LIAISON® VZV IgG and VZV IgM assays: A Comparative Study

P. Huynen, P. Melin, J. Mathieu, P. De Mol – University of Liège, Department of Medical Microbiology, Liège, Belgium

Introduction

Varicella-zoster virus (VZV) belongs to the Herpesvirus family. Varicella (chickenpox) is the full-blown primary infection and zoster (shingles) is caused by the reactivation of latent VZV. Varicella and zoster are mainly diagnosed clinically because of the specificity of the symptoms, but serology plays an important role, especially in diagnosis of non-typical forms and in assessment of immunity. VZV serology is currently carried out by microplate analysers in our institute. The aim of this study was to evaluate if the LIAISON® VZV IgG and VZV IgM (DiaSorin, Saluggia, Italy), two fully automated immunoassays, based on chemiluminescence technology (CLIA) could be an alternative method, quick and easy to perform, whose performance meets our current quality requirements. We therefore performed a comparative evaluation and investigated the overall agreement between LIAISON® VZV IgG and IBL VZV IgG ELISA (Immuno Biological Laboratories, Hamburg, Germany) as well as between LIAISON® VZV IgM and Enzygnost VZV IgM ELISA (Dade Behring Enzygnost, Marburg, Germany).

Materials and Methods

The performances of **LIAISON® VZV IgG** and **IBL VZV IgG ELISA** were compared for a total of 165 selected routine serum samples from different patient categories (table 1).

Table 1

Patient categories	Nr of samples
Pregnant women	13
Patients with haematological diseases	15
Hospitalised patients	20
Teenagers	13
Not characterized	104
Total	**165**

Discordant results were solved by Euroimmun VZV IgG (Euroimmun AG, Luebeck, Germany) ELISA. The detection of VZV antibodies using IBL VZV IgG ELISA and Euroimmun VZV IgG was performed on ETI-MAX 3000 instrument, a fully automated microplate analyzer (DiaSorin).

LIAISON® VZV IgG assay is an indirect chemiluminescence immunoassay (CLIA) for the quantitative determination of specific IgG antibodies to Varicella-zoster virus in human serum or plasma samples. For interpretation of results of the LIAISON® VZV IgG assay, a cut-off value of 150 mIU/mL was used, in order to achieve the highest diagnostic specificity and sensitivity.

IBL VZV IgG ELISA is a sandwich two steps enzyme immunoassay for the qualitative and quantitative determination of IgG antibodies to VZV. The microplate wells are coated with VZV viral lysate.
The results were evaluated plotting the OD of calibrators against their concentrations and reading the concentration of the samples from the standard curve.

Table 2: interpretation of results

	LIAISON® VZV IgG	IBL VZV IgG
pos	≥150 mIU/mL	≥12 U/mL
neg	<150 mIU/mL	< 8 U/mL
eqv		8-12 mIU/mL

The performances of **LIAISON® VZV IgM** and **Enzygnost VZV IgM ELISA** were compared for a total of 160 selected routine serum samples from different patient categories (table 3).

Table 3

Patient categories	Nr of samples
Pregnant women	13
Patients with haematological diseases	15
Hospitalised patients	20
Teenagers	13
Not characterized	99
Total	**160**

Discordant results were solved by Euroimmun VZV IgM and NovaTec VZV IgM ELISA (NovaTec Immunodiagnostica GmbH, Dietzenbach, Germany), and performed on ETI-MAX 3000 instrument. The detection of VZV antibodies using the Enzygnost assay was performed on BEP III analyzer (Dade Behring).

LIAISON® VZV IgM assay is an indirect chemiluminescence immunoassay (CLIA) for the qualitative determination of specific IgM antibodies to Varicella-zoster virus in human serum or plasma samples. Results were evaluated using a cut-off Index value of 1, with a grey zone of +/- 10%.

Enzygnost anti-VZV IgM is an indirect immunoenzymatic assay for qualitative determination of IgM antibodies to VZV. The microplate wells are coated with purified VZV antigens.
The results were evaluated using a Cut Off Index.

Table 4: interpretation of results

	LIAISON® VZV IgM	Enzygnost anti-VZV IgM
pos	≥1.1 Index	sample absorbance > 0.200 OD
eqv	0.9-1.1 Index	sample absorbance 0.100-0.200 OD
neg	<0.9 Index	sample absorbance < 0.100 OD

Results

LIAISON® VZV IgG versus VZV IgG ELISA IBL

A total of 165 selected routine serum samples were tested with **LIAISON® VZV IgG** and **IBL VZV IgG ELISA**.

LIAISON® VZV IgG \ VZV IgG IBL	pos	eqv	neg	
pos	139	4	12	155
eqv	0	0	0	0
neg	0	1	9	10
	139	5	21	165

The overall agreement between LIAISON® and IBL VZV IgG assays was 89.7% (148/165).

All discordant samples (17 out of 165) were further characterized with Euroimmun VZV IgG Elisa, when the sample volume was sufficient, and a consensus between at least two out of three tests was applied.

Nr of samples	LIAISON® VZV IgG	IBL VZV IgG	Euroimmun VZV IgG	Consensus
3	pos (*)	neg	pos	pos
3	pos (*)	eqv	pos	pos
1	neg	eqv	neg	neg
3	pos (*)	neg	neg	neg
Unresolved				
1	pos (*)	eqv	neg	?
2	pos (*)	neg	-	?
1	pos (345) mIU/mL	neg	eqv	?
3	pos (*)	neg	-	?

(*) low positive value

LIAISON® VZV IgG \ VZV IgG IBL+Euroimmun VZV IgG	pos	eqv	neg	
pos	145	1	6	152
eqv	0	0	0	0
neg	0	0	13	13
	146	0	19	165

The overall agreement between LIAISON® and IBL VZV IgG assays after consensus was 95.8% (158/165).
Almost all the discordant results were close to the cut-off in each technique.
The intra- and inter- assay variation were <10% (reproducibility: 30 days; repeatability: 30 samples).

LIAISON® VZV IgM versus Enzygnost VZV IgM Behring

A total of 160 selected routine serum samples were tested with LIAISON® VZV IgM and Enzygnost VZV IgM by Behring.

LIAISON® VZV IgM \ VZV IgM Enzygnost	pos	eqv	neg	
pos	12	1	0	13
eqv	0	4	2	6
neg	10	19	112	141
	22	0	114	160

The overall agreement between LIAISON® and Enzygnost VZV IgM assays was 80% (128/160).
30 out 36 discordant samples were further characterized with Euroimmun and Novatec VZV IgM assays, when the sample volume was sufficient, and a consensus between at least two out of three tests was applied.

Nr of samples	LIAISON® VZV IgM	Behring VZV IgM	Euroimmun VZV IgM	Novatec VZV IgM	Consensus
16	neg	eqv	neg	neg	**neg (°)**
1	neg	eqv	neg	neg	**neg**
1	neg	eqv	-	-	**neg** (°)
1	neg	eqv	pos (*)	neg	**neg** (°)
1	pos	eqv	pos	-	**pos**
2	neg	pos	neg	neg	**neg**
3	neg	pos	eqv	neg	**neg** (°)
1	neg	pos	pos (*)	neg	**neg** (°)
2	neg	pos	pos	neg	**neg (§)**
Unresolved					
2	neg	pos	eqv	eqv	**?** (°)

(*) low positive value
(°) probably residual VZV IgM; high positive VZV IgG
(§) non specific or persistent VZV IgM

LIAISON® VZV IgM \ VZV IgM Enzygnost+VZV IgM Euroimmun	pos	eqv	neg	
pos	13	0	0	13
eqv	0	4	2	6
neg	2	0	139	141
	15	4	141	160

The overall agreement between LIAISON® and Behring VZV IgM assay after consensus was 97.5% (156/160).
The comparison results shows the selection of the LIAISON® VZV IgM cut-off in order to avoid the detection of residual VZV IgM.
The intra- and inter- assay variation were <10% (reproducibility: 30 days; repeatability: 30 samples).

Conclusions

The LIAISON® VZV IgG assay is a valid alternative for the quantitative detection of VZV IgG antibodies, since the kit performance was at least equivalent to that of the kits currently available on the market.
With its high specificity, the LIAISON® VZV IgM test, a fully automated method, is also a good alternative for the detection of IgM antibodies.