Journal of Virological Methods 237 (2016) 38–39

Contents lists available at ScienceDirect

Journal of Virological Methods

journal homepage: www.elsevier.com/locate/jviromet

Short communication

Comparison of two chemiluminescent immunoassays in the detection of measles IgM antibodies

Cristina Gómez-Camarasa, Ana Lara-Oya, Fernando Cobo, Antonio Sampedro-Martínez*, Javier Rodríguez-Granger, José Gutierrez-Fernández, José María Navarro-Marí

Microbiology Department; University Hospital Virgen de las Nieves, Avenida de Fuerzas Armadas s/n, 18014, Granada, Spain

Article history:
Received 20 May 2016
Received in revised form 24 August 2016
Accepted 25 August 2016
Available online 26 August 2016

Keywords:
Measles
Serology
Chemiluminescent immunoassay

A B S T R A C T

Serological confirmation of measles is achieved by detecting the specific immunoglobulin M (IgM), and it is important to evaluate new commercial inmunoassays in order to ensure the quality of results. The objective of this study was to compare the performance of a novel automated chemiluminescent immunoassay (CLIA), Virclia IgM measles (Vircell, Spain), with that of the widely used Liaison measles IgM assay (DiaSorin, Italy). A panel of 86 sera from laboratory-confirmed cases was used for the sensitivity calculation, and 59 sera from healthy individuals and those with other viral infections were used for the specificity calculation. Sensitivity values were 96.5% for Virclia and 97.6% for Liaison; specificity values were 93.2% for Virclia and 96.6% for Liaison; neither difference was statistically significant VirClia IgM measles is a good alternative to other immunoassays for the serological confirmation of measles.

Measles is an acute, vaccine-preventable disease capable of causing epidemics. It is no longer endemic in most European countries due to vaccination programs, but outbreaks remain common in countries containing population subgroups with low immunity levels (European Centre for Disease Prevention and Control, 2016).

Laboratory diagnosis of measles cases is a vital aspect of surveillance at all stages of control programs due to the inadequate reliability of clinical diagnosis. In countries with a low incidence, the majority of suspected cases have other etiologies (parvovirus B19, rubella virus, human herpes virus 6, and enteroviruses). Laboratory confirmation is primarily based on detection of the specific immunoglobulin M (IgM) in serum samples and/or on detection of measles RNA by real-time polymerase chain reaction (RT-PCR) in oral fluid or urine (World Health Organization, 2007).

Other procedures include the isolation of measles virus in oral fluid, nasopharyngeal secretions, or urine, and the detection of a significant rise in specific IgG antibody level in paired sera (World Health Organization, 2007).

Assays used to detect measles antibodies include indirect immunofluorescence (IFI), enzyme immunoassay (ELISA) in indirect or capture format, and recently, a chemiluminescent immunoassay (CLIA) (Liaison, Diasorin, Italy) (Ratnam et al., 2000; Sampedro et al., 2013).

The objective of this study was to compare the diagnostic performance of VirClia measles IgM (Vircell, Spain), a novel automated CLIA, with that of Liaison measles IgM CLIA (DiaSorin, Spain). VirClia measles IgM is an indirect CLIA of IgM against the measles virus in human serum/plasma for application with the Thunderbolt® (Gold Standard Diagnostics, USA) instrument. The analyzer can perform 24 monotests simultaneously, and each includes a calibrator and negative control, allowing validation and interpretation of the results for each individual sample. The Liaison Measles IgM is a CLIA based in μ-capture metology for use on the DiaSorin Liaison automated platform. This assay has been widely validated for serologic diagnostic of measles (de Ory et al., 2015).

Two groups of stored (−20 °C) sera were used for the study: (i) Positive group of serum samples from 86 patients with measles; laboratory confirmation was done by culture and/or RT-PCR from urine or nasopharyngeal samples (Sampedro et al., 2013); and (ii) Negative group of 59 sera, including 35 from healthy individuals with no history of measles, received by our laboratory for immunity study against measles, and 24 from individuals with positive IgM against cytomegalovirus (CMV) (n = 5), Epstein Barr virus (EVB) (n = 7), rubella virus (n = 4), and parvovirus B19 (n = 8), which may produce a false-positive reaction. No information on vaccina-

* Corresponding author.
E-mail addresses: gomezcamarasa@gmail.com (C. Gómez-Camarasa), ana.lara.sspa@juntadeandalucia.es (A. Lara-Oya), fernando.cobo.sspa@juntadeandalucia.es (F. Cobo), antonioj.sampedro.sspa@juntadeandalucia.es (A. Sampedro-Martínez), javierm.rodriguez.sspa@juntadeandalucia.es (J. Rodríguez-Granger), josegf@ugr.es (J. Gutierrez-Fernández), josem.navarro.sspa@juntadeandalucia.es (J.M. Navarro-Marí).

http://dx.doi.org/10.1016/j.jviromet.2016.08.018
0166-0934/

Table 1
Comparison of Virclia and Liaison measles IgM results.

Virclia	Liaison Measles IgM			
measles IgM	Positive	Negative	Equivocal	Total
Positive	81	3	0	84
Negative	2	54	1	57
Equivocal	1	3	0	4
Total	84	60	1	145

Table 2
Sensitivity and specificity values (%) of CLIA Liaison and Virclia.

	Positves/ Positives total	Sensitivity (CI95%)	Negatives/ negatives total	Specificity (CI%95)
VirClia	83/86	96.5% (90.2–98.8)	55/59	93.2% (83.8–97.3)
Liaison	84/86	97.6% (91.9–99.3)	58/59	96.6% (88.4–99)

tion was available from these samples. All samples received from healthy persons had specific IgG anti – measles.

The sera from measles, parvovirus B19, and rubella patients were obtained during outbreaks in Granada in 2010 and 2015 as part of the Measles/Rubella Surveillance Program in Andalusia, Spain (Dirección General de Salud Pública y Participación, Consejería de Salud, 2001).

Commercially available Immulite kits (Siemens) were used to detect the presence of specific IgM against CMV (Immulite 2000 CMV IgM assay), EBV (Immulite 2000 EBV VCA IgM), and rubella virus (Immulite 2000 Rubella IgM). LIAISON kit (Dia Sorin) was used for IgM against parvovirus B19 (Liaison Biotrin Parvovirus B19 IgM) and IgG against measles (Liaison Measles IgG). Assays were performed and results interpreted according to the manufacturers' instructions.

Sensitivity and specificity values were calculated with their 95% confidence intervals (95% CI). The more adverse possibility was assumed when a result was equivocal. The significance of inter-assay differences in sensitivity and specificity was determined with a z –test, considering $P < 0.05$ to be statistically significant.

As shown in Table 1, concordant results were obtained for 135 (93.1%) of the 145 sera; the high kappa value ($K = 0.82$) indicates excellent assays beetwent agreement. Fifty-four sera were negative and eighty-one were positive with both assays; three Liaison positives specimens gave 2 negative and one equivocal by Virclia; six were negative by Liaison but three of these were positive and the other three equivocal by Virclia; and one serum was equivocal by Liaison but negative by Virclia.

Table 2 exhibits the sensitivity and specificity values for the two assays. The sensitivity was 96.5% for Virclia and 97.6% for Liaison, a non-significant difference ($p = 0.6$). Liaison was previously reported to offer excellent sensitivity in a comparison with ELISA Enzygnost for measles diagnosis (de Ory et al., 2015). All false-negative results in our study (three for Virclia and two for Liaison) were in samples drawn early (within the first few days) after appearance of a rash; both assays showed 100% sensitivity in samples drawn more than 3 days after rash onset ($n = 75$). It has been widely reported that early serum collection produces a higher rate of false-negative IgM results (Ratnam et al., 2000; Sampedro et al., 2013).

The specificity of both assays was excellent (Table 2), with no statistically significant difference between them ($P = 0.1$). A good positive predictive value is especially important in countries with a low incidence of measles. In the present study, three false-positive results were obtained with Virclia and one with Liaison in samples from patients with EBV infections, and a false-positive was also obtained with Liaison in a sample from a patient with recent CMV. No false-positive results were obtained with Virclia or Liaison in samples from healthy individuals. In previous studies, false-positive results were reported in sera from patients with EBV, CMV, mycoplasma, or exanthematous viral infection (Ratnam et al., 2000; Thomas et al., 1999).

In summary, VirClia IgM measles is a good alternative to other immunoassays for the detection of IgM against measles. This rapid and easy-to use assay appears to be a highly useful technique for laboratory measles confirmation.

References

Dirección General de Salud Pública y Participación, Consejería de Salud, J. de A. 2011. Action plan for measles elimination in Andalusia Sevilla.

European Centre for Disease Prevention and Control, 2016. Measles and rubella monitoring, January 2016–Reporting on January 2015–December 2015 surveillance data and epidemic intelligence data until 31 January 2016.

Ratnam, S., Tipples, G., Head, C., Fauvel, M., Fearon, M., Ward, B.J., 2000. Performance of indirect immunoglobulin M (IgM) serology tests and IgM capture assays for laboratory diagnosis of measles. J. Clin. Microbiol. 38, 99–104.

Sampedro, A., Rodríguez-Granger, J., Gómez, C., Lara, A., Gutierrez, J., Otero, A., 2013. Comparative evaluation of a new chemiluminiscent assay and an ELISA for the detection of IgM against measles. J. Clin. Lab. Anal. 27, 477–480, http://dx.doi.org/10.1002/jcla.21630.

Thomas, H.I., Barrett, E., Hesketh, L.M., Wynne, A., Morgan-Capner, P., 1999. Simultaneous IgM reactivity by EIA against more than one virus in measles, parvovirus B19 and rubella infection. J. Clin. Virol. 14, 107–118.

World Health Organization, 2007. Manual for the Laboratory Diagnosis of Measles and Rubella Virus Infection, second ed. Geneva, Switzerland.

de Ory, F., Minguito, T., Balfagón, P., Sanz, J.C., 2015. Comparison of chemiluminescent immunoassay and ELISA for measles IgG and IgM. APMIS 123, 648–651, http://dx.doi.org/10.1111/apm.12413.