Detection of Enterovirus and Parechovirus in Plasma Specimens of Pediatric Patients in Chicago

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Updated Abstract

Human Enteroviruses (EV) and Parechoviruses (HPeVs) are well known causes of meningitis and other serious infections in young children. The typical presentation of children infected with these viruses can involve fever, irritability, non-specific rash, vomiting, diarrhea, congestions, tachycardia, or sepsis-like symptoms. Data involving detection of these pathogens in plasma is limited.

The aims of this study therefore were to examine the prevalence and clinical characteristics of EV and HPeV infections in plasma specimens of patients <2 months of age in the U.S. from September to November of 2015 using different PCR platforms.

Methods

As a proof of concept, 10 plasma specimens were collected from patients whose cerebrospinal fluid (CSF) was enterovirus-negative either the same day (N = 9) or within 1 day (N = 1) of the plasma being collected. All samples were tested for EV and/or HPeV by real-time RT-PCR, either by ARIES®, GeneXpert®, and/or LightCycler®. Additionally, the CDC confirmed samples as positive or negative via genotype sequencing. Clinical information was gathered by reviewing patient electronic medical record.

All samples were extracted using the NucliSENS easyMAG® instrument (bioMérieux Inc., Durham, NC). RT-PCR was performed on all specimens (N = 74) for the detection of enteroviruses and/or HPeV using a previously developed assay1 using the LightCycler® (Roche, Indianapolis, IN). The test group consisted of 64 plasma samples from young infants, of which none was positive for enterovirus using GeneXpert®. Five of the 64 young infants were positive for enterovirus using GeneXpert®. Four of these five were confirmed as EV-positive at the CDC; one each were identified as Coxsackievirus B5, Coxsackievirus A9, Echovirus 5, and Echovirus 8 (Table 5). One additional sample was EV-positive from the CDC (identified as Coxsackievirus B5) that was negative by GeneXpert® (Table 4). All positive samples by either methodology had compatible clinical symptoms (all had fever; and many had other signs of a viral illness such as rash, diarrhea, or congestion).

The negative data from the young infant group is very consistent (Table 4). Fifty-eight out of 64 young infant plasma samples were negative for EV on both GeneXpert® and at the CDC; both the clinical specificity and negative predictive value (NPV) were 98%. The clinical sensitivity and positive predictive value (PPV) were 80%.

TABLE 4. A comparison of enterovirus detection methods using plasma specimens from young infants.

Methods

All of the targets for specificity testing were negative. The ARIES® EV assay detected all 3 aliquots at the level of 1 x 10<sup>3</sup> CC<sub>50</sub>/mL. Among the 10 plasma specimens from the validation group, 7/10 were EV-positive using ARIES® and 9/10 were EV-positive using GeneXpert®. Five were confirmed via genotyping by the CDC; two were identified as Echovirus 18 and one each were identified as Coxsackievirus A5, Echovirus 30, and Echovirus 5 (Table 3). The discrepant samples (C7, C16, and C17) were negative for specific enterovirus testing at the CDC.

Conclusion

In summary, GeneXpert® was able to identify a 7.8% (5/64) prevalence of enterovirus infection in our patient sample. When excluding young infants who were afebrile and lacked symptoms or signs of a viral illness, GeneXpert® was able to identify an enteroviral etiology in 11/48 (23%) of febrile young infants who otherwise did not have a specific etiologic diagnosis. Two of these five (40%) received 2 days of antibiotics pending bacterial cultures, which were negative. Using plasma to detect EV may allow for quicker diagnosis, sparing young infants from unnecessary hospital admission or antibiotic exposure.

References


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