Human bocavirus 1 (HBoV1) was described for the first time in 2005 in children with respiratory tract infection (RTI) [1]. Seroepidemiology studies in the United States [4] and Italy [5] indicated that over 90% of children had antibodies for HBoV. Three other HBoVs, designated HBoV2, HBoV3 and HBoV4, have mainly been detected in faeces, but a causal relation with disease such as gastroenteritis is still unclear [2]. Prevalence of HBoV1 has been estimated to be 6 days. The true clinical impact of a positive PCR result is often difficult to assess as HBoV1 DNA may persist for months in the respiratory tract. The DNA can be encountered in both symptomatic patients and asymptomatic individuals, as well as a co-infection with other respiratory viruses [6].

HBoV1 can be detected in 1.6 to 21.5% of children with respiratory symptoms of RTI, particularly during winter and spring [3]. Nevertheless, causative associations between HBoV1 infection and severe illness, including unexplained severe lower RTI [7] and encephalitis [8], have been described. This emphasizes the need for novel diagnostic methods for accurate and rapid detection of HBoV1 in a paediatric patient with respiratory tract infection symptoms. We describe for the first time the use of an antigen detection assay for the rapid identification of HBoV1 in a respiratory sample. However, the true clinical impact of a positive PCR result is often difficult to assess as HBoV1 DNA may persist for months in the respiratory tract. The DNA can be encountered in both symptomatic patients and asymptomatic individuals, as well as a co-infection with other respiratory viruses [6].

Currently four HBoV species have been identified. HBoV1, HBoV2, HBoV3 and HBoV4. HBoV1 and HBoV2 are isolates of human bocaviruses (HBoVs) which belong to the family Parvoviridae (subfamily Parvovirinae) and type 1, 2 and 3 viruses) and Streptococcus pneumoniae from a respiratory sample. Detection of antigens is based on separation-free two-photon excitation fluorescence. The mariPOC test system (ArcDia International Oy Ltd., Turku, Finland) provides a rapid alternative for HBoV1 detection. The mariPOC test system (ArcDia International Oy Ltd., Turku, Finland) provides a rapid alternative for HBoV1 detection. The mariPOC test system (ArcDia International Oy Ltd., Turku, Finland) provides a rapid alternative for HBoV1 detection.
(VP2), and it has shown good correlation with HBoV1 mRNA PCR designed to detect acute infection cases only (Toivola et al., poster presented at 25th European Congress of Clinical Microbiology and Infectious Diseases, 2015).

Here we describe the use of the HBoV1 antigen test for the detection and monitoring of HBoV1 in nasopharyngeal samples.

**Case Report**

A previously healthy girl, 5 months of age, developed symptoms of rhinorrhoea, cough and fever (temperature up to 39°C). The consulting paediatrician diagnosed an upper RTI with no lower respiratory tract involvement or signs of otitis. After written parental consent was obtained, a nasopharyngeal swab was taken on day 2 of illness and tested by the mariPOC for virologic diagnosis. Within 20 minutes the sample tested positive for HBoV1 antigen. Retrospective PCR testing confirmed the diagnosis: the nasopharyngeal sample tested positive for HBoV1 DNA by quantitative PCR[13] with a load of 7.7 × 10⁷ copies/mL and for HBoV1 mRNA by RT-PCR[10] with a Ct value of 26. To follow the course of infection, nasopharyngeal samples were taken on days 3, 4 and 5 from the onset of symptoms. While rhinorrhoea and mild cough continued, the fever declined on day 3. An initial increase in mariPOC assay signal was followed by a gradual decrease (Fig. 1). The viral antigen concentrations were extrapolated from a dose–response curve of a positive control dilution series. On day 6, the RTI symptoms were mild, which coincided with a decreasing HBoV1 antigen load.

**Discussion**

With the mariPOC rapid test system, we were able to in vitro diagnose and monitor for the first time the course of a primary HBoV1 RTI by directly targeting the virus proteins. Compared to standard laboratory diagnostics, this rapid test is easy to perform and may allow for a clinically accurate diagnosis of HBoV1 infection. The initial HBoV1 antigen detection was confirmed by both DNA and mRNA PCR. The costs of the mariPOC multianalyte tests are comparable with other antigen detection assays, such as direct fluorescent antibody testing. Compared to rapid and easy to perform nucleic acid detection methods, e.g. PCR assays with integrated sample preparation, mariPOC immunoassay is a less expensive alternative.

mariPOC test results are typically reported as qualitative. In this study we followed the course of the HBoV1 infection by using the quantitative property of the underlying two-photon excitation technology. However, the nature of swab sampling limits the quantitativeness of the data to semiquantitative. We showed the duration of this HBoV1 active infection to be approximately 1 week. The patient was HBoV1 antigen positive the morning after onset of symptoms, and HBoV1 antigen positivity lasted until day 5, when the signal barely exceeded the diagnostic threshold. No sample was available beyond day 5, while the decline in antigen since day 3 and the near-cutoff result on day 5 strongly suggest that the patient would have been negative on day 6. These results are in line with the time span of other respiratory viruses[14] and demonstrate once more that rapid testing should be done as soon as possible after the onset of symptoms and at the latest within 5 to 6 days.

While most HBoV1 infections are self-limited, they sometimes lead to life-threatening conditions. The availability of a rapid and accurate test for HBoV1 is likely to be useful in differential diagnoses and development of therapy, and will increase our understanding of the epidemiology and clinical impact of HBoV1 infections.

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**FIG. 1.** Detection of human bocavirus 1 (HBoV1) antigen by mariPOC test (ArcDia International Oy Ltd., Turku, Finland) during course of respiratory infection. Dashed line indicates cutoff for positive finding. For each day of infection, nasopharyngeal sample was analysed by HBoV1 antigen test.
Conflict of Interest

HT, HA and JOK are R&D employees at ArcDia International Oy Ltd. The other authors declare no conflict of interest.

References


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