Original Article

Preoperative Topical Intranasal Fluorescein in Diagnosis of Cerebrospinal Fluid Rhinorrhea

Seyed Mostafa Hashemi Jazi, Zhale Amini, Masih Saboori[1], Mostafa Raisi[2,3]

Departments of Otolaryngology, [1]Neurosurgery and [2]Internal Medicine, [3]Poursina Hakim Digestive Disease Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

ORCID:

Seyed Mostafa Hashemi Jazi: https://orcid.org/0000-0002-4067-6326

Zhale Amini: https://orcid.org/0000-0003-2964-7345

Masih Saboori: https://orcid.org/0000-0002-1782-778X

Mostafa Raisi: https://orcid.org/0000-0001-9925-522X

Abstract

Background and Objectives: The preoperative diagnosis of cerebrospinal fluid (CSF) leak site is necessary for the management of CSF rhinorrhea. At present, intrathecal fluorescein is a common approach for it; however, regarding drawbacks, its value is limited. This study aimed at examining the effects of topical intranasal fluorescein (TINF) on the preoperative diagnosis of CSF rhinorrhea and intraoperative localization of CSF fistula. **Patients and Methods:** In this cross-sectional study, 32 consecutive patients with CSF rhinorrhea were recruited. Topical intranasal 10% fluorescein was placed in common sites of leakage, the middle turbinate meatus, the roof of the ethmoid plate, and sphenoethmoidal recesses. Change of the color of fluorescein indicated the presence of CSF, and thus, the site of the fistula could be outlined. The accuracy rates of diagnosis of leak site identified by TINF were compared with those by available imaging modalities, CSF analysis, intraoperative findings, and follow-up. **Results:** The cause of the leak was traumatic in 22 patients and nontraumatic in 10 patients. Preoperative accuracy rate of the location of CSF fistula was estimated 58.3% by available imaging study. The preoperative diagnosis rate of CSF rhinorrhea and the CSF fistula site localization rate by TINF were both 100%. No recurrence was found during the follow-up for 2–12 months. No complication had been reported. **Conclusions:** Preoperative TINF is an easy, quick, sensitive, safe, and accurate tool in localization of the site of the CSF fistulas and can be considered as a viable noninvasive alternative to the intrathecal fluorescein technique for preoperative diagnosis of CSF rhinorrhea.

Keywords: Cerebrospinal fluid, endoscope, fluorescein, intrathecal, rhinorrhea, skull base, topical

Introduction

Cerebrospinal fluid (CSF) rhinorrhea was described as the leakage of CSF into the nasal cavity.[1] The most important causes of CSF rhinorrhea are traumatic including crash and iatrogenic injuries and nontraumatic including congenital, neoplastic, and spontaneous.[2,3]

For the management of CSF rhinorrhea, there are some guiding principles including leak confirmation, precise site localization, and sufficient closure.[4]

All patients with gross CSF leakage were imaged to find the location of the fistula.[5-7] Regarding limited sensitivity of available imaging modalities, injection of fluorescein into a thecal space is the most common tool to precisely determine the localization of the leak site. In this technique, the site of CSF leakage is established by detecting the green color of intrathecal fluorescein (ITF) in the nasal cavity.[8,9] Some investigations have explained complications and disadvantages of this method,[10,11] while some studies demonstrated the safety of intrathecal injection of diluted low-dose fluorescein.[12,13]

Some authors have recommended the topical application of fluorescein intranasally to localize the site of CSF rhinorrhea. While safety considerations have limited ITF use, the

Access this article online

Quick Response Code:

Website: www.archtrauma.com

DOI: 10.4103/atr.atr_87_18

Address for correspondence: Dr. Zhale Amini, ENT Department, Azzahra Hospital, Isfahan, Iran. E-mail: JA61057@yahoo.com

How to cite this article: Hashemi Jazi SM, Amini Z, Saboori M, Raisi M. Preoperative topical intranasal fluorescein in diagnosis of cerebrospinal fluid rhinorrhea. Arch Trauma Res 2018;7:146-9.

intranasal approach may be a good alternate to decrease the ITF side effects.[14,15] There are only a few published articles in the current English literature regarding topical intranasal fluorescein (TINF) for the diagnosis of CSF rhinorrhea, though interest to use topical fluorescein is increasing nowadays. The present study was conducted to focus on the utility of TINF in the preoperative localization of the site of CSF fistulas and also to examine the results of TINF in identifying and closing skull base defects.

Patients and Methods

This case series included 32 patients (11 women and 21 men) with suspected CSF rhinorrhea. All patients were admitted with clear sweet or salty nasal discharge. All patients were recruited at the Kashani Hospital, Isfahan, Iran, from September 2014 to February 2016. Furthermore, all the patients were evaluated by detailed history taking, neurosurgical, and ear, nose, and throat examination. We used a combination of the available imaging techniques for our cases including axial and coronal computed tomography (CT) scan and/or magnetic resonance imaging (MRI). CT cisternography did not available at that time. The suspected nasal discharge was evaluated for glucose and protein content, a simple test to check whether the rhinorrhea fluid was CSF or not.

In the present study, the patients were divided into two main groups based on the etiology of the leak: (a) nontraumatic and (b) posttraumatic CSF leaks. In Group A, these patients likely have unrecognized raises in intracranial pressure such as benign intracranial hypertension and other neurologic causes. Group B consisted of patients with posttraumatic CSF leaks.

Process

The patients were placed in the supine position, and 1–3 milliliters of CSF was withdrawn and sent to a laboratory. Local anesthesia of the nasal cavity mucous membrane was done with 1% lidocaine and 0.25% phenylephrine, and then, cotton pads soaked with fluorescein were placed. Fluorescein is available in 10% solution in a 5-mL box for ophthalmology usages. We did not dilute it. Three fluorescein-soaked cotton pads were placed in the middle turbinate meatus, the roof of the ethmoid plate, and sphenoethmoidal recesses, respectively. Thereafter, endoscopic examination of the nasal cavity was repeated again carefully by Valsalva maneuver and/or leaning forward. Zero-degree lens rigid 4-mm endoscopes (Chammed, XVS3, China) were used to explore the nasal cavity. As previous studies, a change in the color of the fluorescein from brown to green fluorescence was considered as the presence of CSF, and then, the site of the leak could be outlined.[14]

The accuracy rate of leak site identification was evaluated by comparing with glucose and protein analysis, imaging, intraoperative findings, and follow-up. β2-transferrin assay was not performed because it was not accessible routinely in our region.

Endoscopic repair was carried out in standard fashion.[16] The patients were followed for at least 2-month periods. None of the other individuals needed to endoscopic intervention during the period of follow-up.

The outcome was determined through hospital evidence or telephone with standard questions used to evaluate the recurrence or side effects, such as meningitis, seizures, and chronic sinusitis. Moreover, a history of postnasal discharges, salt tasting, and CSF leakage after strain was obtained.

Informed consent was obtained from all patients, and the protocol of the study was approved by the Ethics Committee at Vice-Chancellor of Research of Isfahan University of Medical Sciences. All procedures and examinations were conducted by the authors of this paper as a collaborative effort of the departments of neurosurgery and otolaryngology.

Results

Patients' characteristics

Thirty-two consecutive patients with suspected rhinorrhea were included in this study. The mean age of the patients was 28.6 years (age range, 7–63 years). Of these patients, 11 cases were female (34.3%) and the remainder were male. Unilateral watery rhinorrhea was the most common preoperative symptom and was found in all cases. Headache, smell disorders (anosmia and hyposmia), and vomiting were also reported [Table 1]. A single episode of meningitis was recorded preoperatively in two patients, but no mortality occurred. In this series, no significant difference was found in rhinorrhea and smell disorders between posttraumatic and non-traumatic groups [Table 1].

In the present study, the preoperative accuracy rate of localization of CSF fistula was estimated 58.3% (13 out of 24) using available imaging studies including coronal and axial spiral CT scan or MRI. TINF was implicated to all patients in this series according to our protocol. The majority of the leaks (22 cases) occurred at the level of the cribriform plate, and only two defects were located in the sphenoid sinus. No case had more than one defect.

In 8 patients (25%), no fistula tract could be identified using multiple modalities [Table 2]. In all of these 8 cases, evaluation including examination, available imaging mostly CT, and follow-up could not identify the site of the CSF fistula.

Suspicious specimens were sent to a laboratory to assess for glucose and protein, and all samples were reported positive for glucose and protein. Topical intranasal application of fluorescein was positive in all these individuals too.

Endoscopic closure was done for six patients who failed to respond conservative treatment including two revision surgeries who failed after previous repairs. Nine other individuals were nominated for surgery but left our center and refused to cooperate for various reasons. In follow-up, six of the patients underwent surgery in other centers and were excluded from the follow-up. In all six patients who were surgically treated, intraoperative ITF verified the site of leakage, which had been reported by TINF previously.

Table 1: Patients' demographic characteristics

	Etiology		Total	*P*
	Nontraumatic	Posttraumatic		
Number of patients	10	22	32	
Gender				
Female	8	3	11	
Male	2	19	21	
Age (range) year	23.2 (7-46)	31.1 (19-63)	28.6 (7-63)	<0.005
Symptoms (%)				
Rhinorrhea	10 (100)	22 (100)	32 (100)	>0.005
Headache	4 (40.0)	13 (59.0)	17 (53.1)	<0.005
Smell disorders	3 (30.0)	7 (30.1)	10 (30.1)	>0.005
Vomiting	4 (40.0)	7 (30.1)	11 (34.3)	<0.005
Meningitis	0	2 (9.0)	2 (6.2)	<0.005
Others	1 (10.0)	2 (9.0)	3 (9.3)	>0.005

Table 2: Location of cerebrospinal fluid leakage base on etiology

	Etiology		Total	*P*
	Nontraumatic	Posttraumatic		
Number of patients	10	22	32	
Site of fistula				
Sphenoid	0	2 (9.0)	2 (6.2)	<0.005
Cribriform plate	5 (50.0)	17 (77.2)	22 (68.7)	<0.005
Ethmoid	0	0	0	>0.005
Frontal sinuses	0	0	0	>0.005
Unknown	5 (50.0)	3 (13.6)	8 (25.0)	<0.005

The authors alerted participants for probable complications such as topical hypersensitivity, vomiting, and sinusitis, but we did not receive related reports in follow-up. No patient developed chronic sinusitis. No major neurological symptoms were described by any patients, but minor symptoms such as dizziness or occasional headaches without neck stiffness or fever were reported by eight patients (25%).

In patients who underwent surgery, the efficacy of closure was complete. There were no persistent leaks after surgery, and no late recurrence was diagnosed during follow-up. One of the patients had transient lower extremity weakness after surgery which may be caused by lumbar drain placement, while no complication was seen in other individuals.

In the present study, the average follow-up for patients who remained in the center was 6 months (range, 2–12 months), but nine patients who left the center were lost during follow-up.

Discussion

CSF rhinorrhea can occur spontaneously, but trauma and iatrogenic injuries are the most common etiologies of it.[17] Regardless of etiology, patients with CSF leakage may have silent symptoms. They may suffer from generally unilateral sweet or salty taste rhinorrhea, nasal obstruction, or meningitis.[6,18] Chronic CSF leakages may cause a low-pressure headache.[19] Unilateral clear rhinorrhea is the most common presentation, although bilateral CSF rhinorrhea has reported.[20] These findings are in accordance with the results of the present study.

Precise pre- and intraoperative localization of the site of CSF leakage has proved particularly significant. The inconvenience and complications attributed to ITF[9,11,21,22] have an obligate physician to explore minimally invasive, simple, and convenient processes for localization of CSF fistula.[19,23] Jones first localized the intraoperative CSF fistula using topical nasal fluorescein in three patients.[15] Saafan acknowledged later that TINF can be considered as a viable noninvasive alternative to ITF.[14] In the present study, no major or minor complication regarding TINF was seen. Moreover, Jones and Saafan reported no complication attributed to TINF in their studies.[14,15] Furthermore, there is no discrepancy between the findings of the current study and those of other studies in this issue.[3,18]

Although in the present study, Trendelenburg positioning and Valsalva maneuvers have been employed to promote CSF leakage, these maneuvers may be impractical in all traumatic patients, but it may be unnecessary in many cases.

Even though both ITF and TINF may have similar inadequacy if the patient is not actively leaking at the time of study and in tiny cracks and subsequent very small CSF leakage, an active leak may be essential for appropriate diagnosis in both of them. However, in temporary CSF leakage, preoperative imaging techniques may be improved diagnostic accuracy.

The finding of this study was similar to the findings of some other studies that denoted preoperative TINF is as sensitive as glucose and protein in detecting CSF leakage.[9,18,24,25] Adding glucose level to TINF can increase accuracy,[18,26] but because sometimes catching sufficient and suitable fluid for this analysis may be impossible, TINF can be helpful in this suspicious rhinorrhea. The results of the present study were in line with those of the previous similar studies in case of safety and accuracy.

The present study had a number of limitations that must be acknowledged. At first, this study was an uncontrolled case series and the results would be more convincing if ITF and preoperative TINF were compared in a double-blind, placebo-controlled, clinical trial. This is a good topic for future studies in collaboration of neurosurgery and otolaryngology departments. Second, our study group was heterogeneous in terms of cause, age, gender, and other demographic factors, and this diversity may conceal some differences. Therefore, further generalization of these results should be done with caution. Longer outcome of patients who managed by this approach as well as the long-term safety and efficacy of TINF is warranted to fully evaluate and remain as a question which needs subsequent systematic and perhaps prospective studies.

Conclusions

Preoperative TINF may be a specific and sensitive tool in identifying preoperative CSF leakage and may identify the leak site in many of the cases regardless of etiology and therefore may be a useful and safe adjunct in endoscopic repair of skull base defects. Preoperative TINF may be easier and less expensive than ITF. Fluorescein can be used even as outpatient investigation for preoperative diagnosis of CSF rhinorrhea in the future because it is a simple, quick, relatively inexpensive, safe, and accurate technique.

Financial support and sponsorship

This study was financially supported by Isfahan University of Medical Sciences.

Conflicts of interest

There are no conflicts of interest.

References

1. Aydin K, Terzibasioglu E, Sencer S, Sencer A, Suoglu Y, Karasu A, *et al.* Localization of cerebrospinal fluid leaks by gadolinium-enhanced magnetic resonance cisternography: A 5-year single-center experience. Neurosurgery 2008;62:584-9.
2. Lindstrom DR, Toohill RJ, Loehrl TA, Smith TL. Management of cerebrospinal fluid rhinorrhea: The Medical College of Wisconsin experience. Laryngoscope 2004;114:969-74.
3. Park JI, Strelzow VV, Friedman WH. Current management of cerebrospinal fluid rhinorrhea. Laryngoscope 1983;93:1294-300.
4. Schlosser RJ, Bolger WE. Nasal cerebrospinal fluid leaks: Critical review and surgical considerations. Laryngoscope 2004;114:255-65.
5. Banu MA, Kim JH, Shin BJ, Woodworth GF, Anand VK, Schwartz TH. Low-dose intrathecal fluorescein and etiology-based graft choice in endoscopic endonasal closure of CSF leaks. Clin Neurol Neurosurg 2014;116:28-34.
6. Kerr JT, Chu FW, Bayles SW. Cerebrospinal fluid rhinorrhea: Diagnosis and management. Otolaryngol Clin North Am 2005;38:597-611.
7. Rice DH. Cerebrospinal fluid rhinorrhea: Diagnosis and treatment. Curr Opin Otolaryngol Head Neck Surg 2003;11:19-22.
8. Javadi SA, Samimi H, Naderi F, Shirani M. The use of low- dose intrathecal fluorescein in endoscopic repair of cerebrospinal fluid rhinorrhea. Arch Iran Med 2013;16:264-6.
9. Oh JW, Kim SH, Whang K. Traumatic cerebrospinal fluid leak: Diagnosis and management. Korean J Neurotrauma 2017;13:63-7.
10. Locatelli D, Rampa F, Acchiardi I, Bignami M, De Bernardi F, Castelnuovo P. Endoscopic endonasal approaches for repair of cerebrospinal fluid leaks: Nine-year experience. Neurosurgery 2006;58:246-56.
11. Lue AJ, Manolidis S. Intrathecal fluorescein to localize cerebrospinal fluid leakage in bilateral Mondini dysplasia. Otol Neurotol 2004;25:50-2.
12. Rodríguez-Navarro MÁ, Díaz-Alejo C, Padilla-Del Rey ML, Alcaraz AB, González-Pérez P, Benítez M, *et al.* Safe intrathecal fluorescein use for identification of cerebrospinal fluid leaks: Case-report and perioperative algorithm description. Rev Esp Anestesiol Reanim 2017;64:533-6.
13. Keerl R, Weber RK, Draf W, Wienke A, Schaefer SD. Use of sodium fluorescein solution for detection of cerebrospinal fluid fistulas: An analysis of 420 administrations and reported complications in Europe and the United States. Laryngoscope 2004;114:266-72.
14. Saafan ME, Ragab SM, Albirmawy OA. Topical intranasal fluorescein: The missing partner in algorithms of cerebrospinal fluid fistula detection. Laryngoscope 2006;116:1158-61.
15. Jones ME, Reino T, Gnoy A, Guillory S, Wackym P, Lawson W, *et al.* Identification of intranasal cerebrospinal fluid leaks by topical application with fluorescein dye. Am J Rhinol 2000;14:93-6.
16. de Divitiis E, Cappabianca P, Cavallo LM. Endoscopic transsphenoidal approach: Adaptability of the procedure to different sellar lesions. Neurosurgery 2002;51:699-705.
17. Hegazy HM, Carrau RL, Snyderman CH, Kassam A, Zweig J. Transnasal endoscopic repair of cerebrospinal fluid rhinorrhea: A meta-analysis. Laryngoscope 2000;110:1166-72.
18. Liu HS, Chen YT, Wang D, Liang H, Wang Y, Wang SJ, *et al.* The use of topical intranasal fluorescein in endoscopic endonasal repair of cerebrospinal fluid rhinorrhea. Surg Neurol 2009;72:341-5.
19. Ozturk K, Karabagli H, Bulut S, Egilmez M, Duran M. Is the use of topical fluorescein helpful for management of CSF leakage? Laryngoscope 2012;122:1215-8.
20. Ramsden JD, Corbridge R, Bates G. Bilateral cerebrospinal fluid rhinorrhoea. J Laryngol Otol 2000;114:137-8.
21. Moseley JI, Carton CA, Stern WE. Spectrum of complications in the use of intrathecal fluorescein. J Neurosurg 1978;48:765-7.
22. Anari S, Waldron M, Carrie S. Delayed absence seizure: A complication of intrathecal fluorescein injection. A case report and literature review. Auris Nasus Larynx 2007;34:515-8.
23. Daele JJ, Goffart Y, Machiels S. Traumatic, iatrogenic, and spontaneous cerebrospinal fluid (CSF) leak: Endoscopic repair. B-ENT 2011;7 Suppl 17:47-60.
24. Chan DT, Poon WS, IP CP, Chiu PW, Goh KY. How useful is glucose detection in diagnosing cerebrospinal fluid leak? The rational use of CT and beta-2 transferrin assay in detection of cerebrospinal fluid fistula. Asian J Surg 2004;27:39-42.
25. Jeng S. 50 years ago in the journal of pediatrics: Diagnosis of cerebrospinal fluid rhinorrhea: Lack of specificity of the glucose oxidase test tape. J Pediatr 2017;190:48.
26. Zhu ZJ, Cheng L, Yang J, Huang Q, Meng GZ, Cao RP, *et al.* Clinical analysis of adult spontaneous cerebrospinal fluid rhinorrhea. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 2018;32:457-61.