Spectrophotometry or Visual Inspection to Most Reliably Detect Xanthochromia in Subarachnoid Hemorrhage: Systematic Review

Kevin Chu, MBBS, MS*; Angus Hann, MBBS (Hons); Jaimi Greenslade, PhD; Julian Williams, MBBS; Anthony Brown, MBChB

*Corresponding Author. E-mail: k.chu@uq.edu.au.

Study objective: We assess the sensitivity and specificity of xanthochromia as adjudicated by visual inspection and spectrophotometry at predicting the presence of cerebral aneurysm in patients with suspected subarachnoid hemorrhage who have a normal computed tomography (CT) head scan result.

Methods: A systematic review was performed. MEDLINE and EMBASE databases were searched. Relevant studies with clinical data on the diagnostic accuracy of visual inspection or spectrophotometry were considered. Patients who had a normal CT head scan result followed by a lumbar puncture were included in this review. Sensitivities, specificities, and heterogeneity (I^2) were calculated. Subgroup analyses were performed to explore reasons for the heterogeneity.

Results: There were major methodological limitations in the studies found. Twenty-two relevant articles were heterogeneous in regard to time to lumbar puncture, spectrophotometry methods, and follow-up of patients not undergoing cerebral angiography. Twelve of the 22 studies selected patients on the basis of a cerebral aneurysm or subarachnoid hemorrhage on imaging, or a positive lumbar puncture result. These studies were excluded from our initial analysis, which included only patients with clinically suspected subarachnoid hemorrhage. In this initial analysis, pooled estimates of sensitivity and specificity for spectrophotometry were 87% (95% confidence interval [CI] 71% to 96%; I^2=26%) and 86% (95% CI 84% to 88%; I^2=96%), respectively. For visual inspection, pooled sensitivity and specificity were 83% (95% CI 59% to 96%; I^2=52%) and 96% (95% CI 93% to 97%; I^2=76%), respectively. Sensitivity estimates are difficult to interpret without knowing time to lumbar puncture.

Conclusion: The heterogeneity in the underlying studies, combined with significant overlap in pooled confidence limits, makes it impossible to provide a definite conclusion about the diagnostic accuracy of spectrophotometry versus visual inspection. [Ann Emerg Med. 2014;64:256-264.]

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INTRODUCTION

Background

Patients complaining of a sudden, severe headache require subarachnoid hemorrhage to be ruled out. The catastrophic but infrequent nature of subarachnoid hemorrhage makes the diagnosis particularly challenging, especially in the neurologically intact patient.[1,2] The standard diagnostic approach is to perform a noncontrast computed tomography (CT) head scan followed by a lumbar puncture, if the result is normal.[3-5]

CT is highly sensitive (98% to 100%) for the detection of subarachnoid hemorrhage if performed within 6 hours of hemorrhage.[6,7] The proportion of subarachnoid hemorrhage left undiagnosed by CT and potentially identifiable by lumbar puncture is small. Nonetheless, the consequences of missing a sentinel bleeding event are grave, so the diagnosis should be pursued even when the CT result is normal.

A lumbar puncture showing a raised red blood cell (RBC) count or xanthochromia in the cerebrospinal fluid implies a subarachnoid hemorrhage and mandates angiography. Historically, *xanthochromia* was used to describe the yellow discoloration of the cerebrospinal fluid supernatant.[8] More recently, it has been defined as the yellow discoloration indicating bilirubin in the cerebrospinal fluid.[9]

Importance

Internationally, spectrophotometry is advocated in the United Kingdom in accordance with their national guidelines.[10] The test is commonly ordered in the United Kingdom where visual

Editor's Capsule Summary

What is already known on this topic

Assessing cerebrospinal fluid for xanthochromia is a pivotal step in managing patients who have suspected subarachnoid hemorrhage but normal noncontrast head computed tomography. The utility of xanthochromia depends on its sensitivity and specificity for detecting blood in cerebrospinal fluid.

What question this study addressed

What are the test performance characteristics of visual inspection and spectrophotometric assessment and how do they compare?

What this study adds to our knowledge

The sensitivity and specificity of xanthochromia in detecting subarachnoid hemorrhage are imperfect for both visual and spectrophotometric measurements. The available clinical information is inadequate to justify recommending one form of assessment over the other.

How this is relevant to clinical practice

Clinicians can accept results based on either form of measurement.

inspection is considered subjective and unreliable and thus should be abandoned.[11,12] The use of spectrophotometry is variable in continental Europe.[13]

The need for spectrophotometry in addition to visual inspection has been questioned by authors in North America and Australasia because of concerns about the test's low specificity.[14,15] Spectrophotometry for xanthochromia is virtually unavailable in the United States.[16] The detection of xanthochromia in North America therefore relies on visual inspection alone.

Goals of This Investigation

Differences in practice across the continents reflect polarized views on the need for spectrophotometry to replace visual inspection.[17-19] The objective of this review is to assess the sensitivity and specificity of xanthochromia as adjudicated by visual inspection and spectrophotometry at predicting the presence of a cerebral aneurysm in patients with suspected subarachnoid hemorrhage who have a normal CT head scan result.

MATERIALS AND METHODS

Selection of Participants

The literature search terms are given in Figure 1; the search strategy, in Appendix E1 (available online at http://www.annemergmed.com). The population was patients complaining of a headache. The index and comparator tests were visual inspection and spectrophotometry of the cerebrospinal fluid. The outcome or target condition was subarachnoid hemorrhage or cerebral aneurysm.

Population	headache
	AND
Index and Comparator Tests	xanthochromia OR spectrophotometry OR heme pigment OR haem pigment OR bilirubin OR oxyhemoglobin OR oxyhaemoglobin OR lumbar puncture OR dural puncture OR spinal puncture OR spinal tap OR cerebrospinal fluid OR spinal fluid
	AND
Outcome	subarachnoid hemorrhage OR subarachnoid haemorrhage OR intracranial aneurysm OR cerebral aneurysm OR berry aneurysm OR saccular aneurysm

Figure 1. Literature search terms.

MEDLINE and EMBASE databases, along with the Cochrane Library, were searched independently by K.C. and A.H. In addition to using the search terms, the related citations in PubMed were also searched. Furthermore, the reference lists of relevant articles were hand searched, but the gray literature, including conference proceedings or meeting abstracts, was not.

The search was limited to the English language but no other filters were used. Studies were considered relevant if they were primary clinical studies that provided data on the diagnostic accuracy of a visual inspection or spectrophotometry. Laboratory-based experimental studies were excluded because they provide only "mechanism-based reasoning."[20]

The methodological quality was assessed by K.C. and A.H. with the Quality Assessment of Diagnostic Accuracy Studies - 2 (QUADAS-2) tool described in Appendix E2 (available online at http://www.annemergmed.com).[21,22] Disagreements were resolved by consensus. We rated the reference standard domain as highly biased if follow-up was (1) not reported or incomplete for a patient not undergoing angiography; or (2) only at the study hospital because the patient may have presented elsewhere or died. The quality assessment was reported with the QUADAS-2 template for tabular display.[22]

Data Collection and Processing and Primary Data Analysis

Data were extracted independently by K.C. and A.H. with a data collection form created for this review. Disagreements were again resolved by consensus. The initial analysis included only studies or patients in which case selection was based on clinical suspicion of subarachnoid hemorrhage plus a normal CT result followed by a lumbar puncture. Studies in which case selection was based on confirmed subarachnoid hemorrhage or abnormal