Clinical Evaluation of the Investigational 3M™ Rapid Detection RSV Test

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CLINICAL EVALUATION OF THE INVESTIGATIONAL 3M™ RAPID DETECTION RSV TEST

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BACKGROUND and AIMS OF STUDY

Easy to use immunochromatographic methods for the detection of respiratory syncytial virus (RSV) can provide clinicians with rapid results. The specificities of the tests are generally good when used during RSV season, but the tests can lack sufficient sensitivity. Therefore, continued improvement of these test methods are desirable. The Investigational 3M™ Rapid Detection RSV Test (3M Health Care, St. Paul, MN) is a qualitative immunochromatographic cartridge test. The test utilizes fluorescent-dyed particles coated with anti-RSV antibodies that bind to RSV antigens, if present in the sample. Detection is performed using the 3M™ Rapid Detection Reader.

The aims of this study were:

1.) To evaluate the Investigational 3M™ Rapid Detection RSV Test for the direct detection of RSV in clinical respiratory samples.

2.) To compare the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the 3M Test to direct fluorescent antibody staining (DFA)(D3 Ultra, Diagnostic Hybrids, Athens, OH), R-Mix culture (Diagnostic Hybrids) and to the BinaxNOW RSV Test (Inverness Medical, Waltham, MA).

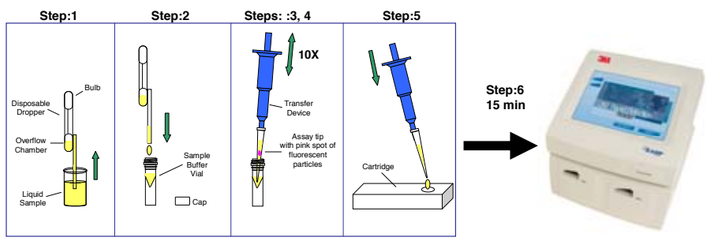
MATERIALS and METHODS

Specimens: A total of 423 respiratory specimens (nasopharyngeal (NP) aspirates, NP washings, NP swabs in universal transport media) submitted for routine viral culture and DFA were tested in this study. After discounting samples QNS for DFA (n=77), inappropriate samples tested (n=3) and samples too viscous to give a valid 3M result (n=5), the final number of samples included in the analysis (valid results for all 4 assays) was 338.

Methods:

1) Neat sample was used to perform both the 3M and BinaxNOW tests, according to the respective manufacturer's instructions.
2) Each specimen was then centrifuged to obtain NP cells to perform DFA for influenza A, B, RSV, adenovirus, parainfluenza 1, 2, 3, and hMPV.
3) The supernatants were micro-filtered and used to inoculate R-Mix trays. R-Mix cultures were performed according to validated laboratory procedures.

3M Influenza A and B Test Format



1. Place the disposable dropper in the liquid sample. Squeeze and release the bulb such that a visible amount of sample flows into the overflow chamber.
2. Remove the cap from the sample buffer vial and dispense the sample into the sample buffer vial. Sample will remain in the overflow chamber.
3. Place a new assay tip on the transfer device.
4. Insert the assay tip into the sample buffer vial and slowly press and depress the transfer device 10 times to mix in the fluorescent particles.
5. Transfer the mixture of sample and fluorescent particles into the cartridge well.
6. Insert the cartridge into the reader.

RESULTS: Samples Types by Age and Result

Sample Types by Age

Sample Type	Patient Age				Total Tested
	<6 yr	6 to 21 yr	22 to 59 yr	≥60 yr	
Nasal Wash/Aspirate	59	7	0	1	67
NP Aspirate	79	8	0	0	87
NP Swab	50	26	55	53	184
Total	189	40	55	54	338

Distribution of all samples tested by types and age groups

Sample Type by Age (RSV+)

Sample Type	Patient Age				Total Tested
	<6 yr	6 to 21 yr	22 to 59 yr	≥60 yr	
Nasal Wash/Aspirate	22	1	0	0	23
NP Aspirate	29	1	0	0	30
NP Swab	23	2	3	4	32
Total	74	4	3	4	85

Distribution of all RSV positive samples by types and age groups

RESULTS: 3M™ Rapid Detection RSV Test Results

Age group	Distribution of Results by Age and Specimen Type															
	<6 yr				6-21 yr				22-59 yr				>60 yr			
Sample Type	TN	FN	TP	FP	TN	FN	TP	FP	TN	FN	TP	FP	TN	FN	TP	FP
Nasal wash/asp	37	2	20	0	5	0	1	1	0	0	0	0	1	0	0	0
NP aspirate	50	5	24	0	7	0	1	0	0	0	0	0	0	0	0	0
NP swab	27	1	22	0	23	0	2	1	49	2	1	3	47	2	2	2
Total	114	8	66	0	35	0	4	2	49	2	1	3	48	2	2	2

TN: true negative; FN: false negative; TP: true positive: FP: false positive

RESULTS: Sensitivity, Specificity, PPV, NPV

< 6 yr	Sensitivity	Specificity	PPV	NPV
DFA	100%	100%	100%	100%
R-Mix culture	64%	100%	100%	81%
BinaxNOW RSV	61%	100%	100%	80%
3M Rapid RSV	89%	100%	100%	93%

All ages	Sensitivity	Specificity	PPV	NPV
DFA	100%	100%	100%	100%
R-Mix culture	65%	100%	100%	89%
BinaxNOW RSV	59%	99.6%	98%	88%
3M Rapid RSV	86%	97%	91%	95%

PPV: positive predictive value; NPV: negative predictive value

RESULTS: 3M and BinaxNOW Analytical Sensitivity

Dilution	RSV Dilution Series													
	1:5		1:10		1:15		1:20		1:30		1:40		1:50	
	Pos/test[a]	% Pos[b]	Pos/test	% Pos	Pos/test	% Pos	Pos/test	% Pos	Pos/test	% Pos	Pos/test	% Pos	Pos/test	% Pos
Sample 1 3M RSV	5/5	100%	0/5	0%	0/5	0%	NA		NA		NA		NA	
3M mean value (Neat = 19,128)	3261		2320		1722									
Sample 1 BinaxNOW	0/5	0%	0/5	0%	NA		NA		NA		NA		NA	
BinaxNow Read (Neat = very weak)	NEG													
Sample 2 3M RSV	5/5	100%	5/5	100%	5/5	100%	5/5	100%	5/5	100%	5/5	100%	0/5	0%
3M mean value (Neat = 32,341)	ND		8330		6654		4666		3167		2872		2106	
Sample 2 BinaxNOW	5/5	100%	5/5	100%	0/5	0%	0/5	0%	NA		NA		NA	
BinaxNow Read (Neat = pos band)	ND		VW		NEG		NEG							

3M Test: Add 150 µl to buffer, mix and add 75 µl to test cartridge

BinaxNOW is tested with 100 µl neat sample

a. Number positive/number tested; b. Percent positive; POS = positive; NEG = negative; VW= very weak band; NA = not applicable. When indicated 5 replicates of serial dilutions of two RSV positive clinical samples were tested in parallel with the 3M and BinaxNOW Tests. Positive 3M Test cut off value =2500.

SUMMARY AND CONCLUSIONS

- Overall, the 3M™ Rapid Detection RSV Test demonstrated superior sensitivity for the detection of RSV (86%) as compared to the BinaxNOW RSV Test (59%) and to R-Mix culture (65%).
- Comparable results were obtained for specimens collected from children < 6yr.
- The only noted difference between age and specimen type was a lower sensitivity for NP swabs tested from patients >21 yr.
- The 3M Test was less sensitive than DFA. However, there were 77 samples for which no DFA result was obtained due to insufficient cellular material. The 3M Test detected RSV in 3 of the 77 QNS samples. For 2 samples R-Mix(+), RSV reporting was delayed for 24 hr and a RSV(+) diagnosis would have been missed for one sample R-Mix(-).
- A few highly mucoid samples were unable to flow properly through the test cartridge and required diluting the samples with UTM.
- False positives were noted in 7 samples.
- The analytical sensitivity of the 3M Test was greater than BinaxNOW, despite the fact that the final sample volume tested in the 3M Test cartridge is 75 µl (containing 37.5 µl of sample) as compared to 100 µl for BinaxNOW.
- The easy to use reader and printer provided documentation of instrument quality control and test results. The automated reading of test results eliminated the potential for user misreading or misinterpretation of test results.

REFERENCES

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