



Original Article

Efficacy and safety of polyethylene glycol dural sealant system in cranial and spinal neurosurgical procedures: Meta-analysis

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ABSTRACT

Background: We aimed to assess the efficacy of polyethylene glycol (PEG) dural sealant to achieve watertight closure, prevention of cerebrospinal fluid (CSF) leak and to investigate its possible side effects.

Methods: We searched Medline (through PubMed), Scopus, and the Cochrane Library through December 2019. We included articles demonstrating cranial or spinal procedures with the use of PEG material as a dural sealant. Data on intraoperative watertight closure, CSF leak, and surgical complications were extracted and pooled in a meta-analysis model using RevMan version 5.3 and OpenMeta (Analyst).

Results: Pooling the controlled trials showed that PEG resulted in significantly more intraoperative watertight closures than standard care (risk ratio [RR] = 1.44, 95% confidence interval [CI] [1.24, 1.66]). However, the combined effect estimate did not reveal any significant difference between both groups in terms of CSF leaks, the incidence of surgical site infections, and neurological deficits ($P = 0.7, 0.45, \text{ and } 0.92$, respectively). On the other hand, pooling both controlled and noncontrolled trials showed significance in terms of leak and neurological complications (RR = 0.0238, 95% CI [0.0102, 0.0373] and RR = 0.035, 95% CI [0.018, 0.052]). Regarding intraoperative watertight closure, the overall effect estimate showed no significant results (RR=0.994, 95% CI [0.986, 1.002]).

Conclusion: Dura seal material is an acceptable adjuvant for dural closure when the integrity of the dura is questionable. However, marketing it as a factor for the prevention of surgical site infection is not scientifically proved. We suggest that, for neurosurgeons, using the dural sealants are highly recommended for duraplasty, skull base approaches, and in keyhole approaches.

Keywords: Dura sealant, Dural closure, Hydrogel, Polyethylene glycol

INTRODUCTION

Cerebrospinal fluid (CSF) leakage after neurosurgical operations is a common phenomenon at either infratentorial or supratentorial surgeries. It ranges from 10 to 25%.^[12,28] Indeed, it is regarded as one of the most important causes of morbidity after neurosurgical operations;

complications of CSF leak include wound dehiscence, wound infections, meningitis, and encephalitis.^[3,25] CSF leakage is frequently and significantly cost-effective across all types of neurosurgical operations.^[1]

The main method of dural closure is the primary surgical closure; however, this is not enough to achieve a watertight approximation.^[20,24,31] The pinholes created by the suture itself may increase the incidence of leakage when intracranial pressure increases as well and moving back in a ball and valve mechanism.^[25,29]

At present, the techniques used to achieve a watertight dural closure include the application of interrupted sutures, dural replacement materials (duraplasty), and hemostatic agents.^[9,15] Tissue adhesives are mostly used as an adjunct to primary dural closure to achieve a watertight dural closure. Tissue adhesives are of two types; fibrin sealants and hydrogel-based sealant systems.^[23,26,28,36] The most widely used method is fibrin sealants, a two-component system with one containing fibrin, factor XIII, and calcium; it forms a coagulum which prevents CSF leak on the suture sites.^[23] However, many side effects have been reported about fibrin sealant systems. Bovine fibrin may induce allergic reactions and even cause anaphylaxis or aseptic meningitis.^[2,16,34]

Polyethylene glycol (PEG)-based hydrogel is a new sealant used as an adjuvant to augment primary dural closure after craniotomy.^[4] A synthetic hydrogel is effective in sealing the suture pinholes and tiny gaps between the suture stitches. Data from preclinical animal studies provided objective evidence that the PEG sealant was safe and effective.^[25] PEG is also superior to fibrin sealants in being nonimmunogenic and with no risk of transmitting infection.^[3,5,17] One study showed that the reduction of CSF leakage high costs was achieved using the PEG sealant system.^[13]

In this meta-analysis of clinical trials, we aimed to assess the efficacy of PEG to achieve watertight closure of the dura and prevention of CSF leak and to investigate its possible side effects.

MATERIAL'S AND METHODS

We performed all steps of this systematic review in strict accordance with the Cochrane handbook of systematic reviews and meta-analysis. We also followed the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement guidelines while drafting our manuscript.^[14,27,33]

Literature search strategy

We searched Medline (through PubMed), Scopus, and the Cochrane Library through December 2019, using the

following keywords: "PEG," "Hydrogel," "Dural Sealant," "Dural Closure," "Neurosurgery," "Cranial," and "Spinal."

No restrictions by language, country, or publication date were employed. We also searched the bibliography of eligible studies for relevant articles.

Eligibility criteria

We included both randomized controlled trials and noncontrolled studies assessing the use of PEG hydrogel for dura matter closure in cranial or spinal neurosurgical procedures.

We excluded nonhuman studies, studies from which data cannot be reliably extracted, duplicate references, case reports, and conference abstracts.

Selection of studies

We independently applied the selection criteria; eligibility screening was conducted in two steps, (a) titles and abstracts screening for matching the inclusion criteria and (b) full-text screening for eligibility to meta-analysis. Disagreements were resolved on discussion.

Outcomes of interest

We included studies reported at least one of the following outcomes: (1) intraoperative watertight closure, (2) CSF leak, and (3) surgical complications such as meningocele, surgical site infection, sepsis, subarachnoid hemorrhage, and pneumocephalus.

Data extraction

We independently extracted and tabulated data on the first author, publication year, study design, baseline characteristics of the study population, type of intervention including the type of prosthesis, study period, follow-up period, and relevant outcomes data. Disagreements were resolved on discussion.

Risk of bias (ROB) assessment

Two independent reviewers used the Cochrane ROB assessment tool, clearly described in Chapter 8.5 of the Cochrane handbook of systematic reviews of interventions 5.1.0. The Cochrane ROB assessment tool is designed to detect five types of bias, including selection bias (sequence generation and allocation concealment), performance bias (blinding of participants and investigators), detection bias (blinding of outcome assessors), attrition bias (incomplete outcome data), and reporting bias (selective outcome reporting).^[6-8,10] Each study is classified in each domain as low, high, or unclear ROB.

Data analysis

We included both controlled and noncontrolled studies. We used OpenMeta (Analyst) software to calculate an overall estimate and 95% confidence interval (CI) for the outcome in the experimental groups in both sets of studies. We used Review Manager software (version 5.3) to calculate the risk ratio (RR) and 95% CI for outcomes of the controlled studies.

Assessment of heterogeneity

Heterogeneity was assessed by visual inspection of the forest plots and measured by Q statistic and I^2 statistic. Significant statistical heterogeneity was indicated by Q statistic $P < 0.1$ or by I^2 more than 50%.

Publication bias

According to Egger's *et al.*, publication bias is not reliable for <10 pooled studies. Therefore, in the present study, we could not assess the existence of publication bias by Egger's test for funnel plot asymmetry.

RESULTS

Literature search results

The results of searching databases yielded 255 studies. After excluding duplicates, 169 studies entered the screening phase. Twelve studies entered full-text screening, and a total of six studies were finally included in our study. Half of the included trials were controlled trials, and the other three studies were noncontrolled. [Figure 1] shows a PRISMA flow diagram summarizing our literature search.

Characteristics of the included studies' population

The included studies were six studies. Controlled and uncontrolled studies were in a ratio of 3:3. The total number of recruited patients from randomized studies was 493 patients. The uncontrolled studies contain 181 patients. The controlled trials measured PEG efficacy against conventional method used for dural closure. The summary of the baseline characteristics of the included studies is shown in [Table 1].

Assessment of study validity

We detected an overall moderate ROB for the included clinical trials. Regarding randomization and blinding of outcome assessors, three studies did not report the methodology of randomization nor blinding of outcome assessors, therefore, were categorized as unclear ROB. As for allocation concealment, blinding of patients, attrition bias, and selective reporting, all studies were put to low

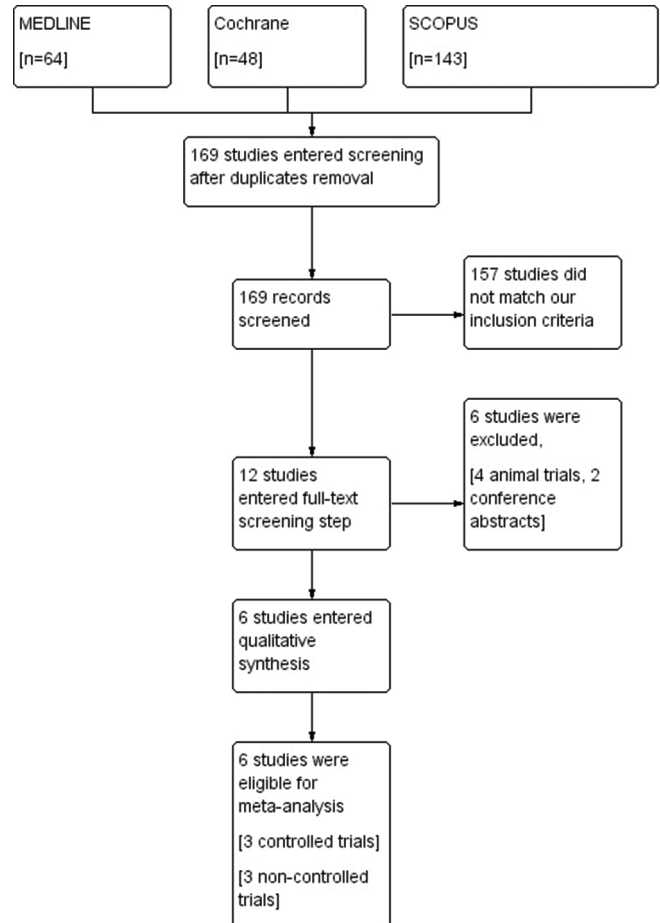


Figure 1: Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart. Figure 1 shows PRISMA flowchart summarizing our literature search.

risk, as they provided sufficient data for supporting these domains. Except for Osbun *et al.*,^[22] we could not assure proper allocation concealment, therefore, the study was put to unclear risk for this domain. [Figure 2] shows a summary and a graph for the overall ROB.

Synthesis of results

We conducted two analyses for selected outcomes; one for controlled trials and another single-arm analysis for both controlled and noncontrolled studies.

Analysis of controlled trials [Figure 3]

Intraoperative watertight closure

The overall RR showed that PEG resulted in significantly more intraoperative watertight closures than standard care (RR = 1.44, 95% CI [1.24, 1.66], $P < 0.001$). Pooled results were homogeneous ($I^2 = 59%$, $P = 0.12$), Figure 3.1.

Table 1: Summary of baseline characteristics of included studies.

Study	Study design	Patients number		Age		Gender				Intervention	Population	Main finding
		Exp. group	Control group	Exp. group	Control group	Exp. group		Control				
						Males	Females	Males	Females			
Wright <i>et al.</i> , 2015	Randomized single-blind, multicenter trial.	74	24	44.3	44.7	30	44	9	15	PEG hydrogel sealant versus any standard method	Patients were having elective spinal surgeries	Patients treated with the PEG hydrogel spinal sealant had a significantly higher rate of watertight closure than the control (98.6% vs. 79.2%, $P=0.003$). No statistical differences were seen in postoperative cerebrospinal fluid, infection, and wound healing. No neurological deficits were seen attributable to the sealant.
Kim <i>et al.</i> , 2011	Randomized single-blind, multicenter trial.	102	56	47.7	42.3	48	56	26	30	PEG hydrogel sealant versus any standard method	Patients were having elective spinal surgeries	Patients treated with the PEG hydrogel spinal sealant had a significantly higher rate of watertight closure than the control (100% vs. 64.3%, $P<0.001$). No statistical differences were seen in the postoperative cerebrospinal fluid leak, infection, and wound healing. No neurologic deficits were seen attributable to the sealant.
Osburn, Ellenbogen, Chesnut <i>et al.</i> , 2012	Randomized single-blind, multicenter trial.	120	117	49.6	48.2	42	78	43	74	PEG hydrogel sealant versus any standard method	Patients were having elective cranial surgeries	The incidences of neurosurgical complications, surgical site infections, and CSF leaks were similar between treatment and control groups, with no statistically significant difference between the measures.
Cosgrove <i>et al.</i> , 2007	Single-arm, multicenter trial	111	49	49	35	76	76			PEG hydrogel sealant	Patients were having elective cranial surgeries	The PEG hydrogel sealant was 100% effective in stopping CSF leakage in all patients. There were no sealant-related adverse events, and all clinical outcomes were consistent with expectations for seriously ill patients undergoing prolonged neurosurgical procedures.

(Contd...)

Table 1: (Continued)

Study	Study design	Patients number		Age		Gender		Intervention	Population	Main finding		
		Exp. group	Control group	Exp. group	Control	Exp. group					Control	
						Males	Females				Males	Females
Boogaarts et al., 2005	Single-arm, multicenter trial.	46	52	24	22	24	22	PEG hydrogel sealant	Patients were having elective cranial and spinal surgeries	Of the 46 patients included, there was one case of overt CSF leak. One patient had a pseudomeningocele. There were no adverse events other than those related to the disease or to the surgical procedure itself.		
Nishimura et al., 2012	Single-arm trial	24	Not available	16	8	16	8	PEG hydrogel sealant	Patients treated by STA-MCA anastomosis for symptomatic major artery stenosis or occlusion or aneurysms	Of the 24 patients included, only two patients developed subcutaneous CSF collection.		

In all patients, intraoperative watertight closure of the dura could not be obtained after primary closure. CSF: Cerebrospinal fluid, PEG: Polyethylene glycol

CSF leak

The combined effect estimate did not reveal any significant difference between both groups in terms of CSF leaks (RR = 0.87, 95% CI [0.37, 2.04], $P = 0.7$). Pooled results were homogenous ($I^2 = 0\%$, $P = 0.5$), Figure 3.2.

Surgical site infections

The net result of analysis did not favor any of the two groups regarding the incidence of surgical site infections (RR = 0.74, 95% CI [0.33, 1.63], $P = 0.45$). Pooled results were homogeneous ($I^2 = 0\%$, $P = 0.8$), Figure 3.3.

Neurological deficits

The combined RR did not show a significant difference between PEG and standard care (RR = 0.96, 95% CI [0.46, 2.03], $P = 0.92$). Pooled results were homogenous ($I^2 = 0\%$, $P = 0.5$), Figure 3.4.

Analysis for both controlled and noncontrolled trials [Figure 4]

Intraoperative watertight closure

The overall effect estimate did not reveal significant results (RR = 0.994, 95% CI [0.986, 1.002]). Pooled results were homogenous ($I^2 = 0\%$, $P = 0.9$), Figure 4.1.

CSF leak

Combined effect estimates and 95% CI showed marked significance (RR = 0.0238, 95% CI [0.0102, 0.0373]). Pooled results were heterogeneous ($I^2 = 61\%$, $P = 0.026$), Figure 4.2.

Neurological complications

The net results of neurological complications (pseudomeningocele, surgical site infection, and neurological deficit) from surgery revealed significant results (RR = 0.035, 95% CI [0.018, 0.052]). Pooled results were heterogeneous ($I^2 = 50\%$, $P = 0.089$), Figure 4.3.

DISCUSSION

Summary of main results

Analysis of controlled trials only revealed that PEG increases intraoperative watertight closures. However, it did not show any difference between PEG and standard care in terms of neurological deficits, postoperative CSF leaks, and surgical site infections.

Single-arm analysis of all trials showed no difference in terms of intraoperative watertight closures; this may be

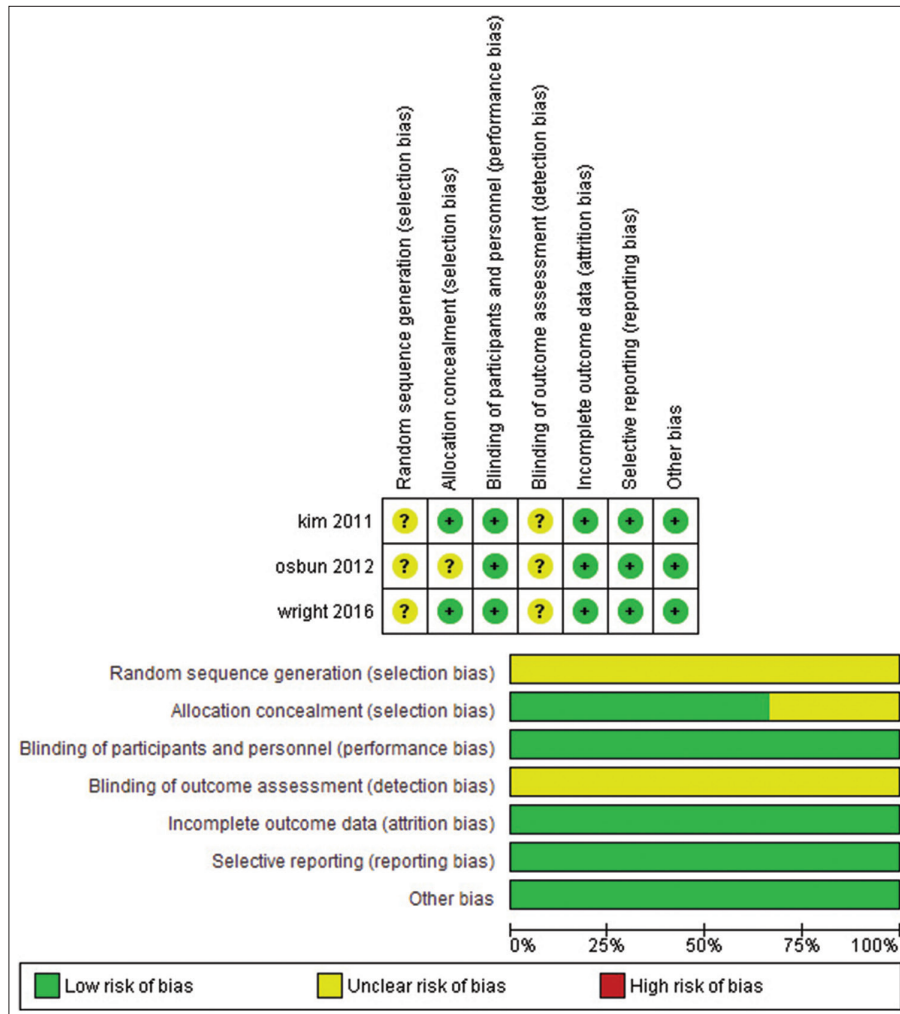


Figure 2: Risk of bias summary and graph. Figure 2 shows summary and graph for risk of bias of controlled trials.

stronger evidence than controlled trials, as the strength of meta-analysis is increased by increasing the number of included studies, provided that results remain homogeneous. However, postoperative CSF leaks and surgical site infections were significant.

Significance of main results

Watertight closure is critical, and the dura seal is an excellent material to achieve zero leakage intraoperatively. However, stopping postoperative leakage cannot be guaranteed by the dura seal in controlled trials. Prevention of surgical site infection is the matter of achieving a good medium for healing and infection control rather than the application of foreign material.

Agreement and disagreement with the previous studies

Kim *et al.* studied the dural sealant in various procedures in neurosurgery; they found that using it was effective in the

prevention of CSF fistula.^[17] Nakamura *et al.* conducted a randomized controlled trial for using dural sealants in spine surgery; they observed a different outcome between as regard drainage fluid between controlled and studied groups.^[19] Kim *et al.* studied the usage of sealants against the standard of care in case of spinal CSF leakage intraoperative; they found that superior results with dural sealants over traditional methods with no neurological injury can be attributed to it.^[17] Wright *et al.* conducted a randomized controlled trial to study the incidence of CSF leakage after unintended durotomies; they found that dural sealants were superior to standard of care techniques for closing dural defects after Valsalva trials.^[35] Watertight closure was a primary goal in Boogaarts *et al.* study;^[3] they found a marvellous reduction in CSF leakage (100%) with no undesired effects in cranial surgery. The same results were achieved by Cosgrove *et al.*^[5] when compared to dural sealants with traditional dural closure in cranial surgeries. Nishimura *et al.* studied the application of dura seal in a specific type of cranial surgeries (bypass surgery).

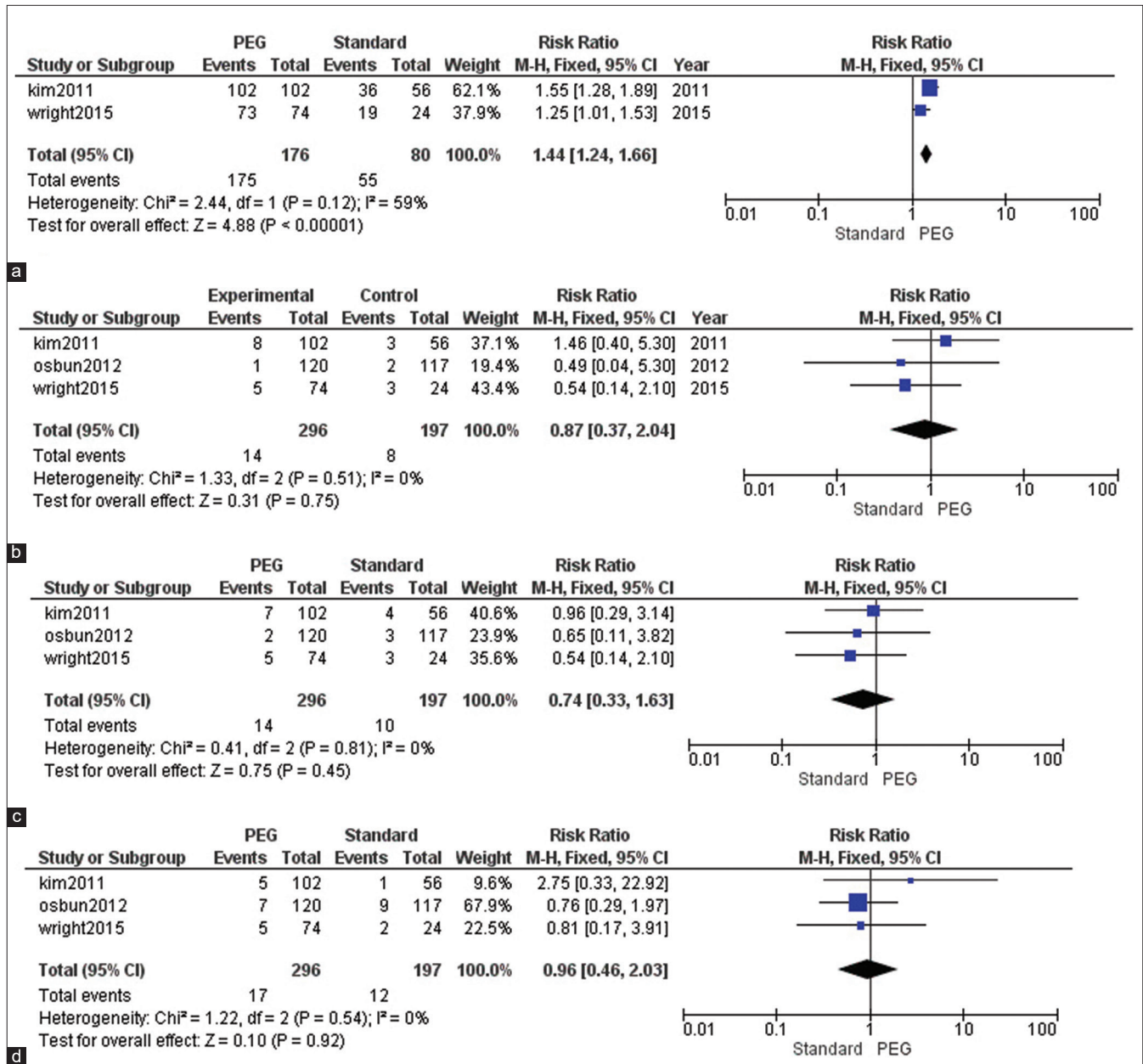


Figure 3: Forest plots of Controlled trials. It shows analysis of controlled trials, (a) intra-operative watertight closures, (b) CSF leaks after operation, (c) surgical site infections, and (d) neurological deficits

They found that easy and effective sealing of the field was achieved by the dura seal.^[21] Only 2/24 patients developed subcutaneous CSF fistula later on. The usage of the dura seal gave no negative effects on the patency of the anastomosis. Takumi *et al.* designated a prospective study but in functional neurosurgery (deep brain stimulation) to assess CSF leakage and brain shifting after DBS in a controlled trial. They found that the application of such material reduces CSF leakage and brain shifting to a minimum if compared to traditional methods. In the skull base surgery field, this material has been studied heavily by George *et al.*^[11] Up to date, it is the

largest trial conducted in this field, with 726 patients who underwent skull base surgery were enrolled and randomized into classic control and study groups. They found CSF leakage events in 25 (6.9%) patients versus 30 (8.2%) current practice patients with no statistically significant difference (odds ratio: 0.82; 95% CI: 0.47, 1.43; P = 0.485). Despite its safety, easy method of application, and low rate of CSF leakage, George *et al.* found that both treatments were well tolerated with similar frequency of adverse events.

Osbun *et al.* conducted a randomized controlled trial used the same material in cranial surgeries in a group (n = 120) against

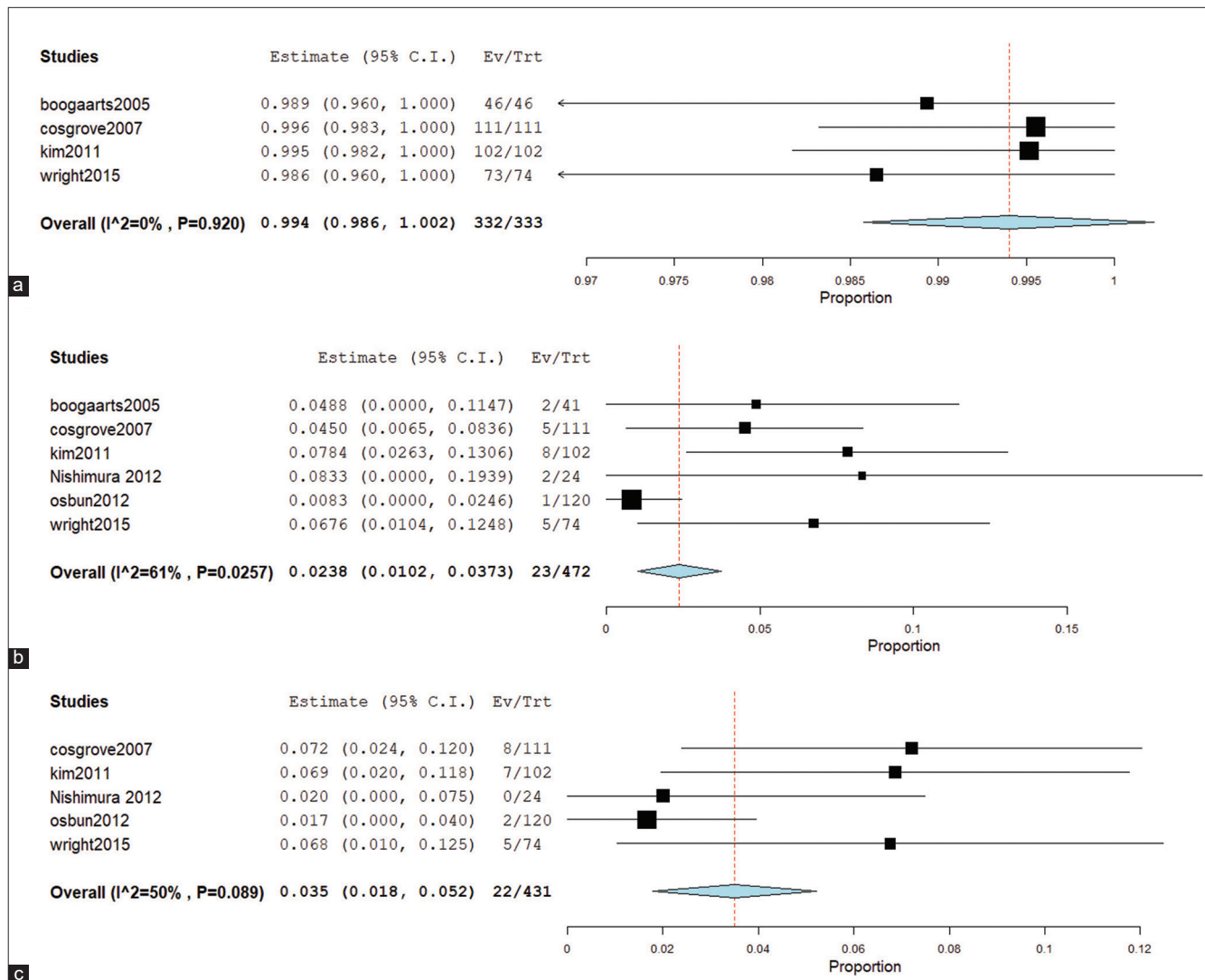


Figure 4: Analysis of non-controlled trials, (a) intra-operative watertight closures, (b) CSF leaks after operation, and (c) surgical site infections.

the traditional method group ($n = 117$).^[22] In the dural sealant group, the incidence of neurosurgical complications was 5.8% ($n = 7$), the incidence of surgical site infections was 1.7% ($n = 2$), and the incidence of CSF leak was 0.8% ($n = 1$). In the control group, the incidence of neurosurgical complications was 7.7% ($n = 9$), the incidence of surgical site infection was 2.6% ($n = 3$), and the incidence of CSF leak was 1.7% ($n = 2$). Hutter *et al.* studied the factors responsible for CSF leakage in elective cranial surgeries.^[15] They found several factors responsible for CSF leakage and observed that cases treated with dura sealant showed a minimum amount of leakage if compared to others.

In contrast, a different outcome was achieved by Green *et al.*^[12] Green *et al.* conducted a multicenter cohort study to assess the safety and effectiveness of dural sealant in cranial surgeries. Safety was assessed to 30 days postsurgery, including the incidence of CSF leakage. No deaths or

unexpected serious adverse drug reactions were reported. CSF leakage within 30 days postoperatively was 2.2% and 2.0% in study and control groups, respectively.

Tew *et al.* conducted a large cohort study that included 17 centers to study the effectiveness of dural sealant versus traditional methods of dural closure in cranial surgeries.^[32]

CONCLUSION AND RECOMMENDATIONS

Dura seal material is an acceptable adjuvant for dural closure when the integrity of the dura is in question. However, marketing it as a factor for the prevention of surgical site infection is not scientifically proved. We suggest that, for neurosurgeons, using the dural sealants are highly recommended for duraplasty, skull base approaches, and in keyhole approaches.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Cardona-Durán RF, Uribe JS. Spinal biologics. In: Baaj AA, Uribe J, Greenberg MS, editors. Handbook of Spine Surgery. 2nd ed. New York: Thieme; 2016. p. 948.
- Beierlein W, Scheule AM, Antoniadis G, Braun C, Schosser R. An immediate, allergic skin reaction to aprotinin after reexposure to fibrin sealant. *Transfusion* 2000;40:302-5.
- Boogaarts JD, Grotenhuis JA, Bartels RH, Beems T. Use of a novel absorbable hydrogel for augmentation of dural repair: Results of a preliminary clinical study. *Neurosurgery* 2005;57:146-51.
- Wei SM, Pei MY, Pan WL, Thissen H, Tsai SW. Gelatin hydrogels reinforced by absorbable nanoparticles and fibrils cured in situ by visible light for tissue adhesive applications. *Polymers* 2020;12:1113.
- Cosgrove GR, Delashaw JB, Grotenhuis JA, Tew JM, van Loveren H, Spetzler RF, *et al.* Safety and efficacy of a novel polyethylene glycol hydrogel sealant for watertight dural repair. *J Neurosurg* 2007;106:52-8.
- Ebada MA, Alkanj S, Ebada M, Abdelkarim AH, Diab A, Aziz MA, *et al.* Safety and efficacy of levetiracetam for the management of levodopa-induced dyskinesia in patients with Parkinson's disease: A systematic review. *CNS Neurol Disord Drug Targets* 2019;18:317-25.
- Ebada MA, Elmatboly AM, Ali AS, Ibrahim AM, Fayed N, Faisal AF, *et al.* An updated systematic review and meta-analysis about the safety and efficacy of infliximab biosimilar, CT-P13, for patients with inflammatory bowel disease. *Int J Colorectal Dis* 2019;34:1633-52.
- Ebada MA, Fayed N, Fayed L, Alkanj S, Abdelkarim A, Farwati H, *et al.* Efficacy of alpha-lipoic acid in the management of diabetes mellitus: A systematic review and meta-analysis. *Iran J Pharm Res* 2019;18:2144-56.
- Eseonu CI, Goodwin CR, Zhou X, Theodros D, Bender MT, Mathios D, *et al.* Reduced CSF leak in complete calvarial reconstructions of microvascular decompression craniectomies using calcium phosphate cement. *J Neurosurg* 2015;123:1476-9.
- Gadallah AH, Ebada MA, Gadallah A, Ahmed H, Rashad W, Eid KA, *et al.* Efficacy and safety of N-acetylcysteine as add-on therapy in the treatment of obsessive-compulsive disorder: A systematic review and meta-analysis. *J Obsess Compuls Relat Disord* 2020;25:100529.
- George B, Matula C, Kihlström L, Ferrer E, Tetens V. Safety and efficacy of tachosil (absorbable fibrin sealant patch) compared with current practice for the prevention of cerebrospinal fluid leaks in patients undergoing skull base surgery: A randomized controlled trial. *Neurosurgery* 2017;80:847-53.
- Green AL, Arnaud A, Batiller J, Eljamel S, Gauld J, Jones P, *et al.* A multicentre, prospective, randomized, controlled study to evaluate the use of a fibrin sealant as an adjunct to sutured dural repair. *Br J Neurosurg* 2015;29:11-7.
- Grotenhuis JA. Costs of postoperative cerebrospinal fluid leakage: 1-year, retrospective analysis of 412 consecutive nontrauma cases. *Surg Neurol* 2005;64:490-3.
- Higgins JP, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions*-I doStatistics; 2008.
- Hutter G, von Felten S, Sailer MH, Schulz M, Mariani L. Risk factors for postoperative CSF leakage after elective craniotomy and the efficacy of fleece-bound tissue sealing against dural suturing alone: A randomized controlled trial. *J Neurosurg* 2014;121:735-44.
- Kanazawa R, Sato S, Iwamoto N, Teramoto A. Allergic reaction following arachnoid plasty with a fibrin sealant. *Neurol Med Chir* 2010;50:608-10.
- Kim KD, Wright NM. Polyethylene glycol hydrogel spinal sealant (duraseal spinal sealant) as an adjunct to sutured dural repair in the Spine. *Spine* 2011;36:1906-12.
- Messerer M, Cossu G, Daniel RT, Jouanneau E. Letter to the editor: Knosp Grades 2-3 nonfunctioning pituitary adenomas. *J Neurosurg* 2015;122:986-7.
- Nakamura H, Matsuyama Y, Yoshihara H, Sakai Y, Katayama Y, Nakashima S, *et al.* The effect of autologous fibrin tissue adhesive on postoperative cerebrospinal fluid leak in spinal cord surgery: A randomized controlled trial. *Spine* 2005;30:E347-51.
- Nakayama N, Yano H, Egashira Y, Enomoto Y, Ohe N, Kanemura N, *et al.* Efficacy, reliability, and safety of completely autologous fibrin glue in neurosurgical procedures: Single-center retrospective large-number case study. *World Neurosurg* 2018;109:e819-28.
- Nishimura K, Kimura T, Morita A. Watertight dural closure constructed with DuraSeal™ for bypass surgery. *Neurol Med Chir* 2012;52:521-4.
- Osborn JW, Ellenbogen RG, Chesnut RM, Chin LS, Connolly PJ, Cosgrove GR, *et al.* A multicenter, single-blind, prospective randomized trial to evaluate the safety of a polyethylene glycol hydrogel (duraseal dural sealant system) as a dural sealant in cranial surgery. *World Neurosurg* 2012;78:498-504.
- Patel MR, Caruso PA, Yousuf N, Rachlin J, Fibrin P. Glue therapy of cerebrospinal fluid. *Am Roentgen Ray Soc* 2000;175:443-6.
- Pereira EA, Grandidge CA, Nowak VA, Cudlip SA. Cerebrospinal fluid leaks after transsphenoidal surgery effect of a polyethylene glycol hydrogel dural sealant. *J Clin Neurosci* 2017;44:6-10.
- Preul MC, Bichard WD, Muench TR, Spetzler RF. Toward optimal tissue sealants for neurosurgery: Use of a novel hydrogel sealant in a canine durotomy repair model. *Neurosurgery* 2003;53:1189-99.
- Shaffrey CI, Spotnitz WD, Shaffrey ME, Jane JA, Laws ER, Sekhar LN, *et al.* Neurosurgical applications of fibrin glue: Augmentation of dural closure in 134 patients. *Neurosurgery*

- 1990;26:207-10.
27. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, *et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: Elaboration and explanation. *BMJ* 2015;350:g7647.
 28. Shimada Y, Hongo M, Miyakoshi N, Sugawara T, Kasukawa Y, Ando S, *et al.* Dural substitute with polyglycolic acid mesh and fibrin glue for dural repair: Technical note and preliminary results. *J Orthop Sci* 2006;11:454-8.
 29. Stoker M, Forbes J, Hanif R, Cooper C, Nian H, Konrad P, *et al.* Decreased rate of CSF leakage associated with complete reconstruction of suboccipital cranial defects. *J Neurol Surg Part B Skull Base* 2012;73:281-6.
 30. Takumi I, Mishina M, Hironaka K, Oyama K, Yamada A, Adachi K, *et al.* Simple solution for preventing cerebrospinal fluid loss and brain shift during multitrack deep brain stimulation surgery in the semisupine position: Polyethylene glycol hydrogel dural sealant capping. *Neurol Med Chir* 2013;53:1-6.
 31. Terasaka S, Taoka T, Kuroda S, Mikuni N, Nishi T, Nakase H, *et al.* Efficacy and safety of non-suture dural closure using a novel dural substitute consisting of polyglycolic acid felt and fibrin glue to prevent cerebrospinal fluid leakage a non-controlled, open-label, multicenter clinical trial. *J Mater Sci* 2017;28:69.
 32. Tew JM, Strong MJ, Alexanderwest G, Woo H, Couture DE, Wilson JA, *et al.* A pivotal randomized clinical trial evaluating the safety and effectiveness of a novel hydrogel dural sealant as an adjunct to dural repair. *Oper Neurosurg (Hagerstown)* 2017;13:204-12.
 33. Allah AW, Yahya M, Elsaedy KS, Alkanj S, Hamam K, El-Saady M, *et al.* Clinical assessment of miRNA-23b as a prognostic factor for various carcinomas: A systematic review and meta-analysis. *Meta Gene* 2020;24:100651.
 34. Wakamoto H, Miyazaki H, Orii M, Ishiyama N, Akiyama K, Konohana I. Aseptic meningitis as a complication caused by an allergic reaction after microvascular decompression: Two case reports. *No Shinkei Geka* 2002;30:1331-5.
 35. Wright NM, Park J, Tew JM, Kim KD, Shaffrey ME, Cheng J, *et al.* Spinal sealant system provides better intraoperative watertight closure than standard of care during spinal surgery: A prospective, multicenter, randomized controlled study. *Spine* 2015;40:505-13.
 36. Yeom JS, Buchowski JM, Shen HX, Liu G, Bunmaprasert T, Riew KD. Effect of fibrin sealant on drain output and duration of hospitalization after multilevel anterior cervical fusion: A retrospective matched pair analysis. *Spine* 2008;33:543-7.

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