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Background

- Point-of-care rapid antigen detection tests for Group A Strep (GAS) have a limited sensitivity of ~85% with some variability.
- Current guidelines recommend confirming negative results with a backup test in children; this two-step process adds additional time, costs and risk of lost patient follow-up.
- The Alere i Strep A is a new isothermal nucleic acid amplification test, with results in ~8 minutes in a point-of-care (POC) setting.

Objective

To evaluate the performance of the Alere™ i Strep A in comparison to bacterial culture as a reference standard, with PCR adjudication for discrepant results.

Figure 1: Overview of the Alere™ i Strep A



Methods

- Subjects** Prospectively enrolled at 10 sites: Emergency Departments (EDs), Urgent Cares (UCs) and Offices, from Jan – Mar 2014. Inclusion: sore throat, stigmata of pharyngitis, assent/consent. Exclusion: antibiotic use < 2 weeks, enrolled in a drug trial, vulnerable populations. With IRB approval, 2 throat swabs collected per subject.
- Alere i Strep A** Run by untrained test operators in a CLIA waived setting (schematic Fig. 1).¹ Controls (+/-) were processed daily prior to enrollments. Results were considered invalid given 2 failed attempts.
- Reference testing** A central lab performed standard bacterial throat culture, with discrepancies adjudicated by real-time polymerase chain reaction (PCR) using the PrimerDesign™ genesig Kit.
- Statistical analysis** Summary statistics of demographics and clinical characteristics were calculated. Data were summarized in 2x2 tables with the number of specimens in 4 categories: true positive (TP), true negative (TN), false positive (FP) and false negative (FN). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) and their associated confidence intervals (CIs) were determined based on calculated proportions, by the Wald method. Fisher's exact test was used to test the associations. SAS© statistical software (version 9.3).

Results

505 subjects were enrolled: 24 excluded of whom 14 had invalid results (2.8%). 481 subjects were analyzed: median age of 11 (7-19 IQR) years; 355 (74%) children < 18 years; 299 (62%) female, 222 (46%) from ED/UC. The prevalence of GAS by culture was 35% in children and 14% in adults. The overall sensitivity and specificity of the Alere™ i Strep A was 96% and 95%, respectively. Discrepant results (n = 24) adjudicated by PCR, resulted in a sensitivity and specificity of the Alere™ i Strep A of 99% and 99%, respectively. (Table 1). No differences were found based on age or setting (ED/UC versus Office), Fischer's exact test.

Table 1: Detection of GAS by Alere™ i Strep A in comparison with culture and after adjudication by RT-PCR (PCR*)

<18 years old

	TP	FP	TN	FN	Total	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Culture	123	15	212	5	355	96 (93-100)	93 (90-97)	89 (84-94)	98 (96-100)
PCR*	134	4	215	2	355	99 (97-100)	98 (96-100)	97 (94-100)	99 (98-100)

≥18 years old

	TP	FP	TN	FN	Total	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Culture	18	3	104	1	126	95 (85-100)	97 (94-100)	86 (71-100)	99 (97-100)
PCR*	20	1	105	0	126	100 (100-100)	99 (97-100)	95 (86-100)	100 (100-100)

All Ages

	TP	FP	TN	FN	Total	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Culture	141	18	316	6	481	96 (93-99)	95 (92-97)	89 (84-94)	98 (97-100)
PCR*	154	5	320	2	481	99 (97-100)	99 (97-100)	97 (94-100)	99 (99-100)

Discussion

- The Alere™ i Strep A has excellent test characteristics compared to culture and with PCR adjudication for discrepant results.
- The test is performed by clinical staff with results available in ~8 minutes at the point-of-care.
- The test is more sensitive than rapid antigen tests² and faster than other nucleic acid amplification tests³
- As with all other tests for GAS pharyngitis, colonization can not be differentiated from infection.
- The test had excellent negative predictive value, despite the relatively high prevalence of GAS in this study
- Overall, the Alere™ i Strep A has excellent performance and could obviate the need for backup testing.⁴

References

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