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ARAŞTIRMA/RESEARCH

Human bocavirus infection in İstanbul

İstanbul'da human bocavirüs enfeksiyonu

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Abstract

Purpose: Human bocavirus (HBoV) is a recently discovered virus which is a member of Parvoviridae family. It is mostly detected in respiratory tract and stool specimens in pediatric patients with the diagnosis of acute respiratory tract infections and gastroenteritis, respectively.
Material and Methods: Hospitalized children aged 1-56 months with the diagnosis of lower respiratory tract infection (LRTI) were included in this prospective study between February 1st 2009 and May 21st 2009. HBoV DNA was investigated by PCR method. A questionarrie form was applied for all of the patients. Written informed consent of a parent or legal guardian was required
Results: Among the total of 120 hospitalized children who were investigated for HBoV the mean age was 9.9 months (1-56 months). HBoV DNA PCR in nasopharyngeal swabs was positive in 8 (6.7%) of 120 patients. In HBoV (+) lower respiratory tract infection group, to have an ill subling with similar symptoms and number of sublings (≥3 or more) were found to be risk factors. In HBoV (+) group serum level of C-reactive protein was significantly lower than HBoV (-) group.
Conclusion: The clinical spectrum of HBoV infection ranges from no symptoms or mild respiratory symptoms to severe acute respiratory disease. Since there is lack of data investigating the frequency of HBoV respiratory tract infections in our region, our study has importance for providing new data.

Key words: Human bocavirus (HBoV), children

Öz

Amaç: İnsan Bocavirüsü (HBoV) Parvoviridae ailesinden yeni keşfedilmiş bir virüstür. Çoğunlukla çocuk hastalarda solunum yolu ve dışkı örneklerinde tespit edilir ve sırasıyla solunum yolu enfeksiyonlarına ve gastroenterit tablosuna neden olur.
Gereç ve Yöntem: 1 Şubat 2009- 21 Mayıs 2009 tarihleri arasında alt solunum yolu enfeksiyonu (ASYE) nedeniyle hastaneye yatırılan, yaşları 1-59 ay arasında değişen 120 çocuk bu prospektif çalışmaya dahil edildi. Hastaların solunum örneklerinden PCR yöntemi ile HBoV DNA'sı araştırıldı. Tüm hastalara risk faktörlerini belirlemek amacıyla anket uygulandı. Çocukların ailelerinden ya da yasal bakıcılarından yazılı onam formu alındı.
Bulgular: Çalışmaya alınan hastaların yaş ortalaması 9.9 ay (1-56 ay) idi. 120 hastanın 8 (%6.7)'inde nazofarengeal aspirat örneğinde PCR yöntemiyle bakılan HBoV DNA pozitif olarak bulundu. HBoV (+) alt solunum yolu enfeksiyonu grubunda, benzer semptomlara sahip kardeşe sahip olmak ve kardeş sayısının ≥3 ya da fazla olması risk faktörleri olarak belirlendi. HBoV (+) alt solunum yolu enfeksiyonu grubunda HBoV (-) alt solunum yolu enfeksiyonu grubuna göre serum C-reaktif protein (CRP) değerleri anlamlı olarak düşük bulundu. **Sonuç:** HBoV ile enfeksiyon bulguları, hiçbir klinik semptomun olmamasından ciddi akut solunum yolu enfeksiyonlarına kadar değişiklik gösterebilmektedir. Yeni keşfedilmiş bir virüs olması nedeniyle patojenitesi ve enfeksiyon için risk faktörlerini araştıran daha çok çalışmaya ihtiyaç vardır. Bölgemizde bu konu ile ilgili çok veri olmaması nedeniyle, çalışmamızın önemli bir kaynak olduğunu düşünmekteyiz.

Anahtar kelimeler: Human bocavirus (HBoV), çocuk

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INTRODUCTION

HBoV is a small, nonenveloped virus with a single stranded DNA genome which belongs to Parvoviridae family, genus Bocavirus. HBoVs are classified into four species; HBoV1 is mostly found in the upper and lower respiratory tract specimens and causes upper and lower respiratory infections during the fall and winter months[1]. On the other hand, HBoV2, HBoV3, and HBoV4 are primarily enteric viruses and found predominantly in stool[2]. It was firstly described in 2005 in a Sweden pediatric patient from upper respiratory secretions[1]. Later, various reports showed that HBoV are detected in humans worlwide especially in children under two years[3]. The most common clinical presentations in children are; acute respiratory tract infections with the symptoms of rhinorrhea, fever, cough, wheezing and acute gastroenteritis. Bronchiolitis and pertussis-like illness may occur. However, there are also few reports which showed the association between HBoV and encephalitis, erythematous rashes and exanthems[4-6].

The microorganism is recently discovered, for this reason its clinical profile and role as a causative agent of respiratory tract disease are not clear. Since there is lack of the data of HBoV frequency and risk factors from our country, we aimed to determine the frequency and possible risk factors in hospitalized children with LRTI under 56 months old in our region.

MATERIAL AND METHODS

This prospective study was performed in a tertiary hospital of Kartal Dr. Lütfi Kırdar Training and Research Hospital. A total of 120 hospitalized children between 1- 56 months with LRTI between February 2009- May 2009 were included in this study. Children in our neonatal intensive care unit (NICU) were excluded. Informed consent was obtained from parents of all study patients. The study protocol was approved by the Institutional Ethics Committee.

All the children hospitalized with the diagnosis of LRTI into our Pediatrics departments had been investigated for HBoV genome in nasopharengeal swabs. Nasopharyngeal samples were obtained with the standard method of nasopharyngeal swab[7]. A questionnaire was conducted to all parents to asses the associated factors of HBoV infection. Maternal age, education level and economical status of the parents, number of siblings, having an ill sibling with similar symptoms, number of persons in the household, breastfeeding, exposure to cigarette smoke, a day-care attendance and family history of asthma were questioned. After a detailed physical examinations, clinical presentations of fever, rhinorrhea, cough, wheezing, tacypnea, subcostal retraction, dyspnea, stridor, vomiting and diarrhea were recorded. O_2 saturation with pulse oximeter, peripheral blood count, C-reactive protein (CRP) (< 3.5 mg/L normal), chest x-ray were performed in all children.

Microbiological methods

A nasopharyngeal swab was collected from each patient and then dipped into 1 ml saline and stored at −20°C until transfer to reference laboratory for nucleic acid extraction. Nucleic acids were extracted from samples using with a commercial nucleic acid extraction kit (High Pure Viral Nucleic Acid Kit, Roch Diagnostics, Germany) according to instruction of manufacturer. HBov DNA was investigated by PCR method described elsewhere using HBoV-F 5'-TAT GGC CAA GGC AAT CGT CCA AG-3' and HBoV-R 5'-GCC GCG TGA ACA TGA GAA ACA GA-3' primers that targeting NP1 gene of HBoV[8].

Statistical analysis

Stastistical calculations were performed with NCSS (Number Cruncher Statistical System), 2007 for Windows (NCSS Corporation, Kaysville, UT, USA). Besides descriptive statistical calculations (mean and Standard deviation and frequency), Pearson chi-square test, Fischer's exact tests were used for evaluation of qualitative data. Statistical significancy was set at $p<0.05$.

RESULTS

Among the total of 120 hospitalized children whom were investigated for HBoV DNA PCR, 43 (35.8%) were female and 77 (64.2%) were male and the male/female ratio was 1.8. The mean age of the group was 9.9 months (1-56 months). The mean age of HBoV (+) group was 9 months (4-19 months). HBoV DNA PCR in nasopharyngeal swabs was positive in 8 (6.7%) of 120 patients. In HBoV (+) LRTI group, to have an ill subling with similar symptoms (p=0.044, OR:4.091; %95 CI: 0.948-

17.654) and number of sublings (≥3 or more) (p=0.038, OR: 4.355; %95 CI: 0.981-19.323) were found to be associated factors. In HBoV (+) group serum level of CRP was significantly lower than HBoV (-) group (p=0.011). There was no difference in age, gender, maternal age, socioeconomic status, duration of breastfeeding, cigarette smoke exposure, attending a day-care center and family history of asthma between HBoV (+) and HBoV (-) groups. Demographic characteristics and associated factors of children with HBoV-positive and HBoV-negative LRTI is shown in Table 1.

Table 1. Demographic characteristics and associated factors of children with HBoV-positive and HBoV-negative LRTI

Variables		HBoV-positive	HBoV-negative	p value
		n (%)	n (%)	
Gender	Male	6 (75)	71 (63)	0.508
	Female	2 (25)	41 (37)	
Age	1-6 months	3 (38)	53 (47)	0,612
	6-12 months	4 (50)	37 (33)	
	>12 months	1 (12)	22 (20)	
Number of siblings	≤2	3 (38)	81 (72)	**0,038**
	≥3	5 (62)	31 (28)	
Having an ill sibling with similar symptoms	Yes	4 (50)	22 (20)	**0,044**
	No	4 (50)	90 (80)	
Exposure to cigarette smoke	Yes	1 (12)	45 (40)	0,152
	No	7 (88)	67 (60)	
Maternal age	18-23	1 (12)	27 (24)	0,755
	24-29	4 (50)	49 (44)	
	≥30	3 (38)	36 (32)	
Education level	Low	6 (75)	93 (83)	0,563
	High	2 (25)	19 (17)	

Clinical presentations in HBoV (+) patients were; cough (100%), subcostal retraction (75%), rhinorrhea (75%), dyspnea (62%), fever (37%), wheezing (37%), vomiting (12%) and diarrhea (12%). Stridor was not observed in our patients with HBoV (+). Statistically no significant difference between HBoV positive and negative patients could be demonstrated for clinical presentations such as cough, subcostal retraction, rhinorrhea, dyspnea, fever, wheezing, vomiting and diarrhea. There was no difference in O_2 saturation with pulse oximeter, white blood cell count, corticosteroid use, antibiotic use, mechanical ventilation support and severity of illness between the two groups.

HBoV infection was detected higher in March and April, however there was no statistically difference between the months. The median duration of hospitalization in patients with HBoV (+) and HBoV (-) were 9.5±8.5 and 8.08±5.7 days, respectively (p=0.960). No mortality was observed during the study.

DISCUSSION

HBoV is a recently described causative agent of LRTI such as human metapneumovirus (hMPV), human coronavirus NL63 (HCoV-NL63) and coronavirus HKU1 (HCoV-HKU1)[3]. HBoV is usually associated with mild symptoms of acute respiratory infections and almost all children improve serologic confirmation of prior infection with HBoV by five years of age[9]. It is identified worldwide throughout the year and no specific antiviral therapy is available.

In our study, the frequency of HBoV infection among children with LRTI was 6.7% similar to many studies in different countries that reported HBoV positivity lower than 8% in respiratory samples[10-11]. The first study detected HBoV DNA in throat swab and/or washing specimens in 76 children with acute respiratory diseases found HBoV positivity 6.5%[12]. The largest study conducted in our country investigated nasal samples

of 1,143 pediatric patients who had respiratory symptoms found HBoV positivity as 2.6%[13]. On the other hand, Günel et al.[14] reported that HBoV positivity was 43.1% in adenoid specimens in asymptomatic children which indicates that the virus can remain persistently and making difficult etiologic association with clinical disease. Obuchi et al. investigated 104 children with acute respiratory infections who were shown to be negative for influenza and found that HBoV (n=21) was the most frequently detected virus[15].

Characteristics of HBoV positive patients in our study were similar to previous studies[16,17]. In our study, we investigated the associated factors for HBoV positivity. In HBoV (+) LRTI group, to have an ill subling with similar symptoms and number of sublings (≥3 or more) were found to be risk factors. In one of study, Caccia et al.[18] reported that HBoV positivity was found in children with respiratory infections who had underlying risk factors as heart disease. In another study, maternal smoking and being born in winter season were found to be associated with HBoV infection[19]. Because of being a novel viral pathogen, there is lack of data investigating risk factors. For this reason, further studies with large study populations are needed.

Co-detection with other viral pathogens is common in HBoV-positive patients as shown in previous studies[20,21]. In our study we did not investigate any other potential pathogens for this reason, it is difficult to say that all the symptoms are associated with only HBoV positivity.

In different studies, it is shown that seasonal peak of HBoV differs according to climate and some factors, however higher detection rates in winter is shown in previous reports[10,22]. On the other hand, in a study it was shown that HBoV was observed between May and June in a higher frequency[23]. In our study, HBoV infection was detected higher in March and April, however we could not observe seasonal variation of HBoV because of short duration of the study.

In conclusion, HBoV is a novel virus identified especially in respiratory and stool specimens, however we believe that further studies are needed to define the pathogenity in other systems. Although there are studies investigated the risk factors for HBoV infection, the data is still missing and long-term studies are required in large populations which investigates possible other viral pathogens.

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