DEVELOPMENT AND VALIDATION OF A NEW mariPOC® INFLUENZA A VIRUS TEST WITH ENHANCED SENSITIVITY

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Introduction

mariPOC® (**Figure 1**) is an automated diagnostic test system for rapid multianalyte decentralized testing of acute infectious diseases. Most of the positives are reported in preliminary reporting phase in 20 minutes, and low positives and negatives are reported in final reporting phase in 2 hours.

mariPOC® respi test identifies 11 pathogens causing respiratory tract infections. The influenza A virus (IAV) test method of the respi test has shown 71–92% sensitivity and 98–100% specificity compared to PCR and DFA (Ivaska et al. 2013; Tuuminen et al. 2013; Sanbonmatsu-Gámez et al. 2015). Compared to lateral flow (LF) tests the mariPOC® IAV test has been shown to be more sensitive (Petrova et al. 2015). The mariPOC® IAV test has been shown to broadly detect different subtypes, including avian influenzas.

Figure 1. mariPOC® test system (ArcDia International Ltd, Finland)

Our aim was to improve the sensitivity of the IAV antigen detection test in order to bridge the sensitivity gap against PCR and DFA (direct fluorescent antibody) techniques.

Methods

A new IAV test was developed using next generation antibodies with higher affinity targeting a conserved epitope within the viral nucleoprotein.

Analytical sensitivity of the new IAV test was studied against the old IAV test with dilution series of purified seasonal IAV subtypes (H1N1, H1N1 swine and H3N2). IAV subtype recognition of the new IAV test was also studied against potentially pandemic IAV subtypes (H2N2, H5N1, H7N3, H7N9 and H9N2).

The performance of the new IAV test was studied against a LF test (CerTest Biotec, ZV862001P) with 198 frozen nasopharyngeal aspirates that were leftovers from routine diagnostics (ISLAB, Finland). The samples were collected during the influenza season of 2015–2016. The samples were pretreated and analysed according to manufacturers' instructions. The LF results were analysed blind by two persons. Samples with discrepant results were resolved using PCR and/or DFA.

Results

The new mariPOC® IAV test showed one order of magnitude better analytical sensitivity (1.5 ng/mL for H1N1) than the old IAV test with seasonal IAV subtypes (**Table 1**). The improvement in sensitivity was most remarkable with H1N1 swine influenza, for which the new test was about 30-fold more sensitive. The new IAV test was confirmed to also detect all the other tested IAV subtypes with high sensitivity.

Table 1. Qualitative results for comparison of the old and new mariPOC® IAV tests with dilution series of seasonal IAV subtypes. Viral samples had different stock concentrations.

H1N1

Dilution factor	Old	New
16 000	+	+
32 000	+	+
64 000	-	+
128 000	-	+
256 000	-	+
512 000	-	-
	8x difference	

H1N1 swine

Dilution factor	Old	New
25	+	+
50	+	+
100	-	+
200	-	+
400	-	+
800	-	+
1 600	-	+
3 200	-	-
	32x difference	

H3N2

Dilution factor	Old	New
1 000	+	+
2 000	+	+
4 000	-	+
8 000	-	+
16 000	-	+
32 000	-	-
	8x difference	

In the retrospective study, the new mariPOC® IAV test detected 13 IAV true positive clinical samples and no false positives (**Table 2**). The new IAV test found 30% more positives compared to the LF test (10 positives). Specificities for the mariPOC® IAV test and the LF test were 100% (185/185) and 96% (178/185), respectively.

The new IAV test was more sensitive than the LF test already in the preliminary reporting phase, where it reported 85% (11/13) of the final positives.

Table 2. Comparison of the new mariPOC® IAV test and the LF test in a nasopharyngeal sample cohort.

		LF test		
		Positive	**Negative**	**Total**
mariPOC®	**Positive**	10	3*	13
	Negative	7**	178	185
	Total	17	181	198

*confirmed as true positives with PCR/DFA

**confirmed as false positives with PCR/DFA

Conclusions

The analytical sensitivity of the new mariPOC® IAV test was enhanced by at least an order of magnitude. The test showed broad subtype recognition, suggesting that it is likely able to detect any new arising pandemic variants. It was significantly more sensitive and specific than the LF test. Although the number of IAV positive samples was small, our results indicate that the newly launched IAV test enables the detection of seasonal as well as pandemic subtypes with improved sensitivity. The magnitude of the improvement suggests that the new IAV test considerably bridges the clinical sensitivity gap to PCR.

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