Preliminary Study on the Stability of Beta-2 Transferrin in Extracorporeal Cerebrospinal Fluid


Otolaryngology -- Head and Neck Surgery 2011 144: 101
DOI: 10.1177/0194599810390887

The online version of this article can be found at:
http://oto.sagepub.com/content/144/1/101

Published by:
SAGE
http://www.sagepublications.com

On behalf of:
AMERICAN ACADEMY OF OTOLARYNGOLOGY--HEAD AND NECK SURGERY

American Academy of Otolaryngology- Head and Neck Surgery

Additional services and information for Otolaryngology -- Head and Neck Surgery can be found at:

Email Alerts: http://oto.sagepub.com/cgi/alerts
Subscriptions: http://oto.sagepub.com/subscriptions
Reprints: http://www.sagepub.com/journalsReprints.nav
Permissions: http://www.sagepub.com/journalsPermissions.nav

>> Version of Record - Dec 31, 2010

What is This?
Preliminary Study on the Stability of Beta-2 Transferrin in Extracorporeal Cerebrospinal Fluid

Benjamin S. Bleier, MD1, Indranil Debnath, MD2, Brendan P. O’Connell, MD3, W. Alexander Vandergrift III, MD3, James N. Palmer, MD4, and Rodney J. Schlosser, MD3

No sponsorships or competing interests have been disclosed for this article.

Abstract
Objective. Detection of beta-2 transferrin in rhinorrhea fluid is a sensitive and specific method for the diagnosis of a cerebrospinal fluid (CSF) leak. Patients may be asked to collect this fluid at home to obtain an adequate volume for detection, and thus the age and storage conditions of these specimens may be variable upon analysis. The purpose of this study is to understand how age, storage temperature, and exposure to mucus affect the ability to detect beta-2 transferrin in CSF.

Study Design. Case series with planned data collection.

Setting. Tertiary care university hospital.

Subjects and Methods. This study consists of 6 patients undergoing endoscopic CSF leak repair. CSF was collected directly from a lumbar drain (n = 4) or from nasal drainage (n = 2). Specimens were stored at 4°C (n = 3) or room temperature (n = 3). Samples were tested for the presence of beta-2 transferrin for up to 7 days using standard immunofixation electrophoresis techniques.

Results. Beta-2 transferrin was detected in all specimens through day 7 regardless of storage temperature or collection site (95% exact binomial confidence interval of 0%-46%).

Conclusions. Beta-2 transferrin remains detectable in extracorporeal CSF for up to 7 days regardless of storage at room temperature or exposure to nasal mucus. Negative detection in patient specimens up to a week old is therefore not likely to be caused by protein degradation.

Keywords
CSF Leak, Beta-2 Transferrin, protease, encephalocele, cranial base surgery

Received August 11, 2010; revised September 10, 2010; accepted September 17, 2010.
transferrin. The purpose of this study is therefore to determine the impact of both sample age and storage conditions on the ability to detect the beta-2 transferrin glycoprotein.

Methods

Study Design

This was a case series with planned data collection of 6 patients undergoing endoscopic CSF leak repair at a tertiary care university hospital (study approved by the Medical University of South Carolina Institutional Review Board). Preoperative CSF samples were collected either from the lumbar drain (n = 4) or directly from the nose (n = 2). Samples were stored at 4°C (n = 3) or at room temperature (20-25°C, n = 3) for 7 days. Among the 3 samples stored at 4°C, 2 were collected from the lumbar drain, and 1 was collected directly from the nose. Among the 3 samples stored at room temperature, 2 were collected from the lumbar drain, and 1 was collected directly from the nose (Table 1). All samples were divided into 2 aliquots that were tested on both day 0 and day 7.

Beta-2 Transferrin Testing

The presence of beta-2 transferrin was determined in all samples by the Department of Pathology/Lab Medicine using immunofixation electrophoresis (limit of detection 0.15 mg/dL).

Results

The patient population consisted of 2 male and 4 female patients with a median age of 55 ± 10 years (range, 44-72). In all 6 patients, the diagnosis of CSF leak was confirmed intraoperatively by endoscopy coupled with intrathecal fluorescein. Regardless of storage conditions, beta-2 transferrin was detected in all samples on day 0 and day 7. The 95% exact binomial confidence interval for 0/6 failures is 0% to 46%.

Discussion

Beta-2 transferrin was first described in 1979 by Irjala et al. The unique distribution of beta-2 transferrin in CSF and its derivative fluids has been exploited in the workup of idiopathic rhinorrhea and has been shown to provide a highly sensitive and specific test for CSF leak.

Despite a reported specificity of 97% to 99%, false-positive findings have been reported in patients with alcoholic and non-alcoholic cirrhosis, which results in detectable systemic levels of the beta-2 isoform. Another source of error may occur in the setting of colonization by neuraminidase secreting bacteria, which may convert sialated transferrin in nasal mucus into the desialated form, leading to a false-positive test.

Although sources of type I error have been explored in the literature, type II error has received less attention. Clinically, patients presenting with idiopathic rhinorrhea may be asked to collect nasal specimens at home as a component of a CSF leak workup. As a glycoprotein, the transferrin molecule is subject to potential degradation from a variety of sources, including but not limited to temperature fluctuations, age, and mucus-derived protease exposure. In the uncontrolled home environment, patient specimens may be differentially exposed to each of these variables. However, their impact on the ability to detect the presence of beta-2 transferrin in CSF containing specimens has never been formally explored.

Our study was designed to individually explore the role of age, storage temperature, and exposure to proteolytic enzymes in nasal mucus on the ability to detect beta-2 transferrin within CSF. Our results demonstrate that the glycoprotein remains detectable for at least 7 days regardless of collection site or storage at room temperature. Thus, although each clinical scenario is unique, this study suggests that a negative beta-2 transferrin finding in a specimen less than 7 days old is likely not caused by protein degradation. This has important clinical implications as ambiguity regarding specimen negativity may otherwise require more invasive techniques to rule out the presence of a CSF leak. However, one drawback of this study is that although there were no failures in detection, the upper limit of our 95% confidence interval is 46% or lower, implying that our findings need to be confirmed with larger populations prior to drawing any definitive conclusions.

The elaboration of beta-2 transferrin testing has yielded a highly sensitive and specific method of detecting the presence of CSF within nasal discharge. Regardless of the merits of the test itself, the practical aspects of clinical specimen collection may introduce multiple variables capable of interfering with the outcome. Our study suggests that nasal specimens may be stored at room temperature for up to 7 days without a significant loss of detectable protein. Despite these findings, there may be multiple additional sources of error, including our limited sample size. Thus, each specimen result must be taken in the context of the entire clinical picture.

Acknowledgments

The authors thank the Department of Pathology/Lab Medicine at the Medical University of South Carolina for their assistance with specimen collection and testing.
Author Contributions

Benjamin S. Bleier, design, data acquisition, analysis, drafting, final approval; Indranil Debnath, design, data acquisition, analysis, final approval; Brendan P. O’Connell, design, data acquisition, analysis, drafting, final approval; W. Alexander Vandergrift III, design, data acquisition, analysis, final approval; James N. Palmer, design, data acquisition, final approval; Rodney J. Schlosser, design, data acquisition, analysis, drafting, final approval.

Disclosures
Competing interests: None.
Sponsorships: None.

References