

Primary care

Predicting bacterial cause in infectious conjunctivitis: cohort study on informativeness of combinations of signs and symptoms

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Abstract

Objective To find an efficient set of diagnostic indicators that are optimally informative in the diagnosis of a bacterial origin of acute infectious conjunctivitis.

Design Cohort study involving consecutive patients. Results of index tests and reference standard were collected independently from each other.

Setting 25 Dutch health centres.

Participants 184 adults presenting with a red eye and either (muco)purulent discharge or glued eyelid(s), not wearing contact lenses.

Main outcome measures Probability of a positive bacterial culture, given different combinations of index test results; area under receiver operating characteristics curve.

Results Logistic regression analysis showed optimal diagnostic discrimination for the combination of early morning glued eye(s), itch, and a history of conjunctivitis. The first of these indicators increased the likelihood of a bacterial cause, whereas the other two decreased it. The area under the receiver operating characteristics curve for this combination of symptoms was 0.74 (95% confidence interval 0.63 to 0.80). The overall prevalence of bacterial involvement of 32% could be lowered to 4% or raised to 77%, depending on the pattern of index test results.

Conclusion A bacterial origin of complaints indicative of acute infectious conjunctivitis can be made much more likely or unlikely by the answers to three simple questions posed during clinical history taking (possibly by telephone). These results may have consequences for more targeted prescription of ocular antibiotics.

Introduction

In the developed world, acute infectious conjunctivitis is a common disorder with an annual incidence of 1.5-2% in primary care.¹⁻⁵ Randomised trials in patients with suspected acute bacterial conjunctivitis show a pooled prevalence of bacterial pathogens of 50% (95% confidence interval 45% to 54%).⁶⁻⁹ No more than half of the cases of acute infectious conjunctivitis in primary care probably have a bacterial origin. Confronted with acute infectious conjunctivitis, most

general practitioners feel unable to discriminate between a bacterial and a viral cause. In practice, more than 80% of such patients receive antibiotics.¹⁻⁵ Hence, in cases of acute infectious conjunctivitis, many unnecessary ocular antibiotics are prescribed. In 2001 in the Netherlands, more than 900 000 prescriptions for topical ocular antibiotics were issued, at a cost of €8.85 million (£5.9 million, \$10.9 million). In England 3.4 million community prescriptions for these antibiotics are issued each year, at a cost to the NHS of £4.7 million (€7.1 million, \$8.7 million).^{10 11}

Can general practitioners actually differentiate between bacterial and viral conjunctivitis on the basis of signs and symptoms alone? This is the first empirical study on the diagnostic informativeness of signs and symptoms in acute infectious conjunctivitis.

Methods

Participants

We asked nine designated general practitioners, working in 25 care centres with a total of 41 general practitioners, in the Amsterdam and Alkmaar region to include patients with a red eye and either (muco)purulent discharge or sticking of the eyelids. The exclusion criteria were age younger than 18 years, pre-existing symptoms for longer than seven days, acute loss of vision, wearing of contact lenses, use of systemic or local antibiotics within the previous two weeks, ciliary redness, eye trauma, and a history of eye surgery.

Data collection

At inclusion of each participant, general practitioners completed a standardised questionnaire and physical examination (index tests) (see bmj.com). The general practitioner then took one conjunctival sample of each eye for a bacterial culture. The general practitioners did not receive the culture results, and the microbiologist who analysed the cultures had no knowledge of the results of the index tests.

For each patient one eye was designated as the "study eye." In the case of two diseased eyes, the diseased eye with worse signs or symptoms was the study eye.



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Statistical analysis

We assessed the associations between findings from the index tests and the presence of a positive bacterial culture in the study eye by using a stepwise forward logistic regression analysis (see bmj.com).¹² We quantified the ability of the final model to discriminate between patients with and without a positive bacterial culture by using the area under the receiver operating characteristics curve.¹³

We used the final model to estimate the probability of a positive bacterial culture for each individual patient given his or her combination of test results. We calculated the numbers of correctly treated patients (sensitivity of the chosen cut-off point) and correctly untreated patients (specificity) and the reduction in prescriptions with different treatment cut-off points.

Results

Between September 1999 and December 2002 we enrolled 184 patients; data from 177 (96%) of these could be analysed. The prevalence of a positive bacterial culture in the study eye was 32% (57/177). The groups (culture positive and culture negative) were comparable with respect to baseline demographics, but some notable differences existed in the results of index tests (table 1). A history of conjunctivitis occurred more often in participants with a negative culture (21% *v* 9%). In the group with a positive culture, more patients had two glued eyes in the morning (39% *v* 11%) and bilateral involvement (37% *v* 16%). The most prevalent species was *Streptococcus pneumoniae*, which accounted for 27/57 of the positive cultures (see bmj.com). Three determinants were retained in the multivariable regression analysis: history of conjunctivitis (yes or no), itch (yes or no), and glued eyes in the morning (0, 1, or 2) (table 2).

The area under the receiver operating characteristics curve of the final model was 0.74 (95% confidence interval 0.65 to 0.82). Validation of this model with the bootstrap technique showed hardly any indication of undue influence by particular patients (corrected 95% confidence interval of area under curve 0.63 to 0.80) (see bmj.com).

The logistic regression analysis generated 12 different combinations of test results. These combinations corresponded to nine different clinical scores, varying from +5 to -3. For each clinical score, we calculated the probability of a positive culture. For a patient with a clinical score of +5, this probability was increased from 32% (prevalence in this study) to 77% (table 3). By contrast, a clinical score of -3 lowered this probability to 4%. Table 3 allows the calculation of the numbers of correctly treated patients (sensitivity) and correctly untreated patients (specificity) and the reduction of prescriptions with different treatment cut-off points. For example, if the treatment cut-off point is set at +2, indicating that only patients with a clinical score of +2 or higher receive ocular antibiotics, 38/57 (67%) of patients are correctly treated and 87/120 (73%) patients are correctly untreated. If applied to our study population, the cut-off point of +2 would lead to a reduction in prescriptions of antibiotics from more than 80% (current practice) to 40% (71/177).

Table 1 Baseline demographic characteristics and index test results and their univariate odds ratios. Values are numbers (percentages) unless stated otherwise. The prevalence of a positive culture was 32% (57/177)

Characteristic	Culture positive (n=57)	Culture negative (n=120)	Odds ratio (95% CI)
Mean (SD) age (years)	47 (17)	42 (14)	–
Median (range) duration of symptoms (days)	2 (1-7)	3 (1-7)	–
Female	36 (63)	68 (57)	–
History of hay fever	9 (16)	18 (15)	1.06 (0.45 to 2.54)
History of conjunctivitis	5 (9)	25 (21)	0.37 (0.13 to 1.01)
History of allergic conjunctivitis	3 (5)	6 (5)	1.06 (0.25 to 4.38)
Self treatment*	45 (79)	85 (71)	1.54 (0.73 to 3.26)
Redness:			
Peripheral	16 (28)	50 (42)	1
Whole conjunctiva	29 (51)	50 (42)	1.81 (0.88 to 3.74)
Conjunctival and pericorneal	12 (21)	20 (17)	1.88 (0.75 to 4.66)
Periorbital oedema	20 (35)	41 (34)	1.04 (0.54 to 2.02)
Secretion:			
None or water	20 (35)	47 (39)	1
Mucus	26 (46)	43 (36)	1.42 (0.70 to 2.90)
Purulent	11 (19)	30 (25)	0.86 (0.36 to 2.05)
Bilateral involvement	21 (37)	19 (16)	3.10 (1.50 to 6.42)
Itching	33 (58)	76 (63)	0.80 (0.42 to 1.52)
Foreign body sensation	23 (40)	48 (40)	1.02 (0.53 to 1.93)
Burning sensation	37 (65)	69 (58)	1.37 (0.71 to 2.63)
Glued eyes:			
None	5 (8)	33 (27)	1
One in the morning	30 (53)	74 (62)	2.68 (0.95 to 7.51)
Two in the morning	22 (39)	13 (11)	11.17 (3.49 to 35.77)

*Cleaning with water.

Discussion

The combination of three diagnostic indicators—glued eyes, itch, and a history of conjunctivitis—provided optimal discrimination between patients with and without a positive culture. It is of practical interest that these indicators may all be collected by clinical history taking or by telephone interview.

A history of infectious conjunctivitis and itch both made the probability of current bacterial involvement less likely. This may be explained by assuming that a viral conjunctivitis is more prevalent or has a stronger tendency to recur than a bacterial conjunctivitis and that itch indicates an allergic cause.

The use of the logistic regression model allows for the flexible creation of easy to use clinical rules. However, as long as more formal decision analyses do not exist, the choice of a rational treatment threshold remains somewhat arbitrary. We used the example of a treatment cut-off point of +2 to illustrate an approximate reduction of antibiotic prescriptions from more than 80% to 40%. These data indicate that in the absence of “alarm symptoms” the decision whether to

Table 2 Results of logistic regression analysis. Independent indicators of positive bacterial culture and their clinical score

Indicator	Odds ratio (95% CI)	Regression coefficient	Clinical score*
Two glued eyes	14.99 (4.36 to 51.53)	2.707	5
One glued eye	2.96 (1.03 to 8.51)	1.086	2
Itching	0.54 (0.26 to 1.12)	-0.61	-1
History of conjunctivitis	0.31 (0.10 to 0.96)	-1.161	-2
Area under ROC curve (95% CI)	0.74 (0.65 to 0.82)	–	–

ROC=receiver operating characteristics.

*Clinical scores of every symptom present are added up. For example, a patient with two glued eyes, itch, and no history of conjunctivitis has a clinical score of: 5 + -1 = 4.

Table 3 Clinical scores and their associated probabilities of a positive culture, sensitivity, and specificity

Clinical score	Percentage (No) observed positive cultures*	Percentage (95% CI) predicted positive cultures†	Percentage correctly treated (sensitivity)‡	Percentage correctly untreated (specificity)§
+5	100 (5/5)	77 (57 to 90)	9	100
+4	71 (17/24)	65 (47 to 79)	39	94
+3	0 (0/3)	51 (23 to 79)	39	92
+2¶	41 (16/39)	40 (26 to 55)	67	73
+1	20 (10/51)	27 (17 to 39)	84	38
0	13 (3/23)	18 (7 to 38)	89	22
-1	20 (5/25)	11 (4 to 26)	98	5
-2	0 (0/1)	7 (2 to 28)	98	4
-3	17 (1/6)	4 (1 to 15)	100	0

*Overall prevalence of positive culture=32% (57/177). In parenthesis are the number of positive cultures (numerator) and total number of cultures (denominator) in that row.

†Predicted probability is the probability of a positive culture calculated by regression analysis.

‡Fraction of patients with a positive culture who would be correctly treated if the clinical score in that row was used as treatment cut-off point.

§Fraction of all patients with a negative culture who would be correctly untreated if the clinical score in that row was used as treatment cut-off point.

¶Clinical score of +2 used in the text to illustrate its use for treatment decisions.

What is already known on this topic

No evidence has been published to show that clinical signs, symptoms, or both help to distinguish bacterial from viral conjunctivitis

General practitioners would benefit from an easy to use diagnostic tool to make this distinction

What this study adds

General practitioners can increase or reduce the chances that conjunctivitis is bacterial by asking about the number of glued eyes, itch, and history of infectious conjunctivitis

General practitioners could use this diagnostic information in their decisions about antibiotic treatment

A considerable reduction in the number of prescriptions for topical ocular antibiotics could be achieved, while avoiding harm or much discomfort

in other populations or the same indicators may be associated with different degrees of informativeness.¹³ On the other hand, we took some precautions against overoptimism in regression analysis by limiting the number of variables to four, which is below the rule of thumb stating that this number should be no bigger than the number of cases of the target disease divided by 10.¹³ As we had 57 cases, the use of four variables complies with that rule. In addition, the bootstrap procedure should be a safeguard against finding a regression model that is influenced too much by particular patients that are not found outside our dataset.

This study was limited to adult patients. The incidence of acute infectious conjunctivitis in children is higher than in adults, and the spectrum of causative micro-organisms may differ from that in adults. Therefore, these results cannot automatically be applied in children.

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prescribe antibiotics could be made without any additional diagnostic tests. This could lead to a substantial reduction in the costs associated with prescription of topical antibiotics. Use of a treatment cut-off point means that some patients with a positive culture will not receive treatment. The question is whether this is acceptable. A meta-analysis indicated that suspected acute bacterial conjunctivitis is mostly a self limiting disorder, with no serious complications in the placebo arms of the included studies. However, this meta-analysis also showed that treatment with antibiotic was associated with significantly better rates of early (days 2 to 5) clinical remission (relative risk 1.3, 95% confidence interval 1.1 to 1.6).⁴

Doctors who feel inclined to use these results in their daily practice should be aware of several factors. Firstly, the clinical domain to which our results apply does, of course, not formally include patient types that were excluded—for example, patients with acute loss of vision and contact lens wearers. Secondly, as we instructed the general practitioners especially for the study, the results may not be fully replicated if used by general practitioners not similarly instructed. Thirdly, an independent replication of our study would be useful, as other diagnostic indicators may perform better

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