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Comparing tests for Group A Streptococcus bacteria in children with throat infections

Submission date	Recruitment status	[_] Prospectively registered
11/09/2018	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
16/10/2018	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
24/02/2020	Infections and Infestations	

Plain English summary of protocol

Background and study aims
Strep A (Streptococcus pyogenes) is a bacterium that commonly causes a sore throat in humans. Some people who get Strep A infections have complications affecting other organs, such as the heart or kidneys, as a result. It is important for physicians to have tests to help them determine which patients have Strep A so they can treat them correctly with antibiotics. The aim of this study is to compare the cobas Liat Strep A test (a test for bacterial DNA that can be performed at the site of patient care) with the rapid antigen detection test (which tests for proteins or carbohydrates in the bacteria) currently used by physicians, and laboratory testing using bacterial culture (growing the bacteria) to confirm that negative results are correct. The study will look at the ability of the tests to correctly classify patients as positive or negative for Strep A infection. The study will also look at differences in the treatment and management by physicians based on the test results.

Who can participate?
Children aged 3 to 18 years with symptoms of Strep A infection. These include throat pain, difficulty swallowing, red and swollen tonsils, swollen and tender lymph glands (nodes) in the neck, fever, headache, fatigue.

What does the study involve?
Two throat swabs will be taken from each participant. All patient samples will be tested using all of the diagnostic methods in the study. Patients will be divided into two groups. One group will be managed by the clinician after the result of the antigen test is given. The other group will be managed by the clinician after the result of the DNA test is given. The study will alternate the test result given on a weekly basis to divide the patients into the two groups.

What are the possible benefits and risks of participating?
Participants in the DNA test group will have the benefit of the physician using a test result that is more likely to be correct and not have to wait several days for the laboratory test.

Where is the study run from?
The study is run at a single large primary pediatric care clinic within the Baylor Scott and White integrated system located in the suburbs of Austin, TX (Scott and White Round Rock Clinic, 7 providers, 100 to 150 patients per day).

When is the study starting and how long is it expected to run for:
The study will start in September 2016 and is expected to run for 6 months.

Who is funding the study?
This study is sponsored by Roche Molecular Systems Inc, the company that sells the cobas® Liat Strep A DNA test.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
LIAT-STP-407

Study information

Scientific Title
Diagnosis and antibiotic treatment of GAS pharyngitis in children in a primary care setting

Acronym
Strep A_POC_Pediatric

Study objectives

Rapid antigen detection tests (RADT) and bacterial culture are the current standard of care for diagnosing Group A Strep in pediatric patients. Polymerase Chain Reaction (PCR) tests offer improved turn-around-times at the point-of-care (POC) or in the laboratory. PCR has demonstrated improved sensitivity over reference culture in previous studies. The study hypothesis is that POC PCR has high sensitivity and specificity and rapid turnaround times, and leads to more appropriate antibiotic use.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Baylor Scott & White Institutional Review Board (Temple, TX), April 2016, IRB Submission Reference 056357

Study design
Prospective open-label single-center study

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Pharyngitis due to group A Streptococcus infection

Interventions
A primary care site will be selected based on patient population (pediatric) and workflow. The site will execute the standard-of-care Strep A rapid antigen detection test (RADT) with bacterial culture to confirm negative results. This takes several days to produce a result. The standard of care for the site is consistent with the IDSA Guidelines: Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis.

For the study, the cobas® Liat Strep A assay (POC PCR) will also be used at the POC. Strep A RADT tests are easy-to-use POC tests that provide results in ~5 minutes. The person's throat is first swabbed to collect a sample of mucus. The swab is inserted into the lateral flow test and the reagent is manually added. A positive result is signified by a visible pink test line and is visually read for interpretation. For a negative results a confirmatory bacterial culture test is recommended.

POC PCR tests are only recently available and provide lab quality results in ~15 minutes. The person's throat is first swabbed to collect a sample of mucus. The swab is inserted into collection media. 200 microl of the collection media is added to the test tube with the disposable pipette included in the kit. The tube is inserted into the PCR machine for amplification and analysis. The device reports positive or negative results automatically. Confirmatory culture is not recommended.

Two simultaneous throat swab specimens will be collected from patients who present with symptoms characteristic of Strep A pharyngitis and who have provided written informed consent. One swab will be used for the Quidel QuickVue RADT point-of-care (POC) test, the

other swab will be used for the cobas® Liat Strep A assay nucleic acid amplification technique (NAAT) POC test and then transported to the lab for bacterial culture and stored for confirmation with sequencing if needed.

For the intervention, the site will alternate on a weekly basis which POC result will be used to manage patients. The second result will be blinded to the site. Hence, one week RADT will be used, the next week POC PCR, the next week RADT, etc. This will randomize the patients to the RADT or POC PCR arm of the study. Bacterial culture will be conducted for all patients to confirm positive POC tests in addition to confirmatory testing for negative POC results.

Chart review will be conducted to collect patient management data. Follow-up timeline is after culture results have been received (2-5 days post initial visit). Analytical performance between assays and a laboratory based nucleic acid amplification test, (using DNA sequencing to adjudicate discrepancies) will be calculated . The impact on appropriate patient management (antibiotic prescription) will be compared between the two arms (RADT and POC NAAT).

Intervention Type
Other

Primary outcome(s)
Diagnostic test results will be recorded by the site staff at the time of testing for POC tests and weekly for laboratory-based tests. The overall sensitivity, specificity, and percentage agreement between the different testing methods and the respective 95% CIs (via Clopper–Pearson, exact) will be calculated by using the laboratory-based Quidel Solana GAS NAAT test as the reference method. All discordant results will be adjudicated with bidirectional sequencing.

Key secondary outcome(s))
1. Anti-infective prescriptions assessed using the patient's electronic medical record at time of first visit and after the bacterial culture result is available
2. Additional tests ordered, assessed using the patient's electronic medical record at time of first visit and after the bacterial culture result is available
3. Follow-up appointments scheduled, assessed using the patient's electronic medical record at time of first visit and after the bacterial culture result is available

Completion date
02/10/2017

Eligibility

Key inclusion criteria
1. Aged 3–18 years
2. Clinical signs and symptoms of GAS pharyngitis, defined as the presence of sore throat and at least one other symptom (redness of the posterior pharyngeal wall, pharyngeal or tonsillar exudate, tonsillar swelling, tender cervical lymphadenopathy, and/or fever >100°F)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
3 years

Upper age limit
18 years

Sex
All

Total final enrolment
255

Key exclusion criteria
Treated with antibiotics currently or within the previous 7 days

Date of first enrolment
26/09/2016

Date of final enrolment
01/01/2017

Locations

Countries of recruitment
United States of America

Study participating centre
White Round Rock Clinic (Baylor Scott & White Health's)
Austin
United States of America
78665

Sponsor information

Organisation
Roche Molecular Systems Inc

ROR
https://ror.org/011qkaj49

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available upon request from Joanna Sickler (joanna.sickler@roche.com). The raw data spreadsheet including fields used for analysis will be available from October 2018 to September 2020. The data will be available to researchers conducting a formal study confirmed by a protocol, to enable meta-analysis and other types of analysis to answer future research questions. The trial participants consented to inclusion in the study and all data is de-identified.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	16/01/2019	24/02/2020	Yes	No
Abstract results	results presented at ID Week	04/10/2017		No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes