Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Infection (2010) **61**, 351–359

ELSEVIER

www.elsevierhealth.com/journals/jinf

LETTERS TO THE EDITOR

Procalcitonin in children with suspected novel influenza A (H1N1) infection

Rapid diagnosis of children with flu-like symptoms is of great clinical importance.[1] It has been shown that the discrimination of influenza from other viral and bacterial infections in children during an influenza epidemic, either based on clinical findings or on laboratory parameters, is unreliable.[2–4]

In a number of pediatric studies, circulating levels of procalcitonin (PCT) were raised in bacterial infection and only mildly raised in the absence of bacteria.[5–7] We hypothesized that PCT might be a useful tool for the discrimination of children with bacterial infection from children with viral infection during the Novel Influenza A (H1N1) pandemic.

From October until December 2009, 30 consecutive children with suspected Novel Influenza A (H1N1) infection were included at the freely accessible (i.e., no referral needed) influenza outpatient clinic. Standard blood tests at presentation included C-reactive protein (CRP), differentiated white blood count and PCT. A pharyngeal swab for polymerase chain reaction (PCR) for Influenza A and B, rhinovirus, adenovirus, para-influenza virus 1–4, enterovirus, human coronavirus, human metapneumovirus and respiratory syncytial virus, as well as for *Legionella* spp., *M. pneumoniae* and *C. pneumoniae*, were standardly performed, using primers as advised by the World Health Organization. Blood and sputum cultures, lumbar punctures and radiological examinations were routinely ordered at the discretion of the treating physician.

Values are presented as numbers with percentages or as medians with interquartile ranges (IQR). Correlations between CRP, leukocytes and PCT were assessed using Spearman's correlation test. Student's *t*-test was used for inter-group comparison. $P < 0.05$ was considered significant.

30 Consecutive patients were included (mean age 24 months). 25 Patients (83.3%) were diagnosed with a confirmed viral illness. Three patients were diagnosed with a – clinically suspected – viral upper airway infection without positive PCR, one patient was diagnosed with a *M. Pneumoniae* infection and one patient was diagnosed with a non-confirmed bacterial pneumonia.

In the subgroup with confirmed viral infections, nine cases of novel influenza A (H1N1)(30%), eleven cases of rhinovirus (36.7%), five cases of respiratory syncytial virus (16.7%), four cases of adenovirus (13.3%) and one case of human metapneumovirus were diagnosed (Table 1).

Median PCT values in the subgroup with confirmed viral infections were 0.153 ng/mL with IQR 0.094–0.261 ng/mL, median CRP values were 19.0 mg/L with IQR 5.6–28.3 mg/L and median leukocyte count was 13.1 giga/L with IQR 9.5–16.0 giga/L. The one case with non-confirmed bacterial pneumonia showed a marked acute phase response (PCT 32.17 ng/mL, CRP 444.1 mg/L). The negative predictive value (NPV) of PCT for bacterial infection was 88%, at a cut-off <0.71 ng/mL – the earlier described lower cut-off point in healthy neonates[8] – whereas the NPV of CRP was 28% at a cut-off <10 mg/L and 78% at a cut-off <30 mg/L (Fig. 1).

A significant correlation between PCT and CRP (ρ 0.531, $P = 0.003$), between CRP and leukocyte count (ρ 0.445, $P = 0.016$), but not between PCT and leukocyte count (ρ 0.041, $P = 0.83$) could be observed.

Our study was aimed to assess the value of PCT in children with suspected Novel Influenza A (H1N1) infection during the pandemic. Based on the results of this small cohort study, we can conclude that the acute phase response in children with Novel Influenza A (H1N1) infection and other viral infections is mild, with low levels of CRP, PCT and leukocyte count. For CRP and leukocyte count, this is in conjuncture with earlier studies in children and adults.[2,4,8,9] We show that values of PCT are generally below <0.71 ng/mL – the earlier described lower cut-off point in healthy neonates[8] – in children with viral infection of any cause.

Levels of CRP were considerably low in the subgroup with viral infections and showed a significant correlation with PCT levels. However, seven patients had CRP values >30 mg/L, whereas the generally accepted lower cut-off point is <10 mg/L[10].

PCT measurement in children with suspected Novel Influenza A (H1N1) infection seems to be of added value. Low circulating levels of PCT appear to correlate with the presence of viral infection and/or the absence of bacterial infection. Although circulating levels of CRP show a correlation with PCT and are generally low in patients with viral infection, a considerable amount of patients had moderately

Table 1 Detected viruses by means of PCR in children with suspected Novel Influenza A (H1N1) during the H1N1 pandemic. Total exceeds 100% due to double infections.

Virus	*n*
Influenza A (H1N1)	9
Rhinovirus	11
Adenovirus	4
Respiratory syncytial virus	5
Human metapneumovirus	1
Suspected viral infection	3

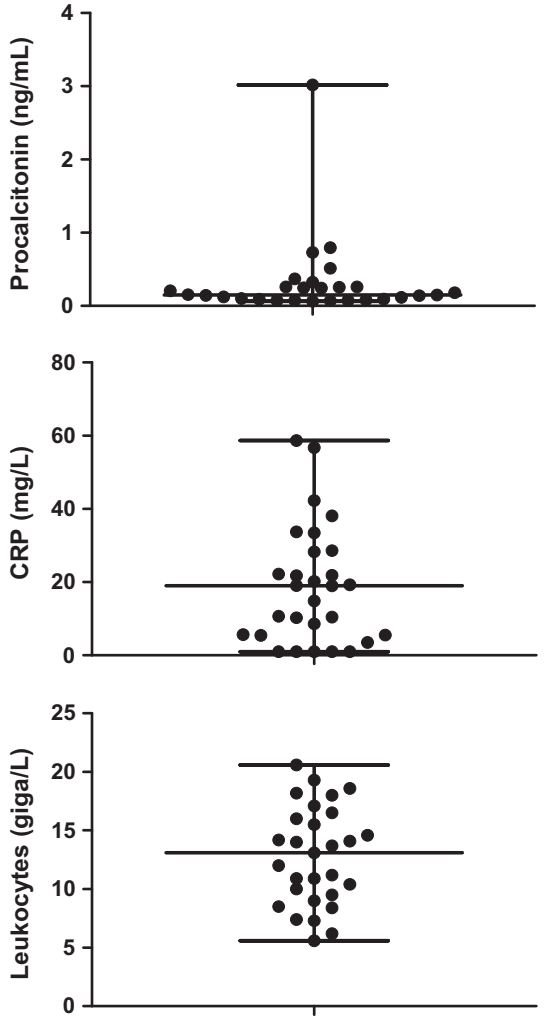

Figure 1 PCT levels (ng/mL), CRP levels (mg/mL) and leukocyte counts (giga/L) in patients with a confirmed viral infection at presentation.

elevated levels of CRP. The same holds true for leukocyte counts.

This study has some limitations. Apart from the small cohort size, a major drawback is the fact that we almost uniformly included patients with viral infections. To be able to analyze the diagnostic properties of PCT, CRP and leukocyte counts in differentiating viral and bacterial infections, a group of children with bacterial infection from the same cohort is needed. However, many earlier studies have shown that values of PCT during bacterial infection in children can be elevated.[5–7]

In children with flu-like symptoms, a rapid and adequate diagnosis is of great importance. Reliable biomarkers that are readily available may enhance and quicken the diagnostic process. Based on our findings, PCT may be of added value when the treating physician is uncertain whether to withhold antibiotics.

Disclosures

The authors do not have any conflict of interest to declare. No financial funding for this research was received.

References

1. Sharma V, Dowd MD, Slaughter AJ, Simon SD. Effect of rapid diagnosis of influenza virus type a on the emergency department management of febrile infants and toddlers. *Arch Pediatr Adolesc Med* 2002;**156**:41–3.
2. Appenzeller C, Ammann RA, Duppenthaler A, Gorgievski-Hrisoho M, Aebi C. Serum C-reactive protein in children with adenovirus infection. *Swiss Med Wkly* 2002;**132**:345–50.
3. Hoeven AM, Scholing M, Wever PC, Fijnheer R, Hermans M, Schneeberger PM. Lack of discriminating signs and symptoms in clinical diagnosis of influenza of patients admitted to the hospital. *Infection* 2007;**35**:65–8.
4. Whicher JT, Chambers RE, Higginson J, Nashef L, Higgins PG. Acute phase response of serum amyloid A protein and C reactive protein to the common cold and influenza. *J Clin Pathol* 1985;**38**:312–6.
5. Dubos F, Korczowski B, Aygun DA, Martinot A, Prat C, Galetto-Lacour A, et al. Serum procalcitonin level and other biological markers to distinguish between bacterial and aseptic meningitis in children: a European multicenter case cohort study. *Arch Pediatr Adolesc Med* 2008;**162**:1157–63.
6. Maniaci V, Dauber A, Weiss S, Nylen E, Becker KL, Bachur R. Procalcitonin in young febrile infants for the detection of serious bacterial infections. *Pediatrics* 2008;**122**:701–10.
7. Olaciregui I, Hernandez U, Munoz JA, Emparanza JI, Landa JJ. Markers that predict serious bacterial infection in infants under 3 months of age presenting with fever of unknown origin. *Arch Dis Child* 2009;**94**:501–5.
8. Edelbauer M, Wurzner R, Jahn B, Zimmerhackl LB. C-reactive protein and leukocytes do not reliably indicate severity of influenza a infection in childhood. *Clin Pediatr (Phila)* 2006;**45**:531–6.
9. Falsey AR, Walsh EE, Francis CW, Looney RJ, Kolassa JE, Hall WJ, et al. Response of C-reactive protein and serum amyloid A to influenza A infection in older adults. *J Infect Dis* 2001;**183**:995–9.
10. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. *J Clin Invest* 2003;**111**:1805–12.

Maarten Limper*
Patrick M. Smit
Department of Internal Medicine, Slotervaart Hospital, Louwesweg 6, 1066 EC, Amsterdam, The Netherlands
*Corresponding author. Tel.: +31 (0) 20 512 5194; fax: +31 (0) 20 512 4783.
E-mail address: maarten.limper@slz.nl (M. Limper)

Karlien M. Bongers
Department of Pediatrics, Slotervaart Hospital, Louwesweg 6, 1066 EC Amsterdam, The Netherlands

Anton P. van Zanten
Laboratory of Biochemistry, Slotervaart Hospital, Louwesweg 6, 1066 EC, Amsterdam, The Netherlands

Paul H.M. Smits
Laboratory of Molecular Biology, Slotervaart Hospital, Louwesweg 6, 1066 EC, Amsterdam, The Netherlands

Dees P.M. Brandjes
Jan Willem Mulder
Department of Internal Medicine, Slotervaart Hospital, Louwesweg 6, 1066 EC, Amsterdam, The Netherlands

Ines A. von Rosenstiel
Department of Pediatrics, Slotervaart Hospital, Louwesweg 6, 1066 EC Amsterdam, The Netherlands

Eric C.M. van Gorp
Department of Internal Medicine, Slotervaart Hospital, Louwesweg 6, 1066 EC, Amsterdam, The Netherlands

Departmemt of Virology, Erasmus Medical Centre, Dr. Molewaterplein 50, 3015 GE, Rotterdam, The Netherlands

9 July 2010

Available online 16 July 2010

doi:10.1016/j.jinf.2010.07.005

Apropos "Seroprevalence of common vaccine-preventable viral infections in HIV-positive adults"

To the Editor

We appreciate Molten et al.[1] for their comprehensive investigation on sero-prevalence of common vaccine-preventable viral infections in adults.

Aliquots of the representative sera, if available, should better be examined for poliovirus neutralizing antibody to preempt any poliovirus replication among HIV-positives. Recently, the World Health Organization announced the confirmation of wild poliovirus serotype 1 in seven samples from children with acute flaccid paralysis in Tajikistan, in the context of a multidistrict cluster starting in December 2009. As of 28 April, 2010, 32 of 171 reported cases were laboratory-confirmed and closely related to virus from Uttar Pradesh, India.[2]

There might be gaps in immunity to poliomyelitis in the examined subjects. In a sero-epidemiological study at the University of Milan, to investigate immunity against poliomyelitis in a population of drug addicts in a rehabilitative residential centre there was a widespread lack of poliovirus neutralizing antibodies. That was more evident in the HIV-positive subjects, 27% of whom were seronegative for poliovirus type 1, 27% for type 2 and 34% for type 3, with 11% seronegative for all three types. These results indicate a gap in immunity to poliomyelitis in the examined population.[3]

Investigations would also be needed to identify poliovirus sero-negative natives among either the HIV-positive or HIV-negative in the seventh or higher decades. They might have never been vaccinated against poliomyelitis. Vaccines were not available during their infancy or early childhood. They could be afflicted with locally circulating polioviruses or a travel associated poliomyelitis. Two healthy adult males, ages 62 and 65 years, on their trip to Morocco were afflicted with acute flaccid paralysis while on holidays.[4]

Conflict of interest

None.

Ethical clearance

Not required.

Financial support

None.

References

1. Molton J, Smith C, Chaytor S, Maple P, Brown K, Johnson M, et al. Seroprevalence of common vaccine-preventable viral infections in HIV-positive adults. *J Infect* 2010 Jul;**61**(1):73—80 [Epub 2010 Apr 18].
2. World Health Organization Country Office Tajikistan, WHO Regional Office for Europe, European Centre for Disease Prevention and Control. Outbreak of poliomyelitis in Tajikistan in 2010: risk for importation and impact on polio surveillance in Europe? *Euro Surveill* 2010 Apr 29;**15**(17). pii:19558.
3. Pregliasco F, Minolfi V, Boschin A, Andreassi A, Profeta ML. A seroepidemiologic survey of immunity against poliomyelitis in a group of HIV positive and HIV negative drug addicts. *Eur J Epidemiol* 1995 Dec;**11**(6):693—5.
4. Joce R, Wood D, Brown D, Briggs N. Paralytic poliomyelitis in England and Wales. *BMJ* 1992;**305**:79—82.

Subhash C. Arya*
Nirmala Agarwal
Sant Parmanand Hospital, 18 Alipore Road, Delhi-110054, India
*Corresponding author. Tel.: +91 119810642269.
E-mail address: subhashbhapaji@gmail.com (S.C. Arya)

31 July 2010

Available online 5 August 2010

doi:10.1016/j.jinf.2010.07.016

Community associated methicillin resistant *staphylococcus aureus* (CA-MRSA) infective endocarditis in Italy

Dear Editor,

We read with interest the article by Elston and Barlow who reviewed different aspects of community-associated *Staphylococcus aureus* (CA-MRSA) in UK.[1] CA-MRSA has now emerged as a cause of severe infections worldwide.[1] CA-MRSA is often associated with skin and soft tissue infections and less frequently with necrotizing pneumonia and severe sepsis in young healthy individuals.[2—4] Infective endocarditis (IE) due to CA-MRSA has been recently reported in some European and South American countries.[5—7] In these reports