level 1-8

<table>
<thead>
<tr>
<th>Case definition criteria</th>
<th>Sepsis</th>
<th>EV</th>
<th>Coagulopathy</th>
<th>Hepatic Necrosis</th>
<th>Myocarditis</th>
<th>No. of cases identified</th>
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</thead>
<tbody>
<tr>
<td>(Most strict)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
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<tr>
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<td>X</td>
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<td>X</td>
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<td>1</td>
</tr>
<tr>
<td>8 (Least strict)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>3</td>
</tr>
</tbody>
</table>

Conclusions

- NES, identified using diagnosis code based criteria, was rare among hospitalized neonates in this preliminary analysis, and no cases resulted in death.
- This was the first study to examine NES prevalence using inpatient data from the Sentinel System. Future work might include validation of potential NES cases with medical record review. Additional data are needed to characterize factors that might impact clinical outcomes among patients with NES to inform the design of future clinical trials.

Acknowledgements/Disclosure

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References