ACCURACY AND INTEROBSERVER VARIATION OF THREE CLINICAL DECISION RULES FOR THE DIAGNOSIS OF STREPTOCOCCAL PHARYNGITIS

Dulce Helena Gonçalves Orofino, MSc,†*
*Sônia Regina Lambert Passos, PhD,**
*Carlos Augusto Ferreira de Andrade, PhD,**
Daniel Nigri, MD,† Lúcia dos Santos Werneck, BS,‡
*Raquel Carvalhaes de Oliveira, PhD,**
*and Yara Hahr Marques Hökerberg, PhD**

Abstract: We evaluated the accuracy and interobserver variation of 3 clinical decision rules for streptoccocal pharyngitis diagnosis. Oropharyngeal swab culture was the reference. The Abu Reesh rule had the highest sensitivity and the World Health Organization rule showed the highest specificity. The interobserver variation of those rules indicates the need for better training of clinicians.

Key Words: validation study, sensitivity, specificity, test reproducibility, streptococcal pharyngitis, rheumatic fever

From the*Laboratory of Clinical Epidemiology of the Instituto de Pesquisa Clínica Evandro Chagas, Fundação Oswaldo Cruz; †Souza Marques Medical School; and ‡Prontobaby Hospital, Rio de Janeiro, Brazil.

This study was funded by the Technological Research and Development Program (PIPDT-2011) of the IPEC/FIOCRUZ and the Carlos Chagas Foundation of Research Support—FAPERJ (S.R.L.P. had a fellowship JCNE E-26/101–511/2010, and D.N. had a PIBIC CNPq scholarship.). The funding sources had no role in the following: study design and conduct; and data collection, analysis and interpretation. D.H.G.O. had full access to all data and final responsibility for the decision to submit for publication on behalf of all authors. The authors have no other funding or conflicts of interest to disclose.

Address for correspondence: Dulce Helena Gonçalves Orofino, MSc, Laboratory of Clinical Epidemiology of the Instituto de Pesquisa Clínica Evandro Chagas, Fundação Oswaldo Cruz, Avenida Brasil 4036 sala 301-A-Manguinhos, Rio de Janeiro, Brazil. E-mail: dulceorofino@yahoo.com.br.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's web site (www.pidj.com).

ISSN: 0891-3668/13/3206-686
DOI: 10.1097/INF.0b013e3182868b32

Pharyngitis is a common reason for seeking medical care. Viruses are the most frequent causative agents, however, 30% of the cases are caused by *Streptococcus pyogenes* requiring antibiotic treatment to prevent rheumatic fever.[1] In daily practice, Brazilian clinicians decide on antibiotic therapy based exclusively on clinical criteria, which can lead to overuse of antibiotics.

Clinical decision rules for the diagnosis of streptococcal pharyngitis have been proposed in developing countries, one of them by the World Health Organization (WHO) and 2 different rules in Egypt ("Abu Reesh" and "Steinhoff").[2–4] Joachim et al[5] developed an alternative score system using Brazilian data. The accuracy of different decision rules scores[6] and the interobserver variation of the clinical signs included in those rules have already been tested.[7,8] To our knowledge, the interobserver variation of the overall rules has not been evaluated yet. Our study aimed at evaluating the accuracy and interobserver variation of 3 decision rules for the diagnosis of streptoccocal pharyngitis: WHO, Abu Reesh and Steinhoff.

METHODS

We performed a cross-sectional study at 2 pediatric hospitals in the city of Rio de Janeiro, Brazil, from June 2010 to June 2011. The study included 120 patients from 2 to 15 years of age, who sought medical care due to "sore throat." The exclusion criteria were: use of antibiotics up to 72 hours before the medical consultation; previous diagnosis of rheumatic fever; immunosuppression due to diseases or to the use of drugs; and no record on oropharyngeal culture results.

This study was approved by the Committee on Ethics in Research of the Evandro Chagas Clinical Research Institute of the Fundação Oswaldo Cruz, and informed written consent was provided by guardians and patients over the age of 12 years.

Each patient was examined by a trained pediatrician who completed a form about the predictive signs and symptoms of streptococcal pharyngitis: fever, rhinitis, cough, abdominal pain, headache, scarlatiniform rash, Filatov or Pastia signs, tender enlarged anterior or posterior cervical lymph nodes, petechiae on the palate and purulent oropharyngeal exudates.[6]

Swab specimens from the tonsils and posterior pharyngeal wall were collected for rapid antigen detection tests (streptococcus A test dispositive [Acon, San Diego, CA]) and culture onto a blood agar plate. When colony growth showed β-hemolysis and sensitivity to the bacitracin disc, the culture was considered positive.[9]

The following 3 clinical decision rules were assessed: the WHO rule (purulent oropharyngeal exudate and tender enlarged anterior cervical lymph nodes = bacterial pharyngitis); the Abu Reesh rule (purulent oropharyngeal exudate or tender enlarged anterior cervical lymph nodes = bacterial pharyngitis); and the Steinhoff rule (the following 3 variables in isolation or in combinations of 2 or 3 in a cumulative score [range = 0–3]: absence of rash [score = 1], absence of moderate or severe rhinitis [score = 1] and presence of tender enlarged anterior cervical lymph nodes [score = 1]).[2–4]

The prevalence of positive cultures was calculated for patients younger than 5 years and those 5 years or older. The following were calculated for the 3 clinical decision rules and for the rapid test: sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios and diagnostic odds ratio with respective 95% confidence intervals.

To assess interobserver variation of the overall rules, part of the sample was examined by a second independent clinician masked to the findings of the first examination. The κ indices used to calculate interobserver variation were interpreted according to Landis and Koch:[10] poor (κ < 0); slight (κ: 0.00–0.19); fair (κ: 0.20–0.39); moderate (κ: 0.40–0.59); substantial (κ: 0.60–0.79); almost perfect (κ: 0.80–0.99) and perfect (κ = 1.0).

Data masking was elaborated in the Epi Data 3.1 software (The EpiData Association, Odense, Denmark), and statistical analyses were performed by using the Statistical Package for the Social Science (SPSS, Chicago, IL) software, version 16.0.

RESULTS

The analysis of the WHO and Abu Reesh clinical decision rules included 120 patients: 56.2% were males and 69.4% were at least 5 years old. The mean age of the sample was 7.5 years (standard deviation = 4.1). The prevalence of a positive culture among the patients under the age of 5 years was 8.6% and among those at least 5 years of age was 28.9%. In the analysis of the Steinhoff clinical decision rule, 7 patients were excluded due to missing data regarding skin rash and rhinitis. The Abu Reesh clinical decision rule had the greatest sensitivity (85.2%) whereas that of WHO had the greatest specificity (80.8%). The rapid test showed sensitivity of 84.6% and specificity of 74.2% (Table 1). The κ index of the clinical criteria and of the overall rules are shown in Table, Supplemental Digital Content 1, http://links.lww.com/INF/B547.

TABLE 1. Accuracy of Clinical Decision Rules for Diagnosing Streptococcal Pharyngitis (WHO, Abu Reesh and Steinhoff) and of the Rapid Test in 120 Patients Aged From 2 to 15 Years in the City of Rio de Janeiro, Brazil

	Sensitivity	Specificity	PPV	NPV	PLR	NLR	OR
	% (95% CI)	% (95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
WHO (n = 120)	44.4 (35.6–53.3)	80.8 (73.6–87.7)	40.0 (31.2–48.8)	83.3 (76.7–90.0)	2.3 (7.9–2.6)	0.7 (0.6–1.2)	3.3 (1.4–8.2)
Abu Reesh (n = 120)	85.2 (78.8–91.6)	29.0 (20.9–37.2)	25.8 (18.0–33.7)	82.6 (61.2–95.0)	1.2 (0.9–1.3)	0.5 (0.3–1.9)	2.4 (0.8–7.3)
Steinhoff 1 (n = 113)*	7.0 (3.0–12.0)	79.0 (72.0–87.0)	10.0 (4.0–16.0)	73.0 (65.0–81.0)	0.35 (0.16–2.57)	1.2 (0.9–1.3)	1.0 (0.4–2.3)
Steinhoff 2 (n = 113)*	52.0 (43.0–61.0)	51.0 (42.0–60.0)	25.0 (17.0–33.0)	77.0 (69.0–85.0)	1.1 (0.7–1.6)	0.9 (0.6–1.5)	1.8 (0.8–4.4)
Steinhoff 3 (n = 113)*	41.0 (32.0–50.0)	72.0 (54.0–60.0)	31.0 (23.0–40.0)	79.0 (72.0–87.0)	1.5 (0.7–2.0)	0.8 (0.6–1.3)	0.8 (0.3–2.4)
Rapid test (n = 118)†	84.6 (78.1–91.1)	74.2 (66.3–82.6)	47.8 (38.9–56.8)	94.5 (90.4–98.6)	3.3 (1.1–2.4)	0.2 (0.2–1.3)	15.8 (5.1–50.1)

*Seven partial missing data.

†Missing data = 2.

95% CI indicates 95% confidence interval; PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio; OR, diagnostic odds ratio; Steinhoff 1, used only 1 variable; Steinhoff 2, used 2 variables.

DISCUSSION

In the literature, no other study of validation and comparison of those 3 clinical decision rules conducted in Brazil was found. This study represented a "narrow validation of decision rule" in which the rule is tested in a setting different from that in which it was developed. Additionally, the prevalence of positive cultures for the group 5 years or older was similar to that reported in other studies[2–5,7]

The WHO clinical decision rule showed better accuracy than it did in previous validation attempts. In a multicenter study conducted by Rimoin et al,[9] sensitivity ranged from 3.6% to 8.5% and specificity from 93.8% to 97.4%, whereas 91–100% of the children with positive culture were not detected. That rule was considered highly specific (93%), but not sensitive (12%) for streptococcal pharyngitis diagnosis in a sample of Egyptian children.[4,6] Although in our sample the WHO clinical decision rule evidenced better accuracy (44.4% sensitivity and 80.8% specificity), it still would leave untreated 15 of 27 patients with a positive culture (55.5%). Of the clinical decision rules tested, that of the WHO is the one that best guides clinicians to prevent unnecessarily antibiotic treatment if the patient does not meet the rule's clinical criteria (purulent exudate and tender enlarged anterior cervical lymph nodes).

Of the 2 rules proposed in Egypt, the Abu Reesh rule had been validated in 2 previous studies with a result similar to that found in our study.[4,6] It showed the best sensitivity, detecting 23 of 27 patients with a positive culture (85.2%). Nevertheless, it treated unnecessarily 66 of 93 patients with negative culture (71%). In our study, the Steinhoff clinical decision rule showed similar accuracies with the use of 3 variables.

The rapid test evidenced the best accuracy when compared with all clinical decision rules. It determined that treatment was unnecessary of 24 of 96 patients with negative culture (25%) and left untreated only 4 of 26 patients with positive culture (15.4%).

Our study found better interobserver variation of the clinical signs included in those rules than the only study performed in Germany,[9] probably due to previous training of our research team. Therefore, training to identify the relevant clinical signs and symptoms of these rules should be emphasized and maintained in continuing medical education to guarantee better interobserver variation in the application of the most accurate rule.

Our study has some limitations. A larger sample might have provided more precision in the results. The inclusion of only symptomatic patients (with "sore throat") minimized the likelihood of finding positive cultures among healthy carriers of *S. pyogenes*.

Although there is no available vaccine against *S. pyogenes,* this study suggests that countries with high prevalence of rheumatic fever and limited laboratory resources should follow the Abu Reesh clinical decision rule to indicate antibiotic therapy for patients less than 15 years of age complaining of "sore throat" due to its high sensitivity. These findings should be confirmed by a larger study that could explore other clinical findings or refine the available rules.

ACKNOWLEDGMENTS

The authors thank the Technological Research and Development Program (PIPDT-2011) of the IPEC/FIOCRUZ and the Carlos Chagas Foundation of Research Support—FAPERJ for funding this research.

REFERENCES

1. Shaikh N, Leonard E, Martin JM. Prevalence of streptococcal pharyngitis and streptococcal carriage in children: a meta-analysis. *Pediatrics*. 2010;126:e557–e564.
2. World Health Organization. *The Management of Acute Respiratory Infections in Children: Practical Guidelines for Outpatient Care*. Geneva, Switzerland: World Health Organization; 1995.
3. Steinhoff MC, Abd el Khalek MK, Khallaf N, et al. Effectiveness of clinical guidelines for the presumptive treatment of streptococcal pharyngitis in Egyptian children. *Lancet*. 1997;350:918–921.
4. Steinhoff MC, Walker CF, Rimoin AW, et al. A clinical decision rule for management of streptococcal pharyngitis in low-resource settings. *Acta Paediatr*. 2005;94:1038–1042.
5. Joachim L, Campos D Jr, Smeesters P. Pragmatic scoring system for the pharyngitis in low-resource settings. *Pediatrics* 2010;126:e608–e614.
6. Fischer Walker CL, Rimoin AW, Hamza HS, et al. Comparision of clinical predictions rules for the management of pharyngitis in settings with limited resources. *J Pediatr* 2006;149:64–71.
7. Donner-Banzhoff N, Beck C, Meyer F, et al. Clinical findings in patients presenting with sore throat. A study on inter-observer reliability. *Fam Pract*. 2002;19:466–468.
8. Shaikh N, Swaminathan N, Hooper EG. Accuracy and precision of the signs and symptoms of streptococcal pharyngitis in children: a systematic review. *J Pediatr*. 2012;160:487–493.e3.
9. Rimoin AW, Hamza HS, Vince, A, et al. Evaluation of the WHO decision rule for streptococcal pharyngitis. *Arch Dis Child*. 2005; 90: 1066–1070.
10. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33:159–174.