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Postoperative Low-Flow Cerebrospinal Fluid Leak of Endoscopic Endonasal Transsphenoidal Surgery for Pituitary Adenoma—Wait and See, or Lumbar Drain?

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Abstract: To assess the effectiveness of continuous lumbar drainage (LD) for management of postoperative cerebrospinal fluid leaks after endoscopic endonasal transsphenoidal approach for resection of pituitary adenoma.

Three hundred eighty-four medical records of patients who were admitted to our institute during a 2.5-year period were retrospectively reviewed, 33 of them experienced low-flow cerebrospinal fluid leak postoperatively. If LD was used, all patients with low-flow cerebrospinal fluid leak were classified into 2 groups, lumbar drained group and conservatively treated group. The age, sex, management of cerebrospinal fluid leaks, and related complications were reviewed. Statistical comparisons between the 2 groups were made using SPSS 19.0 (IBM Corp, Armonk, NY). The differences were considered statistically significant if the *P* value was less than 0.05.

Thirty-three of 384 (8.6%) experienced low-flow postoperative cerebrospinal fluid leaks. Cured rate of cerebrospinal fluid leak was 94.4% (17/18) in continuous lumbar drained group, and 93.3% (14/15) in control group. There were 2 (11.2%) patients who developed meningitis in the LD group and 1 (5.6%) patient in the control group. One patient required endoscopic repair of skull base because of persistent cerebrospinal fluid leak in both groups, with the rates of 5.6% and 6.7%, respectively. There was no significant difference noted in each rate in both groups.

Placement of LD may not be necessary for the management of low-flow postoperative cerebrospinal fluid leak after using endoscopic endonasal transsphenoidal approach to pituitary adenoma.

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Continuous lumbar drainage (LD) is often used in endoscopic endonasal transsphenoidal approach intraoperatively,[1] postoperatively,[2] or even preoperatively[3] to prevent or manage postoperative cerebrospinal fluid (CSF) in many centers. However, the effect of LD placement remains controversial, especially for low-flow CSF leakage which accounts for majority of CSF hinorrhea after endoscopic sellar region surgery. Is continuous LD in management of low-flow CSF leakage really necessary (effective)? We reported our experience of treatment of CSF leaks after endoscopic transsphenoidal procedure which may answer the question.

MATERIALS AND METHODS

We retrospectively reviewed medical records of 384 patients who were admitted to Qilu Hospital of Shandong University and underwent endoscopic endonasal transsphenoidal approach for resection of pituitary adenoma between January 2012 and June 2014, 33 of them experienced low-flow CSF leak postoperatively. All patients with CSF leak were classified into 2 groups based on LD use, lumbar drained group (LD group) and conservatively treated group (control group). The age, sex, management of CSF leaks, and related complications were reviewed. Patients who experienced high-flow CSF leak postoperatively and returned to operating room for repair and who applied LD intraoperatively were excluded from the study. The protocol for this study was reviewed and approved by the Ethics Committee of Qilu Hospital of Shandong University (KYLL-2013–010).

Surgical Technique

The procedure was performed by the same surgical team with senior neurosurgeon Xingang Li, MD. After general anesthesia with orotracheal intubation, the patient was placed supine with slight rotation of the head toward the right shoulder. Usually, the right lateral thigh was prepared for harvest of fascia lata, fat, or muscle to repair skull base as needed. The nasal mucous membranes were decongested with injection of 1% lidocaine with epinephrine (1:100,000 dilution).

The procedure was performed in the right nostril with a 0 degree endoscope, 4 mm in diameter, and 18 cm in length. The middle turbinate was pushed laterally to obtain more surgical freedom, then the endoscope is angled upward, about 1.5 cm, to reach the sphenoid ostium, a key anatomic landmark. The posterior portion of the nasal septum was dissected, and the anterior wall of the sphenoid sinus was opened widely, exceeding the sphenoid ostium. Sellar floor was opened with a high speed

TABLE 1. Patient Profile of CLD Group

Case No.	Age/Sex	Clinical Presentation	SOT	ETR	Intracranial Infection	Reoperation for Repair	Death
1	71/M	Headache, hypopsia	Mac	TR	N	N	N
2	71/M	Headache, hypopsia	Mac	STR	N	N	N
3	71/M	Headache, hypopsia	Mic	TR	N	N	N
4	55/F	Decreased visual acuity	Mac	STR	N	Y	N
5	54/F	Headache	Mic	TR	N	N	N
6	49/F	Headache, decreased visual acuity	Mac	TR	Y	N	N
7	45/M	Acromegaly	Mic	TR	N	N	N
8	45/F	Headache	Mac	TR	N	N	N
9	41/M	Polydipsia, polyuria	Mac	TR	N	N	N
10	39/F	Headache, left vision loss	Mac	TR	Y	N	N
11	38/F	Headache, acromegaly	Mic	TR	N	N	N
12	35/M	Headache	Mic,	TR	N	N	N
13	33/M	Headache, decreased visual acuity	Mac	TR	N	N	N
14	32/F	Amenorrhea	Mic	TR	N	N	N
15	27/M	Acromegaly	Mac	STR	N	N	N
16	24/F	Cushing disease	Mic	TR	N	N	N
17	20/M	Headache, decreased visual acuity	Mac	TR	N	N	N
18	20/M	Developing fast at age	Mac	TR	N	N	N

ETR, extent of tumor removal; F, female; M, male; Mac, macroadenoma; Mic, microadenoma; SOT, indicates size of tumor.

microdrill. The tumor typically spilled over when the dural opened cruciately. After the lesion was removed with a curette or suction, a 30-degree endoscope was used to detect and remove any residual lesion. The surgical cavity was filled with Gelfoam (Pharmacia & UpJohn Corp, New York City, NY). The technique of reconstruction of skull base varied on whether and how CSF leak occurred. If no CSF leak was informed intraoperatively, surgical cavity was filled with Gelfoam, followed by a synthetic dural graft as an overlay graft, then fibrin glue was applied over the synthetic dura. When low-flow CSF leak was inspected, an autologous fat or fascia lata graft was placed within the dural defect as an inlay graft, a synthetic dural graft was used as an overlay graft. On the situation that high-flow CSF leak occurred, a vascularized pedicled nasoseptal flap (PNSF) was harvested from left nasoseptal and covered on the overlay graft, then fibrin glue was applied on the PNSF. The sphenoid sinus was filled with Gelfoam, and the nasal cavity was packed with pledgets. All patients received prophylaxis with third-generation antibiotics intraoperatively.

Postoperative Management

Patients were instructed to rest with their head elevated about 15° and to avoid any activity that might raise intracranial pressure, such as straining or nose blowing. Nasal packing was generally removed endoscopically 1 to 3 days after surgery. The third-generation antibiotic was continued for 3 to 7 days postoperatively. Leakage from nostrils was monitored for both group of patients, TES-tape (Eli Lilly and Co., Indianapolis, IN) was applied to inform CSF leaks for patient who experienced rhinorrhea. Based on whether LD was used, patients who developed CSF leakage post-operatively were classified into 2 categories as follows, lumbar drained group (LD group) and conservatively treated group (control group). Endoscopic repair of skull base was performed in patient whose CSF leak persisted over 7 days in each group.

Statistical Methods

Statistical comparisons between the 2 groups were made using Chi-squared analysis for categorical variables and Student *t* test for

TABLE 2. Patient Profile of Control Group

Case No.	Age/Sex	Clinical Presentation	SOT	ETR	Intracranial Infection	Reoperation for Repair	Death
1	68/F	Headache, decreased visual acuity	Mac	STR	N	N	N
2	65/M	Decreased visual acuity	Mac	TR	N	N	N
3	57/F	Headache	Mic	TR	N	N	N
4	53/F	Decreased visual acuity	Mac	TR	N	N	N
5	48/M	Headache	Mic	TR	N	N	N
6	46/M	Decreased visual acuity	Mac	TR	N	N	N
7	44/F	Headache, hypopsia	Mac	TR	Y	N	N
8	41/F	Headache, acromegaly, Hypopsia	Mac	STR	N	N	N
9	38/F	Headache, hypopsia	Mac	TR	N	Y	N
10	35/M	Headache, headache, hypopsia	Mac	TR	N	N	N
11	32/F	Asymptomatic	Mic	TR	N	N	N
12	31/F	Headache, amenorrhea	Mic,	TR	N	N	N
13	29/M	Headache, decreased visual acuity	Mac	TR	N	N	N
14	27/F	Amenorrhea, galactorrhea	Mic	TR	N	N	N
15	22/M	Headache, hypopsia	Mac	TR	N	N	N

TABLE 3. Summary of Clinical Outcomes of 2 Groups

	LD Group	Control Group	*P*
Male	8/18 (44.4%)	6/15 (40%)	0.27
Female	10/18 (55.6%)	9/15 (60%)	0.27
Cured	17/18 (94.4%)	14/15 (93.3%)	0.51
Meningitis	2/18 (11.2%)	1/15 (6.7%)	0.42
Reoperation	1/18 (5.6%)	1/15 (6.7%)	0.51

continuous variables. Two-tailed tests were performed for each scenario, and the differences were considered statistically significant if the *P* value was less than 0.05. Data were analyzed using SPSS 19.0 (IBM Corp).

RESULTS

Of the 384 patients who experienced endoscopic endonasal transsphenoidal approach for resection of pituitary adenoma, 33 (8.6%) experienced low-flow postoperative CSF leaks. In the LD group, age ranged from 15 to 71 months (mean, 41.5 months), 11 (61.1%) were macroadenomas, compared to 42.4 years for mean age and 66.7% for macroadenoma in control group. Total resection was achieved in 15 cases (83.8%), and a subtotal resection in 3 (16.2%) in LD group, total resection and subtotal resection were 86.7% and 13.3%, respectively, in the control group. No patient had partial or insufficient resection in each group (Tables 1 and 2). Cured rate of CSF leak was 94.4% (17/18) in the LD group, and 93.3% (14/15) in the control group. There were 2 (11.2%) patients who developed meningitis in the LD group and 1 (5.6%) patient in the control group. One patient required endoscopic repair of skull base because of persistent CSF leak in both groups, with the rates of 5.6% and 6.7%, respectively. No significant difference was noted in each rate in both groups (Table 3). No patient experienced recurrence of CSF leakage in both of the groups during the follow-up period.

DISCUSSION

Cerebrospinal fluid leak, which mostly means CSF rhinorrhea, is a pathologic condition where CSF flows out from defects of dural and skull base. Long-term CSF leak may result in many severe complications, even life-threatening event. Based on the cause of the fistula, the CSF leak was classified into spontaneous, traumatic, and iatrogenic (ie, surgery of skull base). In this study, we focused on patients who underwent endoscopic endonasal transsphenoidal approach for resection of pituitary adenoma and discussed surgical complications.

The first use of modern endoscope in transsphenoidal transnasal approach was reported by Apuzzo et al,[4] after then, endoscopic endonasal transsphenoidal approach has been a mainstay in many medical centers in the last 2 decades. Nevertheless, CSF leak is still the main and common postoperative complication of the endoscopic approach. Cerebrospinal fluid leak was classified into high-flow type and low-flow type. The term high-flow CSF leakage was introduced by Luginbuhl et al,[5] which indicated consistent CSF flow out intraoperatively on the situation of the big defect of cistern or opening of ventricle. Although there were few reports confirming the concept of low-flow CSF leakage postoperatively in the literature, we confined low-flow CSF leakage where CSF leaked in a few drops only on the situation of transient increased intracranial pressure, such as getting up, straining, and coughing. The occurrence of the postoperative CSF leak was associated with many factors, such as surgical technique, aggressiveness of resection, volume and location of tumor, and relationship tumor with surrounding neurovascular structures (ie, tumor adherence). Of the factors, the surgeon's technique of reconstruction of the skull base/sellar defect is probably the most important. Many techniques and materials have been applied to repair the defect of the skull base in an endoscopic transsphenoidal approach.[6,7] In 2006, Hadad et al[8] introduced PNSF reconstruction for skull base repair, which significantly decreased postoperative CSF leakage from 2.4% to 5%.[9,10] Even Eloy et al[6] and Greenfield et al[7] reported their experiences and indicated that rigid structural reconstruction and additional dural sealant were not necessary in the condition that skull base defects were well reconstructed with PNSF. We used different technique depending on the varied condition. If no CSF leak was reported intraoperatively, surgical cavity was filled with Gelfoam, followed by a synthetic dural graft as an overlay graft, then fibrin glue was applied over the synthetic dura. When low-flow CSF leak was inspected intraoperatively, an autologous fat or fascia lata graft was placed within the dural defect as an inlay graft, and a synthetic dural graft was used as an overlay graft. On the situation that high-flow CSF leak occurred, a PNSF was covered on the overlay graft, then fibrin glue was applied. In the present study, the total rate of CSF leakage postoperatively was 8.6%, which was comparable to the rates in the literature.[11–14]

The only negative predictor of postoperative CSF leak was increased intracranial pressure.[15] Thus, any methods decreasing intracranial pressure may prevent or manage CSF leakage, such as head elevation, avoiding of straining or nose blowing, placement of LD, and so on. Of which, LD were adopted and thought previously to be effective by many neurosurgeons to manage postoperative CSF leak.[2,16] However, many authors harbored different viewpoint on the use of LD for treatment of postoperative CSF leaks.[16–20] Ransom et al,[21] indicated in their study that LD may increase the incidence of complications related to postoperative CSF leaks, that is, intracranial infection.[22,23] In addition, continuous LD may have risks of intracranial hypotension and pneumocephalus.[24,25] Francel et al[26] reported that 2 patients resulted in coma state after LD placement. We defined cure of CSF leakage as that no drop of CSF was informed in 48 hours consecutively. In present study, the cured rate of CSF leakage postoperatively in LD group was 94.4%, whereas the rate was 93.3% in control group. No significant difference was noted between the groups ($P = 0.51$). Although the rate (11.2%) of meningitis in LD group was higher than that in control group, there was no difference with statistical significance between the 2 groups ($P = 0.42$). Above results showed that LD may not be significantly effective for the management of postoperative CSF leaks and may have potential risks which might include:

(1) Restricted mobilization of the patient because of continuous LD may increase the risk of thromboembolic and pulmonary complications,[2] especially in elderly patients.
(2) It was difficult to manage the device of continuous LD. The catheter of LD was easy to take off from lumbar subarachnoid when patient mobilized, which also increased utilization of health care resource.[21]
(3) The increased incidence of intracranial infection. Although continuous LD was still one of the factors resulting in intracranial infection, there was no difference found between the 2 groups in our series with infection rates of 11.2% and 6.7%, respectively. Multicentric and large volume sample study may have a different finding about infection rate.

In this study, most CSF leaks stopped automatically in approximately 1 week, only small portion of which need surgical repair. Bell et al[17] reported that 84% of patients who experienced

postoperative CSF leak obtained resolution without treatment in 2 to 10 days, which may be the time adherence of repair materials taken. In our series, there was only 1 patient who experienced endoscopic repair for CSF leakage in both groups. We did not note significant difference in the groups ($P = 0.51$).

CONCLUSIONS

Continuous LD may not be necessary for the management of low-flow postoperative CSF leak after endoscopic endonasal transsphenoidal approach to pituitary adenoma. The study involved only a small-sample volume; further, large-sample volume investigation may evaluate the effectiveness of continuous LD.

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