Original Article

The Use of Low- Dose Intrathecal Fluorescein in Endoscopic Repair of Cerebrospinal Fluid Rhinorrhea

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Abstract

Background: Intrathecal injection of fluorescein is a useful adjuvant method for localization of fistulas in endoscopic endonasal repair of cerebrospinal fluid (CSF) leakage. Although being neurotoxic in commercial doses, a low dose of diluted fluorescein seems to be safe on the basis the existing data in the literature.

Objectives: The purpose of this study was to investigate the role of a low- dose intrathecal fluorescein injection in detection of CSF fistula and potential adverse effects of this technique.

Materials and Methods: CSF rhinorrhea was repaired in 20 patients with an endoscopic endonasal technique. Intraoperative intrathecal fluorescein injection was used for localization of the site of the CSF leak. The accuracy rate of leakage site identification and the incidence of complications and recurrences were recorded.

Results: Intrathecal administration of fluorescein demonstrated CSF leakage in 18 of the 20 patients (90%). There were no intraoperative complications. Definitive closure of the CSF leakage site was achieved in 16 patients (80%) after the initial reconstruction. Recurrence occurred in four cases and all patients were free of CSF leakage after the second surgical attempt.

Conclusions: The present study suggested that a low dose of intraoperative intrathecal fluorescein administration is a safe and sensitive method for localization of CSF leakage sites.

Keywords: Cerebrospinal fluid, endoscopy, fluorescein, rhinorrhea

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Introduction

The cerebrospinal fluid (CSF) rhinorrhea is classically described as the leakage of CSF from the subarachnoid space into the paranasal sinuses and consequently into the nasal cavity.[1] The main causes of CSF rhinorrhea can be classified as traumatic, iatrogenic injury, congenital, neoplastic, and spontaneous.[2,3] In patients who do not respond to conservative treatment, surgical intervention is advised. Surgical repair for CSF leakage was first described by Dandy in 1926.[4] Since 1981, the minimally invasive endoscopic technique provides excellent success rate and near to the ground morbidity and mortality.[5–7]

Identification and localization of dural defects and CSF leaks has always been a challenging problem in this kind of surgery[8] because, CSF is a translucent fluid and the operative field is often blurred with blood or mucosal secretions.[9]

At present, intraoperative intrathecal use of fluorescein, a green fluorescent compound, is the commonly used technique for localization of the site of the CSF leak.[8,10,11] In this method, the green color of injected fluorescein into the intrathecal space can be observed in the nasal cavity; as a result, the point of CSF leakage is detected in patients with CSF rhinorrhea.

A number of studies have described complications and disadvantages of this technique,[10–12] while, some reports showed the safety of intrathecal injection of diluted low- dose fluorescein.[9–11] In the present study, the role of intrathecal fluorescein injection in detection of CSF fistula and potential adverse effects of this technique were investigated.

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Materials and Methods

Patient population

This case series study included 20 patients (five women and 15 men; the mean age: 33.7 years, range: seven to 65 years) with rhinorrhea for a period of at least one month. All patients underwent endoscopic management of CSF rhinorrhea at the Department of Neurosurgery in Sina Hospital, affiliated to Tehran University of Medical Sciences (TUMS) from June 2004 through September 2009. All patients were subjected to detailed history taking, neurosurgical evaluation, and thorough ear, nose, and throat examination, including nasal endoscopy, high-resolution coronal and axial computerized tomography (CT), and CT cisternography. The CSF fluid was diagnosed by a simple laboratory analysis of glucose and chloride level of rhinorrhea fluid in all cases.[13]

Informed consent was obtained from all patients and the study was approved by the Institutional Review Board at Vice-Chancellor of Research of TUMS.

After general anesthesia, the patients were placed in lateral decubitus position and a lumbar puncture (LP) was performed at the level of L3/L4 or L4/L5 intervertebral disc space. Ten milliliters of CSF was withdrawn and mixed with one milliliter of 5% sodium

Table 1. Location of the cerebrospinal fluid fistulas, body mass index, and symptoms of the patients

Variable	Subgroups	No. of Cases	%
BMI*	< 20	2	10
	20–24	9	45
	25–30	6	30
	> 30	2	10
Fistula sites	Lateral sphenoid	2	10
	Frontal sinus	2	10
	Cribriform	7	35
	Ethmoid	7	35
	Sphenoid	1	5
	Unknown	1	5
Symptoms	Rhinorrhea	9	45
	Recurrent meningitis	5	25
	Headache	3	15
	Meningocele	1	5
	0bstruction	1	5

*BMI= body mass index.

fluorescein solution (25 mg) for dilution. Fluorescein solution was slowly reinjected into the intrathecal space over several minutes. The patients remained in the supine position for the duration of the procedure. Zero- and 30-degree rigid 4-mm endoscopes (Karl Storz GmbH & Co., Tuttlingen, Germany) were used.

Endoscopic repair was carried out in all cases in a standard fashion as described in previous studies.[14,15] Fascia, subcutaneous fat, muscle, surgicel, and bone, if necessary, were used for repair. Soft tissue was removed and the hole of leakage was dilated. Fat or muscle was inserted at the site , so that it expanded behind the hole and sealed the site; then surgicel and fascia were applied. External lumbar drainage (ELD) was implanted after surgery and removed after five days. The patients were followed up at one and six months periods. History of postnasal drainage, salt tasting, and CSF leakage after strain was obtained. CT scan was performed for evaluation of pneumocephalus.

Results

The cause of CSF rhinorrhea was trauma in 11 patients (55%), iatrogenic in six patients (30%), and spontaneous in three patients (15%). The most common sites of CSF leakage were in the ethmoidal region in seven (35%) patients and in the cribriform plate in seven (35%) patients (Table 1). Unilateral watery rhinorrhea was the most common preoperative symptom, detected in nine patients (45%) and recurrent meningitis in five patients (25%) (Table 1). Duration of symptoms ranged from one to 60 months (mean ± SD = 19 ± 8 months).

Intrathecal administration of fluorescein demonstrated CSF leakage in 18 of the 20 patients (90%). Definitive closure of the CSF leakage was achieved in 16 patients (80%) after the initial reconstruction.

Recurrence occurred in four cases and three cases underwent a second surgery, and all patients were free of CSF leakage after the second surgical attempt. The only remaining recurrent case underwent bifrontal craniotomy and open closure of fistula with a double- layer fascia graft. No recurrence was obsereved after six months of follow-up.

In sixteen patients (80 %), prophylactic lumbar drains were performed. There were no intraoperative complications with the administration of intrathecal fluorescein. Postoperative complications were observed in four cases (20%). The most common complications in the postoperative period were meningitis in two patients, pnemocephalus in one patient, and pseudoaneurysm in one patient. In the first case with fulminant meningitis, the profile of CSF showed bacterial meningitis. So, soft tissue used for repair, was removed and a dramatic response, without any leakage was observed. The second case had mild hydrocephalus with aseptic meningitis, for whom conservative management with IV antibiotics was performed.

The patient with pneumocephalus had iatrogenic profuse watery CSF leak due to previous surgery for pituitary adenoma. The patient developed tension pneumocephalus, but his condition improved with conservative management.

The last patient had CSF leakage after radiation and shrinkage of a giant pituitary adenoma. Rupture of the internal carotid artery (ICA) occurred and packing made ICA occlusion, but the patient had a competent anterior communicating artery and crossed circulation by contralateral side, as a result did not develop any deficit.

Endoscopic repair was successful in all patients during the follow-up period and none of the cases demonstrated any neurological symptoms or signs that could be attributed to intrathecal fluorescein injection.

Discussion

It is critical to accurately locate the CSF fistula for successful repair surgery in rhinorrhea. At present, intrathecal fluorescein for endoscopic transnasal cerebrospinal leakage repair is the most frequently used adjunct in the intraoperative localization of CSF leaks.[8] Some studies reported this method as a safe technique,[9,14] but other studies showed that intrathecal administration of fluorescein has been associated with some severe side effects including seizures, flash pulmonary edema, headache, and distal lower extremity numbness. One study reported that the United States Food and Drug Administration (US FDA) had received 136 cases of severe side effects of intrathecal administration of fluorescein reports, and 13 patients died of adverse drug reaction between 1969 and 2003.[10] In the present study, no major complications attributable to fluorescein such as seizures, flash pulmonary edema, and distal lower extremity numbness were reported. This result showed that the use of intrathecal fluorescein is a safe technique

for diagnosis and localization of CSF leakage in intraoperative endoscopic surgery for the treatment of CSF rhinorrhea.

This discrepancy between the results of our study and those of other studies, which report severe side effects of intrathecal administration of fluorescein, may be explained by a number of factors. First, the fluorescein-related complications may be dose-related. Based on our knowledge, in the present study, lower dose of fluorescein was administrated. Second, the cases of these studies and the present report, represent a heterogeneous group of patients in terms of site, size, and cause of CSF leakage, as a result these variations may be a cause of this controversy.

In the present study, the intraoperative accuracy rate of localization of CSF fistula was about 85%. This indicated that intraoperative intrathecal fluorescein is a highly accurate method in the localization of the site of CSF leak in rhinorrhea.

This study had a number of limitations that must be acknowledged. First, the study was an uncontrolled case series and a similar cohort of patients without the use of fluorescein did not exist for comparison. A randomized trial is necessary to definitively assess safety and complications of fluorescein in the intraoperative evaluation of CSF leaks. Second, most complications in the present study were similar between surgery and administration of fluorescein; therefore, it is not easy to make a distinction between the causes of these side effects. In conclusion, the present study suggested that low dose of intraoperative intrathecal fluorescein administration is a safe and sensitive method for localization of CSF leakage sites.

Conflict of Interest: *None*.

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