Randomized clinical trial of acetazolamide administration and/or prone positioning in mitigating wound complications following untethering surgeries

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OBJECTIVE No evidence-based guideline has been approved for the postoperative management of pediatric patients with tethered cord syndrome (TCS). The purpose of this randomized clinical trial was to evaluate the effectiveness of prone positioning and acetazolamide administration on complication rates following spinal cord untethering surgeries.

METHODS From October 2012 to February 2015, patients with a primary diagnosis of TCS who were admitted to the Children's Medical Center Hospital of Iran were randomly allocated to 1 of 4 intervention modality groups postoperatively: 1) Group A, acetazolamide administration for 10 days; 2) Group B, prone positioning for 10 days; 3) Group C, acetazolamide administration and prone positioning for 10 days; and 4) Group D, no intervention. CSF leakage, CSF collection, wound dehiscence, operative site infection, and secondary surgical wound repair were considered failure.

RESULTS A total of 161 patients were enrolled in this study (Group A, n = 39 [24.2%]; Group B, n = 41 [25.5%]; Group C, n = 39 [24.2%]; and Group D, n = 42 [26.1%]). The overall failure rate was 12.42% (20 patients). Complication rates through pooled analyses were as follows: CSF leakage (n = 9, 5.6%), CSF collection (n = 12, 7.5%), wound dehiscence (n = 2, 1.2%), and infection of operation site (n = 3, 1.9%). Two patients (1.2%) required surgical secondary wound repair due to complications. CSF leakage and collection rates were significantly lower in patients who underwent prone positioning (p = 0.042 and 0.036, respectively). The administration of acetazolamide, either isolated or in combination with prone positioning, not only could not significantly lower the complication rates, but also added the burden of side effects.

CONCLUSIONS The current study demonstrates the possible role of prone positioning in mitigating the complication rates subsequent to untethering surgeries.

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KEY WORDS prone positioning; acetazolamide; cerebrospinal fluid leakage; cerebrospinal fluid collection; wound dehiscence; spine

TETHERED cord syndrome (TCS) is a clinical condition resulting from traction on the conus medullaris.^{2,14,38} Low positioning of conus medullaris, fatty filum (FF), lipomyelomeningocele (LMMC), myelomeningocele, split cord malformation (SCM), and dermal sinus (DS) are some conditions that can cause TCS.^{2,7,14,29,34,38} While asymptomatic in some patients, TCS can present with pain, neurological deterioration, and orthopedic or urological aggravation.^{2,14,38} An untethering procedure may be associated with serious complications such as CSF leakage, CSF collection, wound dehiscence,

and infection.^{19,27,30,31} Despite a vast investigation of preventive interventions for such complications,^{4,8,18,21,27} no evidenced-based guideline has yet been published.

Although prophylactic administration of acetazolamide and/or bed rest following the intradural operation are acceptably used by both neurosurgeons and orthopedic surgeons, no high-level approved evidence exists regarding whether and how to use these measures.

To the best of our knowledge, no randomized trial has assessed the prophylactic effect of acetazolamide in reducing complications following spinal surgeries. Likewise,

ABBREVIATIONS DS = dermal sinus; FF = fatty filum; LMMC = lipomyelomeningocele; SCM = slit cord malformation; TCS = tethered cord syndrome.

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only a limited number of trials have been published on the duration of postoperative bed rest.^{8,30,31} In this study, we conducted a randomized, 4-arm, controlled clinical trial to assess the effect of acetazolamide administration and/or prone positioning on the outcome of pediatric patients who underwent untethering surgeries and discuss other factors that may influence the rate of failure.

Methods

This study was conducted from October 2012 to February 2015 at the Children's Medical Center Hospital in Tehran, Iran. The study was approved by the Medical Ethics and History of Medicine Research Center of Tehran University of Medical Sciences and registered in the Iranian Registry of Clinical Trials (no. IRCT2012100611023N). This study was also registered with the ClinicalTrials.gov database (<http://clinicaltrials.gov>), and its registration no. is NCT01867268. All patients were enrolled in this study voluntarily and informed consent was obtained from the parents or legal advocates of the patients.

Eligibility Criteria

All the patients who needed spinal cord untethering surgery were screened, and those with an initial diagnosis of primary tethered cord with fatty or thick filum terminale, LMMC, SCM, DS, or any other closed spinal dysraphism requiring intradural intervention were included. Patients with an infected dermoid tumor, intramedullary abscess, myelomeningocele, meningocele, or those who had hydrocephalus were excluded. All patients with a tethered cord and thick filum had a conus medullaris at a level much lower than a normally accepted level (distal to the L-3 level). The presence of neurological symptoms was not mandatory to be included in the study, but all clinically asymptomatic patients had at least 1 pathological finding in their urological studies, including radiological or urodynamic assessment. Other exclusion criteria were patients seeking an untethering reoperation or those older than 18 years of age on admission.

Study Design and Sample Size

Because the main purpose of this study was to evaluate the effect of applying two main factors (prone positioning and acetazolamide administration) on outcome, a factorial study was the most appropriate study design, in which participants were allocated to receive neither postoperative measure, one or the other, or both together. A factorial trial enabled us to evaluate both the separate effects of each intervention and the benefits of receiving a combination of both interventions.²⁹ It is worth noting that the 2 postoperative interventions in our study are independent measures, which is the main assumption of the factorial design. Based on the factorial trial design²⁹ and considering 80% power and an α of 0.05, a minimum of 144 patients was calculated.

Randomization and Allocation of the Patients to Interventions

Randomization was performed through a computer-

based 4-factor randomization block design. All the included cases (161 patients) were randomly assigned to 1 of the 4 intervention modality groups by taking 1 of the opaque enveloped cards postoperatively: Group A, acetazolamide administration for 10 days; Group B, prone positioning for 10 days; Group C, acetazolamide administration and prone positioning for 10 days; and Group D, no intervention.

Both the medical staff and the parents of the patient were kept blinded to the intervention before and through the operation. Thus, the intervention allocated to the patient was not affected by the indication (LMMC, DS, SCM, or FF) or technique of the surgery (e.g., whether or not a fascial patch graft was used). Keeping parents blinded could prevent selection bias, influenced by the parents' desire for allocating their children to a given group. The analyzer was also kept blind from the entity of the interventions and indications.

Surgical Considerations

All surgeries were performed in an elective setting. All patients underwent surgical interventions based on individual indications according to preoperative diagnoses and images. The dura and fascia were closed in a watertight fashion after completing the intradural procedure. In the case of a dural or fascial defect, a fascial patch graft was used to fill the gap. No sealant or adhesive material was used to fortify sutures. Skin closure was performed in a multiple-layer fashion with absorbable sutures. At the end of the procedure, a compressive dressing bandage was applied.

Interventions and Postoperative Care

All patients underwent a routine and similar protocol of wound care following the surgery. Operative sites were cleaned with Povidone-iodine and a compressive dressing was applied daily up to the discharge day. Acetazolamide was administered as tablet or dissolved in water, and dosing was based on the patients' weight (20 mg/kg/day). Due to ethical considerations and poor compliance of the younger patients, we did not use physical restraints for maintaining position; instead, we kept the patients prone with the aid of parents and trained nurses. Toddlers received incentives and older patients were convinced to lay prone. The patients maintained the position to the end of the tenth day, even after being discharged from the hospital.

During hospitalization, the compliance of keeping the prone position was controlled by the staff nurse. Compliance for maintaining the prone position for the entire 10 days was checked on the first visit after discharge by asking the parents. The patients in the no-intervention group were free to maintain any position and/or be out of bed from the day after surgery.

Outcome Assessment

Cerebrospinal fluid leakage, CSF collection, wound dehiscence, operative site infection, and secondary wound repair through the first month following the surgery were considered failure. CSF leakage was defined as fluid rush-

ing out from the wound, confirmed by 2 attending neurosurgeons (F.N. and Z.H.) in separate settings. CSF collection was considered as visible subcutaneous fluid collection or subcutaneous fluctuation confirmed by 2 attending neurosurgeons in separate settings, without any superficial ultrasound probe assessment or MRI. In all patients with CSF subcutaneous fluid collection or subcutaneous fluctuation, subcutaneous fluid tapping was conducted to rule out hematoma formation. Wound dehiscence was defined by wound ruptures along surgical sutures, either because the surface layers separated or the whole wound split open. Wound infection was confirmed with culture and staining of the samples from the operative site. Postoperative evaluations (performed daily during hospitalization and about 4 weeks after discharge) were conducted by 2 attending neurosurgeons.

Complication Management

In the case of CSF leakage, CSF collection, and wound dehiscence, in addition to relevant measures such as surgical debridement or simple wound repair, and regardless of the primary intervention group, the patient received acetazolamide and was kept prone until complete wound healing. In the case of wound infection, an antibiotic was administered according to the culture and antibiogram.

Statistical Analysis

Statistical analyses were performed using SPSS (version 22, IBM) and Stata (version 12.0, StataCorp). Data are presented as either means $\pm$ SDs (range), or proportions. The normality of the parameters was checked using the Kolmogorov-Smirnov test. For comparison of quantitative variables (such as weight, age, and the duration of the surgery) in the 4 intervention groups of the study, 1-way ANOVA was used. The chi-square test was used for comparing the proportions of patients who underwent grafting, in addition to the number of males and females in each group. For the comparison of surgical indications between intervention groups (major indication, as well as second and third associated defect), Fisher's exact test was used, as the frequency of complications in the groups was small.

Sex, age, and weight of the patients on the day of the operation, use of a fascia graft, duration of surgery, and the main indication of the surgery (independent variables) were used to predict complications (dependent variable) in a binary logistic regression analysis. All *p* values less than 0.05 were considered significant in all analyses.

Results

A total of 161 patients were enrolled in this study. Patients were randomly assigned to 1 of the 4 intervention groups after surgery (Group A [*n* = 39, 24.2%]; Group B [*n* = 41, 25.5%]; Group C [*n* = 39, 24.2%]; Group D [*n* = 42, 26.1%]). Among those who were excluded, 87 patients had myelomeningocele, 31 patients were admitted due to repeat surgery for myelomeningocele or LMMC, and 7 patients were treated for complicated DSs with abscess.

Seventy-one patients (44.1%) were male. The mean age of the patient population was 3.14 ± 3.80 years old (range

1–5527 days), and the average weight of the patients on the day of the operation was 12.10 ± 11.11 kg (range 1.4–73 kg; Table 1).

Pooled analysis of all patients in the 4 groups revealed that 78 patients (48.4%) underwent surgery for LMMC. Other indications for surgery were primary TCS (28%), SCM (12.4%), and uncomplicated DS (11.2%). A total of 30 patients (18.6%) had a second associated anomaly, and 2 patients (1.2%) had a third associated abnormality (Table 2). Duraplasty was conducted in 55 patients (34.2%). The mean operative time was 171.79 ± 78.30 minutes (range 40–510 minutes). Data for each intervention group is provided in Table 1.

The distribution of patient sex, age, and weight on the day of the operation, medical indications for surgery (LMMC, SCM, FF, and DS), and the rate of duraplasty were similar among categories of intervention. The mean duration of procedures was not remarkably different among patients who underwent these 4 indications (LMMC, SCM, FF, or DS). However, the duration of the operation varied significantly between the 4 intervention groups (A–D), with the lowest mean in Group B (130 minutes) and highest in Group D (216 minutes; *p* < 0.01). Subsequently, all analyses were performed with adjustment for this factor and by splitting the duration of the operation into 2 subgroups (< 120 minutes and > 120 minutes).

Considering all 4 intervention groups together, the complications and their frequencies were as follows: CSF leak (*n* = 9, 5.6%), CSF collection (*n* = 12, 7.5%), wound dehiscence (*n* = 2, 1.2%), and infection of operative site (*n* = 3, 1.9%; Table 3). Two patients (1.2%) required surgical secondary wound repair due to wound dehiscence. Hematoma was detected in 1 patient (0.62%), which was not considered wound failure. Some patients experienced more than 1 complication, thus the overall failure rate was 12.42% (20 patients). Details on complication rates in each intervention group are presented in Table 3.

The analyses of complications through each intervention group (A–D) yielded a borderline difference in CSF leak and significant difference in CSF collection rates among categories of intervention (*p* = 0.06 and 0.02, respectively; Table 3).

In the factorial design and considering the patients in Groups B and C together, patients who underwent prone positioning had significantly lower rates of CSF leak and collection (*p* = 0.042 and 0.036, respectively). Nonetheless, the association between prone positioning and wound dehiscence or operative site infection was not significant (Table 4).

Rates of complications in patients taking acetazolamide were not significantly different from others. Among all those who received acetazolamide, 2 (2.56%) patients experienced diarrhea without bacteria growth in stool examination, 3 (3.84%) had acidosis, 2 (2.56%) experienced electrolyte imbalance, and 4 (5.12%) had loss of appetite. One patient needed admission to the intensive care unit due to severe acidosis and electrolyte imbalance. Applying both modalities (prone positioning and acetazolamide administration) simultaneously did not mitigate the rate of complications.

Binary logistic regression did not find any meaningful

TABLE 1. Patient characteristics in each intervention group

Characteristics	Intervention				Total	p Value
	Acetazolamide	Prone Positioning	Acetazolamide & Prone Positioning	No Intervention		
No. of patients	39	41	39	42	161	
Sex (%)						0.11
Female	18 (46.2)	19 (46.3)	26 (66.7)	27 (64.3)	90 (55.9)	
Male	21 (53.8)	22 (53.7)	13 (33.3)	15 (35.7)	71 (44.1)	
Age (days)						0.40
Mean $\pm$ SD	828.3 $\pm$ 942.0	1138.1 $\pm$ 1500	1177 $\pm$ 1530.6	1389 $\pm$ 1442.9	1146.5 $\pm$ 1385.6	
Range	1–3285	65–4745	1–5527	1–438	1–5527	
Weight (kg)						0.40
Mean $\pm$ SD	11.08 $\pm$ 12.20	10.96 $\pm$ 8.60	11.33 $\pm$ 8.37	14.66 $\pm$ 14	12.10 $\pm$ 11.11	
Range	2–73	4.2–37	3.8–37	1.4–68	1.4–73	
No. w/ dura graft (%)	14 (35.9)	14 (34.1)	11 (28.2)	16 (38.1)	55 (34.2)	0.81
Duration of operation (min)						0.00
Mean $\pm$ SD	160.8 $\pm$ 66.2	129.7 $\pm$ 67.0	181.3 $\pm$ 58.8	215.9 $\pm$ 90.2	171.79 $\pm$ 78.30	
Range	40–300	40–270	60–345	60–510	40–510	

association between each of the complications (CSF leak, CSF collection, wound dehiscence, and infection) and basal parameters (sex, age, and weight of the patients on operation day), use of fascia graft, and duration of or indication for surgery. Complication rates did not vary among patients with different indications for surgery (LMMC, SCM, FF, DS). We also could not find any increment in

complication rates when comparing the patients who underwent LMMC and the other 3 indications for surgery (Table 5).

Discussion

Several conditions including LMMC, SCM, FF, and DS are associated with TCS. Untethering of a tethered spi-

TABLE 2. Surgical indications in each intervention group

Characteristics	Intervention				Total	p Value*
	Acetazolamide	Prone Positioning	Acetazolamide & Prone Positioning	No Intervention		
Major indication for surgery (%)						0.32
LMMC	18 (46.2)	22 (53.7)	24 (61.5)	14 (33.3)	78 (48.4)	
DS	4 (10.3)	5 (12.2)	1 (2.6)	8 (19.0)	18 (11.2)	
Primary TCS	12 (30.8)	10 (24.4)	10 (25.6)	13 (31.0)	45 (28.0)	
SCM syndrome	5 (12.8)	4 (9.8)	4 (10.3)	7 (16.7)	20 (12.4)	
Second associated defect (%)						0.33
DS	0	1 (2.4)	0	1 (2.4)	2 (1.2)	
Tumor	4 (10.3)	0	0	1 (2.4)	5 (3.1)	
Lipoma	1 (2.6)	0	0	2 (4.8)	3 (1.9)	
Syrinx	2 (5.1)	0	1 (2.6)	1 (2.4)	4 (2.5)	
Arachnoid cyst	3 (7.7)	0	0	3 (7.1)	6 (3.7)	
SCM	0	0	1 (2.6)	2 (4.8)	3 (1.9)	
Scoliosis	2 (5.1)	0	0	0	2 (1.2)	
Twin in twin	1 (2.6)	0	0	1 (2.4)	1 (0.6)	
Sacral agenesis	0	1 (2.4)	1 (2.6)	0	2 (1.2)	
Human tail	0	0	0	1 (2.4)	1 (0.6)	
Intramedullary abscess	0	1 (2.4)	0	0	1 (0.6)	
Third associated defect (%)						0.50
Syrinx	0	0	1 (2.6)	0	1 (0.6)	
Scoliosis	0	0	0	1 (2.4)	1 (0.6)	

* Fisher's exact test.

TABLE 3. Complications following untethering surgeries, considering each intervention group separately*

Complications	Interventions (%)				Total	p Value
	Acetazolamide	Prone Positioning	Acetazolamide & Prone Positioning	No Intervention		
CSF leak	3 (7.7)	0	1 (2.6)	5 (11.9)	9 (5.6)	0.06
CSF collection	5 (12.8)	2 (4.9)	0	5 (11.9)	12 (7.5)	0.02
Wound dehiscence	0	0	2 (5.1)	0	2 (1.2)	0.11
Operative site infection	0	2 (4.9)	1 (2.6)	0	3 (1.9)	0.42
Surgical wound repair	1 (2.6)	1 (2.4)	0	0	2 (1.2)	0.61

* p values were calculated considering each postoperative intervention group separately and without applying factorial analyses.

nal cord is recommended in symptomatic or even asymptomatic patients, although there are some debates on the latter condition.^{25,30,32} The end point of closure in all untethering surgeries (with no respect to the underlying pathology) is the same and contains the watertight closure of dura and fascia. Despite the safety of the technique, complications such as CSF leakage, CSF collection, wound dehiscence, and infection are still reported,^{19,23,27,30,31} and albeit rare, they might be serious, leading to meningitis or encephalitis.^{21,31,34,40}

Although various interventions are introduced as protective modalities for reducing the risk of these complications,^{4,18} no evidenced-based or accepted guideline has yet been suggested. Therefore, we designed this study to evaluate the effectiveness of these two routinely practiced postsurgical measures (acetazolamide administration and prone positioning) in patients who underwent untethering of the spinal cord.

Bed Rest

Bed rest is a broadly accepted postoperative care following numerous surgeries.^{2,4,7,8,28} However, there is no consistency between surgeons on indication, duration, and position of the bed rest for prevention and management of CSF complications following lumbosacral spinal surgeries.^{9,12,16,26,29,31}

Experimental models of the dural reparative process showed that primary fibroblastic bridging of the durotomy appears at postoperative Day 6, and closure of the defect occurs at Day 10.³ Some spine surgeons determine the length of bed rest on this basis.⁴ In the All India Institute of Medical Sciences²⁷ almost all patients with spinal dysraphism are nursed in the prone position, as a routine protocol, for a duration of approximately 7–10 days. However, surveys on current practice in postoperative accidental

durotomy showed a trend toward minimizing the duration of bed rest; the majority of surgeons recommend bed rest up to 72 hours and almost 25% of them allow immediate mobilization of the patients.^{9,11}

Some authors have stated that solitary bed rest is ineffective in preventing the consequences following incidental durotomy,^{10,12} and the rate of revision surgeries is the same in patients who underwent bed rest and in those with early mobilization.^{9,16} Despite this opinion, isolated flat positioning is suggested as an effective CSF leak management strategy following tethered cord release.^{2,29}

Some recent studies were published on this issue to put an end to this discrepancy. Chern and colleagues⁸ studied 3 different postoperative care strategies: supine positioning for 48 hours (1 day in the hospital and then keeping the position for another day at home), or 72 hours either as 3 days in the hospital or discharge after the first day. By their conclusion, bed rest can be minimized to 48 hours without an additive complication rate.

In the study by Ogiwara et al.,³¹ patients were kept supine for 8 days following surgery. In comparison with 2 previously published studies with 24–72 hours of supine positioning,^{8,39} those who kept the position for 8 days had lower pseudomeningocele formation and CSF leakage rates. Further comparison of the patients who were kept supine for either 72 hours or 8 days but with a unique surgical technique and dural closure did not find any significant difference between these 2 cohorts.³⁰ Ogiwara and colleagues also mentioned that the preliminary analysis of 1-day bed rest in their ongoing study was satisfactory, and they suggested future studies on the elimination of bed rest from postoperative care protocols.²⁰

In our study, the analysis of complications in each intervention group (comparison between factorial cells) yielded a borderline association between position and CSF

TABLE 4. Complications following untethering surgeries based on factorial design

Complications	Intervention Modalities (%)			p Values*
	Acetazolamide Administration (n = 78)	Prone Positioning (n = 80)	No Intervention (n = 42)	
CSF leak	4 (5.13)	1 (1.25)	5 (11.9)	0.042
CSF collection	5 (6.41)	2 (2.50)	5 (11.9)	0.036
Wound dehiscence	2 (2.57)	2 (2.50)	0	0.091
Operative site infection	1 (1.28)	3 (3.75)	0	0.320
Surgical wound repair	1 (1.28)	1 (1.25)	0	0.054

* Exact logistic regression.

TABLE 5. Comparison of complication rates between patients with different indications of surgery

Complications	p Values	
	Between Patients w/ Different Indications for Surgery*	Between Those Who Underwent LMMC & Other 3 Indications
CSF leak†	0.15	>0.9
CSF collection‡	0.14	0.07
Wound dehiscence†	0.10	0.23
Operative site infection†	0.15	0.11

* LMMC, DS, SCM, and primary TCS.

† Fisher's exact test.

‡ Pearson's chi-square test.

leakage ($p = 0.06$) and a meaningful association between prone positioning and CSF collection ($p = 0.02$). By the aid of the factorial design and corresponding analyses, we cumulatively considered all patients who underwent prone positioning (78 children [48.4%]) and reduced the effect of acetazolamide administration on those from Group C of the intervention modality. This analysis suggested that prone positioning can significantly eliminate the rate of CSF leakage and collection ($p = 0.042$ and 0.036 , respectively).

Based on our knowledge, this is the first randomized clinical trial that shows the effectiveness of prone positioning in preventing postoperative complications. The dissimilarity of our findings with previous reports can be assigned to the position (prone instead of supine) and longer duration of the bed rest in our study.

Changing the body position from horizontal to standing posture increases the mean lumbar subarachnoid and CSF pressure.⁵ Similarly, dural sac cross-sectional area at the level of intervertebral disc, as a direct function of CSF pressure, is lower in the supine position in comparison with standing posture.¹⁵ The pressure of CSF in the prone position is even lower than in the supine position.^{24,33} Postural variation of CSF pressure affects intracanal pressure (inside the spinal canal) in almost the same patterns^{13,35} and both CSF and intracanal pressure are lowest in the prone position.¹³ Although prone positioning was significantly associated with a lower rate of complications in comparison with the free position, its superiority to the supine position should be evaluated in further studies. Moreover, the 10-day period of keeping pediatric patients prone is unacceptable to most of the parents. Therefore, we are designing another study in which the length of prone positioning is mitigated.

Anatomical factors such as fat tissue thickness at the operation site might be the probable causes for absence of correlation between wound dehiscence and positioning.^{4,9}

Acetazolamide Administration

Acetazolamide reduces CSF production and flow by inhibiting the choroid plexus carbonic anhydrase enzyme, resulting in CSF volume and intracranial pressure reduction.^{1,6,17,37} Acetazolamide had been widely used for

the management of CSF leakage.^{6,22,23,41} It has also been suggested that early acetazolamide administration can prevent CSF leakage in high-risk patients.¹ In the case of intradural spine surgeries, acetazolamide is administered routinely as a prophylactic agent in some centers,^{21,27} but its effectiveness has not yet been studied.

In this study, we assessed the complication rates between patients who received acetazolamide and those who did not. Either through a comparison among 4 groups of intervention or as a cumulative analysis of those who received acetazolamide ($n = 78$, 48.4%), we could not detect any significant reduction in complication rates. Instead, it appears that we added the risk of medication side-effects to these patients.

Acetazolamide prevents hydration of carbon dioxide and dehydration of carbonic acid, causing metabolic acidosis. Acetazolamide also results in renal loss of HCO_3^- ions (that carry sodium, water, and potassium) and makes the patient susceptible to electrolyte imbalances such as hyponatremia, hypokalemia, and metabolic acidosis.³⁶ In the current study, among those who received acetazolamide, 2 patients (2.56%) got diarrhea without any evidence of infection, 3 (3.84%) experienced acidosis, and 2 (2.56%) had hypokalemia. One patient required admission to the ICU due to the severity of the acidosis and electrolyte imbalance. Four patients (5.12%) lost their appetite during the course of treatment, which was ameliorated with cessation of acetazolamide. None of the patients in the control group presented with any of the aforementioned complications.

Other Factors Predicting the Outcome

We could not find any correlation between target outcomes and basal parameters such as sex, age, and weight of the patients on the operation day. Similarly, complication rates were the same in the subgroups of indications for surgery (LMMC, DS, SCM, and FF). Interestingly, in contradiction to the former impression that LMMC surgeries are associated with a high rate of CSF leak and wound complications,⁴² our study showed that LMMC does not increase the aforementioned unwanted events in comparison with the other 3 operative modalities (Table 5). We also could not find any association between the application of duraplasty or duration of the surgery and outcomes.

Discounting the effect of basal parameters as well as postoperative care strategies on the outcome of spinal surgeries will bring more attention to the nature of the defect and operative techniques. One possible predictor of the outcome would be the way fascia and muscles are closed.^{30,43} In this study, we used watertight closure of the dura and multilayer closure of the fascia and muscles to minimize failure.

Limitations of the Study

The most critical limitation of this study is the small sample size. To overcome this limitation, we used the factorial design for determining the sample size and analyzing the intervention groups. We also considered the occurrence of CSF leak and collection based on the opinion of 2 attending neurosurgeons and did not include any biochemical or imaging modalities. Likewise, the volume and duration of CSF complications and the size of prima-

ry lesions and dural incisions were not considered in the analyses.

Conclusions

This study suggests that positioning the patients prone for a duration of 10 days might decrease the rate of CSF complications after an untethering procedure. However, the utility of this measure, and also the possibility of a shorter period of prone positioning, should be assessed. We also recommend that prophylactic acetazolamide administration is not necessary for postoperative spinal surgeries and the rate of side effects might surpass its potential benefit. Further studies on the duration and type of position by considering the size of the dural incision are needed to make a final conclusion.

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Disclosures

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Conception and design: Nejat, Shahjouei. Acquisition of data: Shahjouei, Hanaei, Habibi. Analysis and interpretation of data: all authors. Drafting the article: Shahjouei, Hanaei. Critically revising the article: Nejat, Habibi, Ansari. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Nejat. Statistical analysis: Habibi, Hoseini. Administrative/technical/material support: Nejat, Habibi. Study supervision: Nejat.

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