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A comparison of two ELISA methods for the investigation of anti-cytomegalovirus IgG antibodies

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Key words: IgG antibodies, serodiagnosis, cytomegalovirus

Abstract

The Alpha-method ELISA for detection of anti-cytomegalovirus (CMV) IgG antibodies (test 1) was compared with another ELISA technique MEIA (test 2). Samples (248 sera and 56 cerebrospinal fluid) from patients with suspected CMV infection were investigated. Discordant samples were re-analysed, undiluted, with a latex test. Positive results were considered to be true positives when there was agreement in the results from the two methods. There were fourteen discrepant samples (4.6%). The latex agglutination test confirmed eight positive for test 1 and six positive for test 2. The overall diagnostic yield of tests 1 and 2 was sensitivity, 91% and 100%; specificity, 99% and 96%; positive predictive values, 95% and 85%; and negative predictive values 98% and 100%, respectively.

Introduction

New systems have been recently introduced for the investigation of anti-cytomegalovirus (CMV) IgG antibodies, such as the Alpha-method (Behringwerke, Germany). This system has been validated only by comparison with other tests detecting other antibodies beyond those of the IgG class, such as the complement binding and latex agglutination tests (Gutiérrez *et al.*, 1994).

In the present work we compared the Alpha-method for detection of anti-CMV IgG antibodies (Enzygnost, anti-CMV IgG) with another enzyme-linked immunosorbent assay (ELISA) technique (MEIA, Abbott, U.S.A.).

Materials and methods

A total of 248 sera and 56 cerebrospinal fluid (CSF) samples from patients admitted to our hospital and with suspected cytomegalovirus (CMV) infection were investigated for the presence of IgG antibodies using the Alpha-method (in the case of CSF the assay was repeated using a second dilution of the sample, 1:40, in addition to the 1:231 dilution) and MEIA (IMX CMV; Abbott, U.S.A.) tests. Discordant samples were reanalysed, undiluted, with a latex test (CMV scan; Becton Dickinson, U.S.A.). Positive results were considered to be true positives when there was concordance in the results from the two methods.

Table 1 Correlations between the Alpha-method and MEIA test results for serum and CSF samples

Method	Serum: MEIA (+)	MEIA (-)	CSF: MEIA (+)	MEIA (-)
Alpha (+)	40	0	2	0
Alpha (-)	12	196	2	52

Results

Among the 304 samples studied there were fourteen discrepancies (4.6%). The latex agglutination test confirmed eight positive by the Alpha-method and six positive IMX results as true positives (Tables 1 and 2). The overall diagnostic yield of the Alpha-method was sensitivity, 91%; specificity, 99%; positive predictive values 95%; and negative predictive value, 98%. The corresponding data for the MEIA system were sensitivity, 100%; specificity 96%; positive predictive values 85%; and negative predictive values, 100%. The Alpha-method yielded similar results with the 1:231 and 1:40 dilutions of the samples, with the exception of two samples which were positive at the 1:40 dilution with both methods and negative at the 1:231 dilution (Tables 1 and 2).

Discussion

The ELISA test is one of the most widely used laboratory methods, because of its easy technique and acceptable sensitivity, and is therefore one of the tests most frequently used for investigating the presence of anti-CMV IgG antibodies (Doern *et al.*, 1994; Gutiérrez *et al.*, 1994; Kraat *et al.*, 1992; Kropff *et al.*, 1993; Landini, 1993; Rabalais *et al.*, 1993; Roseff and Campos, 1993; Tomiyama *et al.*, 1993; Van Zanten *et al.*, 1993).

In our experience, the two ELISA techniques had a slightly divergent behaviour, and we cannot definitely state if the new Alpha-method surpassed the MEIA system. Table 3 summarizes the technical characteristics of both systems, which may help in reaching a decision to use either one. Significantly the manufacturers do not recommend either system for the investigation of antibodies in CSF. Despite this, we decided to compare both in these types of samples.

Table 2 Samples which were discordant with the Alpha-method and MEIA tests and results of the latex agglutination test

Sample	Sample absorbance/cutoff absorbance:		Latex	Interpretation
	Alpha-method	MEIA		
Serum	Negative	10.6	(-)	Negative
Serum	Negative	4.7	(+)	Positive
Serum	Negative	4.9	(-)	Negative
Serum	Negative	5.6	(-)	Negative
Serum	Negative	4.1	(-)	Negative
Serum	3.3	(-)	(-)	Negative
Serum	Negative	10	(-)	Negative
Serum	Negative	4.5	(+)	Positive
Serum	Negative	4.7	(-)	Negative
Serum	Negative	5.5	(-)	Negative
Serum	Negative	4	(-)	Negative
Serum	4	(-)	(-)	Negative
CSF	Negative	9.6	(+)	Positive
CSF	Negative	9	(+)	Positive

Table 3 Characteristics of the Alpha-method and the MEIA system

Parameter	Alpha-method	MEIA
Minimum sample volume (µl)	20	150
Usable on CSF samples	No	No
Automated dispensation	Yes	Yes
Automated ELISA	Yes	Yes
Performing time (min)	180	45
Semiquantitative results	Yes	Yes

In one of the samples, true positive antibodies were detected by the MEIA and by the Alpha-method at the 1:40, but not at the 1:231 dilution. The reason may have been that with the latter method, and for reasons related to the antigen used, higher dilutions of the samples were needed in order to avoid false-positive reactions, as the test used an antigen from whole infected cells.

This recommendation from the manufacturer is warranted for plasma or serum samples, but in our opinion it does not hold for CSF samples, in which we observed no false-positive results when comparing the MEIA and the Alpha-methods at 1:40 dilution. However, we must stress that one serum sample yielded a false-positive result with the Alpha-method (Table 2). Both of them are useful for the investigation of antibodies in CSF samples, but a 1:40 sample dilution must be used with the Alpha-method.

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Accepted 25 June 1997

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