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Direct comparison of the Cobas® Liat® System for Influenza A/ B and Respiratory Syncytial Virus with the FastTrack Respiratory syndromic panel on the Roche FLOW system utilising Sigma Virocult® transport media and nasal pharyngeal aspirates

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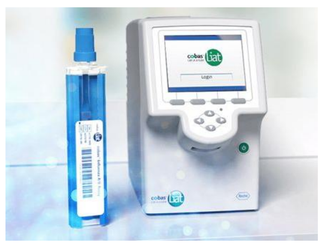
Introduction

Influenza is a significant cause of morbidity and mortality worldwide. Although the diagnosis is often made by clinical signs and symptoms alone, laboratory testing is often needed to guide therapy, determine isolation triaging and provide epidemiologic data. Until recently, point-of-care diagnostic testing has been limited to rapid antigen tests based on chromatographic immunoassay technology, however, this technology has been hampered by lack of sensitivity and specificity.

The Cobas® Liat® System is a fast, easy-to-use, compact PCR system designed for on-demand testing in point-of-care settings. The system is an automated multiplex real-time RT-PCR assay for the rapid in vitro qualitative detection of Influenza A (Flu A), Influenza B (Flu B) and Respiratory syncytial virus (RSV). The assay targets a well-conserved region of the matrix gene of Influenza A, the non-structural protein gene of Influenza B and the matrix gene of RSV with an Internal Process Control (IPC) also included.

In this study, we compared the performance of the Roche Liat versus our routine influenza A and B tests; RSV that are part of the Roche FLOW respiratory panel utilizing the Fast Track Diagnostics (FTD) RESP 21 CE marked multiplex PCR assay with 100 respiratory samples collected in 3 ml Sigma Virocult Medium. To our knowledge, this is the first published direct comparison of the performance characteristics of the Roche FLOW (Fast-Track) and Liat influenza A & B/RSV.



Cobas® Liat ® System

Roche FLOW system

Methods

Clinical specimens. A total of 100 respiratory specimens collected in 3 ml of Sigma Virocult medium (Medical Wire & Equipment) were used in the study. The specimen types included 80 nasopharyngeal swabs, 10 nasal aspirates, and 10 bronchoalveolar lavage (BAL) fluid sample. Specimens were collected from 70 adult patients from 19 to 85 years of age and 30 pediatric patients from 1 month to 10 years of age seen in a variety of outpatient through the A&E setting (70 samples) and inpatient (30 samples) locations.

Study design. The gold standard method utilized was the FTD RESP 21 multiplex PCR assay on the Roche FLOW. The Fast Track Diagnostics (FTD) RESP 21 CE marked multiplex PCR assay comprised of influenza A (FA), influenza A (H1N1), influenza B (FB), coronaviruses NL63, 229E, OC43 and HKU1 (C63, C229, C43, HKU), parainfluenza 1,2,3,4, (PF1,2,3,4), human metapneumovirus A and B (MPV), rhinovirus (RHI), respiratory syncytial viruses A and B (RSV), adenovirus (ADE), enterovirus (ENT), parechovirus (PARE), bocavirus (BOCA) and Mycoplasma pneumoniae (MYCO) including internal control (IC) (Equine arteritis virus).

Sigma Virocult ®

It is currently tested on the Roche FLOW system that includes 2x Hamilton liquid handlers – one for Specimen Handling (PSH) and one for PCR Set-up (PSU) which can be used interchangeably, 2x Roche MagNA Pure 96 (MP96) instruments for automated nucleic acid extraction and 2x Roche Light Cycler 480 II (LC480) Real-Time PCR platforms for amplification and detection.

Where possible, prospective samples were used however where insufficient numbers of Influenza/RSV cases were observed the study was supplemented with archived material for positive samples. These samples were subjected to one freeze thaw cycle and retested concurrently by a single biomedical scientist using a single Roche FLOW line and a single Liat instrument in the clinical laboratory.

In total, 20 influenza A virus (10-2009 H1N1; 5- seasonal H1 and 5- A no subtype), 20 influenza B virus and 20 RSV positive samples were tested. A negative cohort of 40 samples were also analysed. Within the 40 negative cohorts five Rhinovirus positives samples were run through to ensure no cross reactivity existed.

Results

The results of the two nucleic acid amplification tests for detection of influenza A & B virus as well as RSV are shown in table 1. The sensitivities of the Roche Liat test was 100% and the specificity 100% compared to the Roche FLOW system utilising the Fast-Track designed assay.

Table 1: Comparison of Cobas FLOW system and Roche Liat for detection of influenza A & B and RSV utilizing Sigma Virocult.

	Cobas FLOW system			Cobas LIAT		
cycle threshold range value	Influenza A	Influenza B	RSV	Influenza A	Influenza B	RSV
20-29	10	10	10	10	10	10
30-34	5	5	5	5	5	5
35-38	5	5	5	5	5	5
Detected	20	20	20	20	20	20

Within the 40 negative cohorts five Rhinovirus positives samples were run through to ensure no cross reactivity existed.

Table 2: Summary of sensitivity and specificity of the Roche Liat compared to the Roche Flow with the Fast- Track designed assay

Instrument	Influenza A	Influenza B	RSV	Combined Positives	Negative
Roche Liat	20/20 (100%)	20/20 (100%)	20/20 (100%)	60/60 (100%)	40/40 (100%)

Conclusion

The Roche Liat hold promise to significantly improve near-patient diagnostic testing for influenza and has since its implementation facilitated true practice changes in how clinicians manage these patients in the emergency department at St Georges University Hospital in London.

Validating the performance parameters of the Sigma Virocult means continued use of a common collection system currently in place throughout the South West sector of London and the availability of additional specimens without having to collect additional samples for subsequent testing, which may be necessary to clarify respiratory diagnoses, such as coinfections, or address specific infection control requirements

The study demonstrated that the sigma Virocult transport media achieved a 100% sensitivity and specificity when compared to the Roche FLOW system. The prescriptive nature of the package inserts should be adjusted to reflect a wider range of collection devices and certainly include that of the Sigma Virocult (VTM) used extensively across the European market.

Discussion

Although rapid influenza virus antigen testing was available in the St Georges University Hospital adult emergency department as well as in the Croydon Pediatric setting the physicians in these locations rely more heavily on the centralized laboratory based testing on the Roche FLOW system as a primary test because of the poorer sensitivity of rapid antigen tests.

The roll-out of the Roche Liat's at various ED departments which SWLP serves has impacted significantly on the clinicians reliance/confidence in the result. Since its implementation it has facilitated true practice changes in how clinicians manage these patients in the emergency department at St Georges University Hospital in London. Dedicated Flu wards were set-up allowing the triage of patients direct to these wards from the ED setting.

Although Roche has only validated the Copan UTM for this device this study demonstrates the widely utilized Sigma Virocult device is compatible. The ED setting is a high charged area where suppliers must recognize time savings for medical or nursing staff and less confusion in collection device selection when fewer collection devices are being used. This results in time savings for ED staff (fewer samples to access and handle for individual investigations), and patient comfort improvement (multiple sample collection can be avoided). A collection device for several investigations also guarantees quality due to the uniformity of the sample and standardization of procedures (Fontana *et al*., 2013). The flexibility of collection device as demonstrated gives clinicians and laboratorians more flexibility for viral testing. Ease of operation, test complexity, and flexibility are important factors when considering when considering deploy in near-patient locations.

References

Fontana C, Favaro M, Favalli C. (2013). How Liquid Based Microbiology Can Change the Workflow in the Microbiology Laboratories. Advances in Microbiology, Vol. 3, pg. 504-510.

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