Research brief

RAPID ANTIGEN DETECTION TESTING FOR DIAGNOSIS OF GROUP A STREPTOCOCCUS (GAS) IN CHILDREN

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Keywords

Group A streptococcus (GAS), pharyngitis, rapid antigen detection testing (RADT), rheumatic fever.

Aim

THE AIM of this study was to evaluate the use of rapid antigen detection tests to provide timely service for diagnosis and treatment of group A streptococcus (GAS) positive results for children experiencing pharyngitis symptoms. Using rapid antigen detection testing for GAS, as part of diagnostic screening, may be an effective intervention to reduce rheumatic fever hospital admission rates in Aotearoa New Zealand.

Background

Rheumatic fever is an autoimmune disease evolving from a GAS pharyngitis infection (Sika-Paotonu et al., 2017). It is a serious, potentially life-threatening illness and is preventable with early detection and intervention. The most severe complication of rheumatic fever is rheumatic heart disease, which can cause inflammation and scarring of the heart valves (Sika-Paotonu et al., 2017). The Ministry of Health is concerned about rates of rheumatic fever among Māori and Pacific children, which result from the complications of untreated or undiagnosed GAS pharyngitis (Ministry of Health, 2019).

Current practice test for GAS testing involves taking throat swabs from students with sore throats, which are sent to the nearest laboratory for culture. The advantage of sending a throat culture to the laboratory is the ability to detect GAS from small amounts of bacteria on the swab. A limitation of this approach is the waiting time for results, which can take three to five days (Cohen et al., 2013). The waiting time for throat-swab results puts the student and close contacts at risk of spreading GAS pharyngitis infection. In most cases, by the time the results have been received, it is inevitable the infection has spread to close contacts and household family members. School principals are also concerned about the spread within classrooms to classmates and teachers. To reduce transmission, some schools in South Auckland have adopted a policy (guided by the Ministry of Health [2018] recommendations) that students are excluded from school until well and have received antibiotic treatment (from their general practitioner or Mana Kidz Nurse) for at least 24 hours before returning to school.

Bringing in an alternative diagnostic tool such as a rapid antigen detection test (RADT) could improve service delivery and the treatment regime. RADT detects the presence of strep A antigen on a throat-swab specimen and provides GAS results within five to 25 minutes (Ngaio Diagnostics, 2019). Ngaio Diagnostics (2019) argues the RADT has high sensitivity (correctly detecting 95.1 percent of patients with infection) and specificity (correctly detecting 97.8 percent of patients who do not have an infection), and that it has overall accuracy of 97.1 percent. The use of point-of-care testing allows for the best treatment decisions to be made at the time of the consultation, thus saving time, reducing referrals and increasing the efficiency of patient care (American Academy of Paediatrics, 2012; WHO, 2017).

Methods

For this study, meta-ethnography was the approach used to synthesise the findings of published research on this subject. Meta-ethnography uses an interpretive approach to research synthesis, combining and translating the findings of primary studies in ways that preserve the context and concepts in the original studies, but at the same time offers new interpretations of them (Lockwood & Hannes, 2011).

Primary qualitative research articles were searched using key search terms “RADT”, “GAS pharyngitis”, “throat culture”, “streptococcal infection”, “diagnostics and antibiotic prescription”, “rheumatic fever”, and “children”. Search phrases included “point-of-care tests”, “pharyngotonsillitis”, “acute sore throat”, “strep throat”, “pharyngitis”, “streptococcus pyogenes”, “respiratory tract infection”, “rheumatic heart disease”, “acute rheumatic fever microbiology test”, “bacteriology”, “paediatrics” and “child/teens”. Infants (birth to 23 months) and adults (19-plus years) were excluded to target the age range where rheumatic fever is predominant. The articles sourced for the synthesis were published in the Scopus, Medline (OVID), PubMed, Science Direct, Cochrane, Gale, CINAHL, Google Scholar, BMJ, Clinical Key and DOAJ databases.

Using the CASP critical appraisal tool for qualitative studies, the articles selected were evaluated to determine eligibility for inclusion. Twenty-nine studies met the inclusion criteria. The lead researcher then read and evaluated each article to follow France et al’s (2019) process of finding themes in the research studies, translating them into concepts then amalgamating these to reach new interpretations of the material.

Findings

This review found there were advantages to using RADT for GAS infection – these included reducing the spread of GAS infection and reducing rheumatic fever admission rates. The synthesis of the studies identified three key elements: *closure of time gaps*; *antibiotic stewardship*; and *quality assurance*.

Closure of time gaps

RADT reduces time gaps in GAS testing and treatment. The optimised time period to treat a GAS infection safely with antibiotics is nine days before the possible onset of rheumatic fever (Clerc & Greub, 2010). Studies from the United States (US) (Gieseker et al., 2003), Turkey (Küçük et al., 2014), Poland (Stefaniuk et al., 2017), and New Zealand (Upton et al., 2015) found that using RADT reduces the incidence of rheumatic fever through rapid turnaround in detecting GAS-positive pharyngitis. Transmission rate is thus reduced in school classrooms, homes and community settings (Ehrlich et al., 2002). RADT proved a suitable alternative for young, uncomplicated clients who had difficulty accessing their GP at the time of symptom onset (Papastergiou et al., 2018).

RADT testing is more cost-effective than throat swabbing, with fewer processing steps, which reduces service costs (Edmonson & Farwell, 2005; Ehrlich et al., 2002). Internationally, physicians acknowledged that using RADT reduced the waiting time for diagnosis and treatment as results were gained in one consultation (Gieseker et al., 2003; Orda et al., 2016). However, a small minority of practitioners said consultation times were lengthy, because they had to carry out a diagnostic test, physical assessment and treatment all in one consultation (Bourbeau, 2003). Bulk throat swabbing for RADT was not an option as each test needed to be acted on before the child left the clinic (Bourbeau, 2003). Practitioners noted the test was reasonably simple to use and, with practice, they would become more proficient in its use, which would reduce consultation time (Bourbeau, 2003).

Antibiotics stewardship: The need to accurately prescribe antibiotics is essential to antibiotic stewardship (Al-Najjar & Uduman, 2007), and RADT helps general practitioners accurately prescribe antibiotics (Alp et al., 2018; Bulut et al., 2020; Ehrlich et al., 2002). Misuse of antibiotics can contribute to bacterial resistance, therapeutic failure and adverse effects, such as drug toxicity and drug interaction (Llor et al., 2014). Having visual results from the RADT also helped reinforce to practitioners when antibiotic treatment was not required, and helped them reassure clients of this more quickly, than if they were relying on clinical signs and symptoms alone (Al-Najjar & Uduman, 2007). However, some prescribers were reluctant to use the RADT as a differential diagnostic tool, and gave antibiotics based on their own clinical assessment (Leydon et al., 2013), or their judgement that all bacterial infections should be treated with antibiotics (Gröndal et al., 2015; Hedin et al., 2014).

The stopping and starting of antibiotic treatment can create a culture of overuse and misuse (Llor et al., 2014). RADT can prevent this by confirming a result at the time of the initial consultation.

Quality assurance: Quality assurance measures include the implementation of appropriate clinical policies and procedures to ensure RADT tests are used for the right person at the right time and in the right context (Luo et al., 2019). Quality assurance is essential to ensure RADT is used as recommended. Barakat et al (2019) observed that children who have been treated for recent GAS pharyngitis might give a false positive RADT that is rarely seen in children not recently treated. The false positive RADT may be caused by the presence of non-degraded antigenic proteins that stay even in the absence of viable GAS in the pharynx (Barakat et al., 2019). This study found children five years and under had significantly higher false positives than older children. It concluded that RADT testing should be reserved for children who had not been treated for a GAS infection in the previous 28 days (Barakat et al., 2019).

Gieseker et al (2003) said that RADT GAS-negative results in children should be backed up with laboratory throat culture to ensure an accurate result. The American Society of Infectious Diseases (American Academy of Paediatrics, 2012) recommends all RADT GAS-negative results in children should be followed up with laboratory testing.

The need for space to perform RADT testing is critical to its introduction and success in practice (Gazzano et al. 2016). The development of RADT training workshops for practitioners is beneficial, as the person performing the test is a crucial to its success and accuracy (Gazzano et al. 2016). According to Gazzano et al, practitioners agreed that training was essential to ensure competency. RADT training should align with the manufacturer's diagnostic guidelines (Bourbeau, 2003).

Conclusion

This synthesis of research studies found that RADT testing improved outcomes for children with illness associated with GAS infection. It also decreased the severity of illness by allowing early intervention with antibiotics. The introduction of RADT testing may help reduce some of the barriers that exist in the current throat-swabbing practice, and in turn may reduce overall rheumatic fever rates. These findings suggest rheumatic fever programmes need to be realigned to support RADT pilots, as part of public health sector modernisation and change. RADT testing in primary health care settings, especially in areas of high deprivation, would best support the Ministry of Health strategy of reducing rheumatic fever.

References

Al-Najjar, F., & Uduman, S. (2007). Clinical utility of a new rapid test for the detection of Group A Streptococcus and discriminate use of antibiotics for bacterial pharyngitis in an outpatient setting. *International Journal of Infectious Diseases, 12*(3), 308-311. https://doi.org/10.1016/j.ijid.2007.07.006

Alp, E., Dalgıç, N., Kına, N., Bayraktar, B., Öncül, A., & Sepetci, E. (2018). The importance of rapid antigen testing for Group A Streptococcal Tonsillopharyngitis: A single center experience. *Cocuk Enfeksiyon Dergisi, 12*(3), E93-E98. https://doi.org/10.5578/ced.201829

American Academy of Paediatrics. (2012). *Red book: 2012 Report of the committee on infectious diseases (29th ed.)*. Pickering LK.

Barakat, A., Evans, C., Gill, M., & Nelson, D. (2019). Rapid strep testing in children with recently treated streptococcal pharyngitis. *Pediatric Investigation, 3*(1), 27-30. https://doi.org/10.1002/ped4.12109

Bourbeau, P. (2003). Role of the Microbiology Laboratory in diagnosis and management of pharyngitis. *Journal of Clinical Microbiology, 41*(8), 3467-34672. https://doi.org/10.1128/JCM.41.8.3467-3472.2003

Bulut, M., Kına, N., Büyükyanbolu, E., Özer, V., Aktaş, E., & Bayraktar, B. (2020). A highly-sensitive rapid test for the diagnosis of streptococcal pharyngitis: BD Veritor System. *International Journal of Pediatric Otorhinolaryngology, 133,* 109980. https://doi.org/10.1016/j.ijporl.2020.109980

Clerc, O., & Greub, G. (2010). Routine use of point of care tests: usefulness and application in clinical microbiology. *European Society of Clinical Microbi-*

*ology and Infectious Disease, 16,*1054-1061.https://doi.org/10.1111/j.1469-0691.2010.03281.x

Cohen, J. F., Bertille, N., Cohen, R., & Chalumeau, M. (2016). Rapid antigen detection test for group A streptococcus in children with pharyngitis. *Cochrane Database of Systematic Reviews,* (7). https://doi.org/10.1002/14651858.CD010502.pub2

Edmonson, B., & Farwell, K. (2005). Relationship between the clinical likelihood of Group A Streptococcal Pharyngitis and the sensitivity of a rapid antigen-detection test in a pediatric practice. *Pediatrics, 115*(2), 280-285. http://dx.doi.org/10.15421peds.2004-0907

Ehrlich, J., Demopoulos, B., Daniel, K., Ricarte, M., & Glied, S. (2002). Cost-effectiveness of treatment options for prevention of rheumatic heart disease from Group A Streptococcal Pharyngitis in a pediatric population. *Preventive Medicine, 35*(3), 250-257. https://doi.org/10.1006/pmed.2002.1062

France, E., Uny, I., Ring, N., Turley, R., Maxwell, M., Duncan, E., & Noyes, J. (2019). A methodological systematic review of meta-ethnography conduct to articulate the complex analytical phases. *BMC Medical Research Methodology, 19*(1), 35. http://dx.doi.org.ezproxy.auckland.ac.nz/10.1186/s12874-019-0670-7

Gazzano, V., Berger, A., Benito, Y., Freydiere, A., Tristan, A., Boisset, S., Carricajo, A., Poyart, C., Vandenesch, F., Descours, G., & Cheval, C. (2016). Reassessment of the role of rapid antigen detection tests in diagnosis of invasive Group A Streptococcal infections. *Journal of Clinical Microbiology, 54*(4), 994-999. http://doi.org/10.1128/JCM.02516-15

Gieseker, K. E., Roe, M. H., MacKenzie, T., & Todd, J. K. (2003). Evaluating the American Academy of Pediatrics diagnostic standard for Streptococcus Pyogenes Pharyngitis: backup culture versus repeat rapid antigen testing. *Pediatrics, 111*(6), 1424. doi:10.1542/peds.111.6.e666

Gröndal, H., Hedin, K., Strandberg, E. L., André, M., & Brorsson, A. (2015). Near-patient tests and the clinical gaze in decision-making of Swedish GPs not following current guidelines for sore throat – a qualitative interview study. *BMC Family Practice, 16*(1), 81. doi:10.1186/s12875-015-0285-y

Hedin, K., Strandberg, E., Gröndal, H., Brorsson, A., Thulesius, H., & André, M. (2014). Management of patients with sore throats in relation to guidelines: An interview study in Sweden. *Scandinavian Journal of Primary Health Care, 32*(4), 193-199. https://doi.org/10.3109/02813432.2014.972046

Küçük, O., Biçer, S., Giray, T., Çöl, D., Erdağ, G., Gürol,Y., Kaspar, C., & Vitrinel, A. (2014). Validity of rapid antigen detection testing in Group A Beta-Hemolytic Streptococcal Tonsillopharyngitis. *The Indian Journal of Pediatrics, 81*(2), 138-142. doi:10.1007/s12098-013-1067-y

Leydon, G., McDermott, L., Moore, M., Williamson, I., Hobbs, R., Lambton, T., Cooper, R., Henderson, H., & Little, P., on behalf of the PRISM investigators. (2013). A qualitative study of GP, NP and patient views about the use of rapid streptococcal antigen detection tests (RADTs) in primary care: 'Swamped with sore throats?' *BMJ Open, 3*(4): e002460.

Llor, C., Bjerrum, L., Munck, A., Cots, J., Hernandez, S., & Moragas, A. (2014). Access to point-of-care tests reduces the prescription of antibiotics among antibiotic-requesting subjects with respiratory tract infections. *Respiratory Care, 59*(12), 1918-1923. https://www.ncbi.nlm.nih.gov/pubmed/25468986

Lockwood, C., & Hannes, K. (2011). *Synthesizing Qualitative Research: Choosing the Right Approach.* Wiley.

Luo, R., Sickler, J., Vahidnia, F., Lee, Y., Frogner, B., & Thompson, M. (2019). Diagnosis and management of Group A Streptococcal Pharyngitis in the United States, 2011-2015. *BMC Infectious Diseases, 19*(1), 193. http://dx.doi.org.ezproxy.auckland.ac.nz/10.1186/s12879-019-3835-4

Ministry of Health. (2018). *School exclusion.* https://www.health.govt.nz/your-health/conditions-and-treatments/school-exclusion

Ministry of Health. (2019). *Reducing rheumatic fever.* https://www.health.govt.nz/our-work/diseases-and-conditions/rheumatic-fever/reducing-rheumatic-fever

Ngaio Diagnostics. (2019). *Point of care testing.* https://www.ngaio.co.nz/products/point-of-care-testing.

Orda, U., Mitra, B., Orday, S., Fitzgerald, M., Gunnarsson, R., Rofe, G., & Dargan, A. (2016). Point of care testing for Group A Streptococci in patients presenting with pharyngitis will improve appropriate antibiotic prescription. *Emergency Medicine Australasia, 28*(2), 199-204. https://doi-org.ezproxy.auckland.ac.nz/10.1111/1742-6723.12567

Papastergiou, J., Trieu, C., Saltmarche, D., & Diamantouros, A. (2018). Community pharmacist directed point-of-care Group A Streptococcus testing: Evaluation of a Canadian program. *Journal of the American Pharmacists Association, 58*(4), 450-456. https://doi.org/10.1016/j.japh.2018.03.003

Pulcini, C., Pauvif, L., Paraponaris, A., Verger, P., & Ventelou, B. (2012). Perceptions and attitudes of French general practitioners towards rapid antigen diagnostic tests in acute pharyngitis using a randomized case vignette study. *Journal of Antimicrobial Chemotherapy, 67*(6), 1540-1546. https://doi-org.ezproxy.auckland.ac.nz/10.1093/jac/dks073

Ralph, A., Holt, D., Islam, S., Osowicki, J., Carroll, D., Tong, S., & Bowen, A. (2019). Potential for molecular testing for Group A Streptococcus to improve diagnosis and management in a high-risk population: A prospective study. *Open Forum Infectious Diseases, 6*(4), Ofz097.https://doi.org/10.1093/ofid/ofz097

Rao, A., Berg, B., Quezada, T., Fader, R., Walker, K., Tang, S., & Sickler, J. (2019). Diagnosis and antibiotic treatment of Group A Streptococcal Pharyngitis in children in a primary care setting: Impact of point-of-care polymerase chain reaction. *BMC Pediatrics, 19*(1), 24. http://dx.doi.org.ezproxy.auckland.ac.nz/10.1186/s12887-019-1393-y

Sika-Paotonu, D., Beaton, A., Raghu, A., Steer., A., & Carapetis, J. (2017). *Acute rheumatic fever and rheumatic heart disease.* University of Oklahoma Health Sciences Center.

Stefaniuk, E., Bosacka, K., Wanke-Rytt, M., & Hryniewicz, W. (2017). The use of rapid test QuikRead go® Strep A in bacterial pharyngotonsillitis diagnosing and therapeutic decisions. *European Journal of Clinical Microbiology & Infectious Diseases, 36*(10), 1733-1738. doi:10.1007/s10096-017-2986-8

Upton, A., Bissessor, L., Farrell, E., Shulman, S., Zheng, X., & Lennon, D. (2015). Comparison of illumigene Group A Streptococcus Assay with culture of throat swabs from children with sore throats in the New Zealand School-Based Rheumatic Fever Prevention Program. *Journal of Clinical Microbiology, 54*(1), 153-156. https://doi.org/10.1128/JCM.02440-15

World Health Organization. (2017). *Policy and practice.* https://www.who.int/bulletin/volumes/95/9/16-187468/en/