



SCIENTIFIC LETTERS

Community acquired acute respiratory infections caused by enterovirus D68 (EV-D68)[☆]



Infecciones respiratorias agudas comunitarias causadas por enterovirus D68 (EV-D68)

Dear Editor:

Enterovirus D68 (EV-D68) is a virus that belongs to the *D* species of the *Enterovirus* genus in the family Picornaviridae. It was first described in 1962 in California as rhinovirus 87 as an agent involved in paediatric respiratory infections.¹ In 2014 a significant outbreak of respiratory infections caused by EV-D68 was reported in the United States that affected more than one thousand patients.² Due to this circumstance, several countries started assessing for the presence of this virus in cases of upper and lower respiratory tract infections in children and adults. Infection by this virus has been reported in France, Italy, Netherlands and Germany, among other European countries.^{2,3}

In Spain, there have been a few reports of isolated acute respiratory infection (ARI) associated with EV-D68, both in adults and in children, and in the community and in the hospital.^{4–6} We think that there is still little information on this type of infections, and thus believed it would be interesting to analyse the ARIs caused by EV-D68 over a period of eight months.

We analysed the presence of enterovirus and other respiratory viruses in respiratory samples (nasopharyngeal aspirate or throat swab) obtained between July 2015 and March 2016 in paediatric patients (age < 15 years) with suspected ARI.

Viral detection was performed by means of a commercially available real-time RT-PCR gene amplification technique that simultaneously detects and distinguishes 16 different viruses (Allplex[®] Respiratory Full Panel Assay; See-gene, South Korea). This assay can differentiate between enterovirus and rhinovirus, but cannot be used to serotype enteroviruses. Samples that tested positive for enterovirus were submitted to the National Microbiology Centre (Centro Nacional de Microbiología, Madrid), where the final serotyping was performed.

We analysed 2827 respiratory samples collected in the period under study, of which 1646 (58.2%) tested positive (some virus was detected). Of the positive samples, 88 (5.3%) corresponded to enterovirus, and only 78 strains could be serotyped (88.6%), with identification of EV-D68 in nine patients (11.5%). The nine cases of EV-D68 infection amounted to 0.5% of all positive samples and 0.3% of the total samples analysed. Other enteroviruses detected in the sample included coxsackievirus A13 (16.6%), coxsackievirus A6 (76%) and coxsackievirus B4 (7.6%). Table 1 presents the main clinical characteristics of these infections. All were community-acquired infections that occurred in isolation, and all patients had positive outcomes, including the one that required admission to the hospital.

Although there are many studies devoted to most types of enterovirus infection, this is not the case regarding their involvement in ARIs. Historical studies seem to suggest that enteroviruses are the main aetiological agents in ARIs in the summer months, possibly accounting for 23–27% of all viruses detected during this season of the year.^{2,3} Although when its involvement is analysed over the course of an entire year, it declines to 4–6%.³ The incidence of ARIs caused by EV-D68 in Spain corresponds to between 0.94% and 2% of analysed samples^{4,5}; in our study, the percentage found was somewhat lower, of 0.5%, but it appears that its incidence may change based on the season under study (peaking in the summer).^{2,3}

In Spain, twenty cases have been described to present in patients aged 1 month to 5 years^{4–6}; our patients were slightly older, with ages ranging between 1 month and 9 years. The mean age reported in the North American outbreak was 5 years, although the range was 15 days to 15 years.²

Despite the severity of the ARIs caused by EV-D68 reported in relation to the American outbreaks, the cases described in Europe seemed to be less severe.² Our patients only presented with fever and mild to moderate respiratory symptoms that did not require hospital admission. Only one patient (11%) developed pneumonia requiring three days of hospitalisation; however, in the study by Calvo et al.,⁴ 83% of patients had to be admitted. In the United States outbreak, 59% of patients were admitted to paediatric intensive care units due to the severity of their respiratory disease.² In opposition, only 6.8% required admission to intensive care in a study conducted in Canada.²

Some studies have demonstrated that the presence of underlying disease, especially respiratory, could facilitate infection by EV-D68.² In our study, four patients (44.4%) had this type of disease.

[☆] Please cite this article as: Reina J, Cabrerizo M, Ferrés F. Infecciones respiratorias agudas comunitarias causadas por enterovirus D68 (EV-D68). An Pediatr (Barc). 2017;86:158–159.

Table 1 Main characteristics of patients with acute respiratory infections caused by EV-D68.

Patient	Sex	Age	Symptoms	Underlying disease	Admission	Treatment
1	Male	9 years	Fever, bronchospasm, expectoration	None	No	Salbutamol, ipratropium, methylprednisolone
2	Male	5 years	Fever, wheezing, bronchopulmonary dysplasia	Preterm birth	No	Salbutamol, prednisolone
3	Female	2 years	Fever, bronchitis	None	No	Salbutamol
4	Male	6 years	Fever, cold symptoms	Asthma	No	Salbutamol
5	Male	2 years	Fever, bronchitis, pneumonia	Asthma	Yes	Salbutamol, amoxicillin
6	Female	1 month	Fever, bronchiolitis	None	No	Salbutamol
7	Male	2 years	Fever, bronchiolitis	Asthma	No	Salbutamol
8	Male	2 years	Fever, bronchospasm	None	No	Salbutamol
9	Male	5 years	Fever, bronchitis	None	No	Amoxicillin

The evidence from this pilot study suggests that ARIs caused by EV-D68 in Europe are not associated with the clinical severity that has been observed in the outbreaks in North America, although patient comorbidity could be a determinant of its pathogenicity.

References

- Messacar K, Abzug MJ, Domínguez SR. 2014 outbreak of enterovirus D68 in North America. *J Med Virol.* 2016;88:739–45.
- Gimferrer L, Campins M, Codina MG, Esperalba J, Martin MC, Fuentes F, et al. First enterovirus D68 (EV-D68) cases detected in hospitalised patients in a tertiary care university hospital in Spain, October 2014. *Enferm Infecc Microbiol Clin.* 2015;33:585–9.
- Rojo-Rello S, Sanz-Muñoz I, Ortiz de Lejarazu R. El enterovirus D68 sí que existe en España. *Enferm Infecc Microbiol Clin.* 2016, <http://dx.doi.org/10.1016/j.eimc.2015.12.011>.
- Calvo C, Cuevas MT, Pozo F, García-García ML, Molinero M, Calderón A, et al. Respiratory infections by Enterovirus D68 in outpatients and inpatients Spanish children. *Pediatr Infect Dis J.* 2016;35:45–9.

- Renois F, Bouin A, Andreoletti L. Enterovirus 68 in pediatric patients hospitalized for acute airway diseases. *J Clin Microbiol.* 2013;51:640–3.
- Schieble JH, Fox VL, Lennette EH. A probable new human picornavirus associated with respiratory diseases. *Am J Epidemiol.* 1967;85:297–310.

Jordi Reina^{a,*}, María Cabrerizo^b, Francesc Ferrés^c

^a *Unidad de Virología, Servicio de Microbiología, Hospital Universitario Son Espases, Palma de Mallorca, Baleares, Spain*

^b *Unidad de Enterovirus, Centro Nacional de Microbiología, Madrid, Spain*

^c *Sección de Urgencias, Servicio de Pediatría, Hospital Universitario Son Espases, Palma de Mallorca, Baleares, Spain*

* Corresponding author.

E-mail address: jorge.reina@ssib.es (J. Reina).

2341-2879/

© 2016 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. All rights reserved.

Periodic fever, aphthous stomatitis, pharyngitis, and adenitis syndrome: A study and follow-up of 16 cases[☆]



Síndrome de fiebre periódica, estomatitis aftosa, faringitis y adenitis cervical: Estudio y seguimiento de 16 casos

Dear Editor:

Periodic fever, aphthous stomatitis, pharyngitis, and adenitis syndrome (PFAPA) is the most common type of recurrent

[☆] Please cite this article as: Muínelo Segade A, Vila Sexto L. Síndrome de fiebre periódica, estomatitis aftosa, faringitis y adenitis cervical: Estudio y seguimiento de 16 casos. *An Pediatr (Barc).* 2017;86:159–161.

Table 1 Diagnostic criteria used for PFAPA.

Regularly recurrent fevers in any age group
– Regularly recurrent fevers with onset before age 5 years
– Constitutional symptoms in the absence of upper respiratory infection with at least 1 of the following clinical signs:
• Aphthous stomatitis
• Cervical lymphadenitis
• Pharyngitis
– Exclusion of cyclic neutropaenia
– Completely asymptomatic interval between episodes
– Normal growth and development

Source: Thomas et al.²