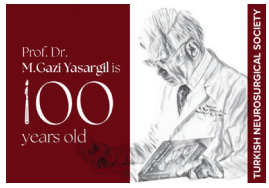
Turk Neurosurg 35(6):839-845, 2025
DOI: 10.5137/1019-5149.JTN.49101-25.3

Original Investigation

General Neurosurgery and Miscellaneous-Others

Received: 12.05.2025
Accepted: 21.08.2025
Published Online: 30.10.2025



The Impact of Hypertonic Dextrose on Dura Mater Regeneration and Fibroblast Activity Following Experimental Cerebrospinal Fluid Leakage

Omer SAHIN[1], Tuncer TASCIOGLU[2], Aysegul FIRAT[3], H. Selcuk SURUCU[4], Muzaffer CAYDERE[5], Duran Berker CEMIL[2]

[1]Bestepe State Hospital, Department of Neurosurgery, Ankara, Türkiye
[2]University of Health Sciences, Ankara Training and Research Hospital, Department of Neurosurgery, Ankara, Türkiye
[3]Hacettepe University Faculty of Medicine, Department of Anatomy, Ankara, Türkiye
[4]Koc University Faculty of Medicine, Department of Anatomy, Istanbul, Türkiye
[5]University of Health Sciences, Ankara Training and Research Hospital, Department of Pathology, Ankara, Türkiye

Corresponding author: Omer SAHIN ✉ dromersahin060@gmail.com

ABSTRACT

AIM: To investigate the effects of 25% dextrose in a rat model of cerebrospinal fluid leakage.

MATERIAL and METHODS: Forty Wistar rats were included in the study. The dura mater of the rats was opened, and 25% dextrose was applied topically at a dose of 0.1 ml. Rats were sacrificed at the end of the third and sixth weeks. Then, pathologic and electron microscopic evaluations were performed.

RESULTS: The results of healing score and fibroblast density evaluations showed that dextrose led to more successful healing than control subjects in early and late postoperative evaluations. In addition, electron microscopic examination showed that fibroblasts had active endoplasmic reticulum and mitochondria in a large cytoplasm, indicating increased collagen secretion.

CONCLUSION: After dura mater injury, 25% dextrose, a cheap and accessible agent, has the potential to be used to enhance healing.

KEYWORDS: Hypertonic glucose, Wound healing, Rat, Cerebrospinal fluid leak

ABBREVIATIONS: CSF: Cerebrospinal fluid, **PDGF:** Platelet-derived growth factor

INTRODUCTION

The leakage of cerebrospinal fluid (CSF), a common complication in spinal surgery, can result in numerous other problems, including impaired wound healing, meningitis, infections in adjacent areas of the body, and pneumocephalus. Such complications frequently prolong hospitalization, require additional surgical procedures, and, as a result, raise the cost of health care (12,33,34). Consequently, various methods have been developed to manage CSF leakage from cranial or spinal procedures. Traditional repair techniques like primary suturing and duraplasty have their limitations. Currently used fibrin sealant is often insufficient, and synthetic membranes, while preventing adhesions, frequently fail to stop postoperative CSF leaks (26).

Omer SAHIN : 0000-0001-9689-0068
Tuncer TASCIOGLU : 0000-0002-0359-7274
Aysegul FIRAT : 0000-0001-5105-0057
H. Selcuk SURUCU : 0000-0002-9244-4236
Muzaffer CAYDERE : 0000-0003-2910-288X
Duran Berker CEMIL : 0000-0001-9192-6674

Prolotherapy, developed in the early 1900s for chronic non-cancer pain, involves injecting dextrose into joints and entheses for musculoskeletal pain relief (31,32). Though its exact mechanism is unclear, hypertonic glucose injections are thought to promote tissue repair by inducing localized cellular dehydration and hyperosmolarity. This triggers local tissue damage, attracting granulocytes and macrophages. These cells release growth factors and deposit collagen, forming new connective tissue, increasing stability, and reducing pain and dysfunction (17). Studies show that even 5% dextrose can stimulate growth factors vital for tissue repair (27,29). High glucose levels can also stimulate platelet-derived growth factor, aiding repair (8,14,28).

Several studies have demonstrated the clinical beneficial effects of hypertonic dextrose in the healing of osteoarthritis, tendinopathies, joint pains, and chondromalacia (18,30). In this study, the effects of 25% glucose solution on dural healing after experimental dural opening in rats were pathologically and ultrastructurally investigated. This is the first time that the effect of dextrose supplementation on dural repair has been evaluated.

MATERIAL and METHODS

Experimentals

For this study, 40 adult male Wistar rats, each weighing between 300 and 400 grams, were used. Their care and experimental procedures adhered to protocols approved by the Institutional Animal Care and Use Committee at the research facility, following authorization from the Ethics Committee of Ankara Training and Research Hospital's Animal Experiments and Local Ethics Committee (Approval No: 781, Date: 14.06.2024). The animals were housed under consistent conditions, including stable room temperature and humidity, a 12-hour light/12-hour dark cycle, and with continuous access to standard rat feed and water.

Anesthesia and Surgical Procedure

Anesthesia was initiated by injecting 35 mg/kg of ketamine hydrochloride (Ketalar; Pfizer, Istanbul, Türkiye) and 10 mg/kg of xylazine (Rompun; Bayer, Istanbul, Türkiye) intraperitoneally. Thirty minutes before surgery, a single 50 mg/kg dose of ceftriaxone (Rocephin; Roche, Basel, Switzerland) was given via intraperitoneal injection.

After placing them in a prone position and shaving their backs, the surgical area was disinfected with a 10% polyvinylpyrrolidone/iodine solution (Batticon; Adeka Pharmaceuticals, Istanbul, Türkiye) (Figure 1A). Employing aseptic techniques and a surgical microscope, a midline incision was made along the lumbar spinous processes. Following dissection of the fascia and paraspinal muscles, the spinous processes of the L-2 and L-4 vertebrae were excised (Figure 1B). A laminectomy was then performed using a high-speed diamond drill (Figure 1C). The dura mater was incised longitudinally for 5 mm with a No. 11 scalpel (Figure 1D), and cerebrospinal fluid leakage was confirmed under an operating microscope. All surgical procedures were carried out by the same surgeon (OS).

The 40 rats were randomly divided into two groups. Group I, the control group, consisted of 20 rats in which only dural defects were performed. Group II, or the dextrose group, also comprised 20 rats, and their dural defects received a topical application of 0.1 ml of 25% dextrose (Dextrose; Polifarma, Ankara, Türkiye) (22,36). Upon completion of the operation, the wounds were closed in layers, excluding the dura mater. All rats underwent postoperative evaluation, and their mobility status and any signs of neurological deficits were documented.

Histological Evaluation

From each group, a subset of 10 rats was selected for pathological examination and transmission electron microscopy (TEM) of the durotomy site. These examinations were conducted at two time points: 21 days post-surgery (designated as Groups IA and IB) and 42 days post-surgery (designated as Groups IIA and IIB). For this assessment, the rats were euthanized via an intraperitoneal injection of 100 mg/kg ketamine hydrochloride (Ketalar; Pfizer, Istanbul, Türkiye). Subsequently, the spinal column segment encompassing the laminectomy–durotomy site, along with the adjacent muscle tissue, was extracted as a single block.

All specimens sent for pathological examination were subjected to tissue decalcification and dehydration, and paraffin blocks were prepared. The specimens were subsequently subjected to staining with hematoxylin and eosin to obtain axial sections. To assess the healing score and fibroblast count, one pathologist who was blinded to the specimens examined all pathological samples. The healing scores of the dura mater were evaluated in accordance with He et al.'s definitions: Grade 0 indicated no fibrous tissue in the dura mater; Grade I indicated thin fibrous band(s) between fibrous tissue and the dura mater; Grade II indicated adhesions in less than two-thirds of the laminectomy defects; and Grade III indicated the presence of extensive fibrous tissue, adhesions extending to more than two-thirds of the laminectomy defects, and/or

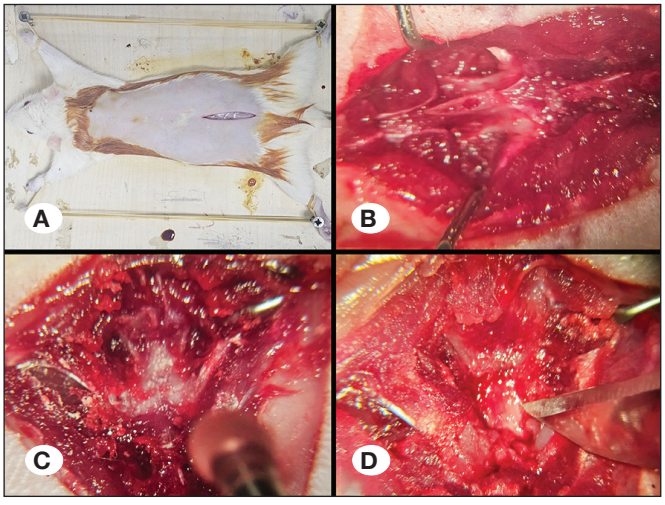


Figure 1: A) An experimental in the prone position, a longitudinal skin incision was made; **B)** Following muscle dissection, the L2-L4 vertebral column was exposed; **C)** A laminectomy was performed; **D)** The dura mater was opened.

fibrous tissue that reached the nerve roots (19). Meanwhile, fibroblast density was evaluated according to Hinton et al.'s classification based on the number of fibroblasts in each region at 400× magnification (i.e., Grade 1 = <100 fibroblasts, Grade 2 = 100–150 fibroblasts, Grade 3 = >150 fibroblasts) (20).

Transmission Electron Microscopy

To preserve the samples, they were initially immersed in a 2.5% glutaraldehyde solution for a duration of 48 hours. This was followed by a secondary fixation step using osmium tetroxide (OsO3), after which the samples underwent dehydration through a series of alcohol solutions with increasing concentrations. After being embedded in Araldite CY212 resin, sections with an approximate thickness of 2 micrometers were cut and subsequently stained with a 1% methylene blue solution. These prepared slides were then placed on a hot plate maintained at a temperature between 100 and 110 ºC for approximately 40 to 45 seconds. Following the heating process, the slides were washed with tap water and then rinsed. For the initial descriptive analysis, the sections were examined using light microscopy. Once the specific area of interest was pinpointed, the tissue blocks were trimmed to facilitate the creation of ultrathin sections, measuring 60 by 90 nanometers, using a Leica EM UC7 ultramicrotome. These ultrathin sections were then stained with uranyl acetate and lead citrate. Finally, the stained sections were observed, and images were captured using a Hitachi HT7800 transmission electron microscope operating at 120 kilovolts.

Statistical Analysis

Frequencies and percentages were reported for categorical variables. To determine statistical significance in the evaluation of healing grading and fibroblast density, we employed the conventional chi-square test, and results with p values less than .05 were statistically significant, with α set at 0.05 for Type I error. All analyses were performed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Every animal included in the study remained alive until the scheduled euthanasia, and none exhibited any signs of neurological impairment or infections at the wound site. Furthermore, there were no visible signs of discharge or any accumulation of CSF beneath the skin in the surgical areas. When healing scores and fibroblast density were evaluated, an increase in fibroblasts was observed as the scores for healing increased (Figure 2A). As a result, the specimens with higher scores for healing at the surgical site were considered to have better results. The findings of the pathological evaluation of the groups appear in Tables I and II. Characteristics of healing scores representing a Grade 3 score were seen only in the dextrose group in 6'th (Figure 2B). The outcomes regarding healing scores and fibroblast density showed statistically significant improvement in the dextrose group compared with the control group, specifically at Weeks 3 and 6 postoperatively (p=0.003 and p=0.000, respectively).

When the groups were examined using electron microscopy, the control group rarely showed active fibroblasts (Figure 3A) and showed no macrophages or other blood cells. Moreover, some specimens in the control group contained striated muscle fibers and nourishing neurovascular bundles possibly belonging to the paravertebral muscles (Figure 3B). In the dextrose group, numerous active fibroblasts with round nuclei and branching cytoplasm were observed in various directions between the collagen fibers (Figure 4A). Those fibroblasts had active endoplasmic reticulum and mitochondria within a large cytoplasm, which suggests increased collagen secretion. Blood cells were also detected in the periphery of epidural scarring (Figure 4B).

DISCUSSION

The dura mater is the toughest layer and plays a key role in protecting the brain tissue (15,16). This structure is a dual-layered connective tissue composed of collagen fibers, elastin filaments, and fibroblasts, which serves to provide structural support for blood vessels and to shield the brain from infectious agents (6,21). Many neurological surgeries and spinal surgeries involving access to the underlying nervous tissues create defects in the dura mater, further resulting in cerebrospinal fluid leakage (15).

For watertight dural closure, suturing is the primary clinical treatment, but it has several drawbacks (2,23). Suturing is time-consuming, technically challenging—especially in hard-

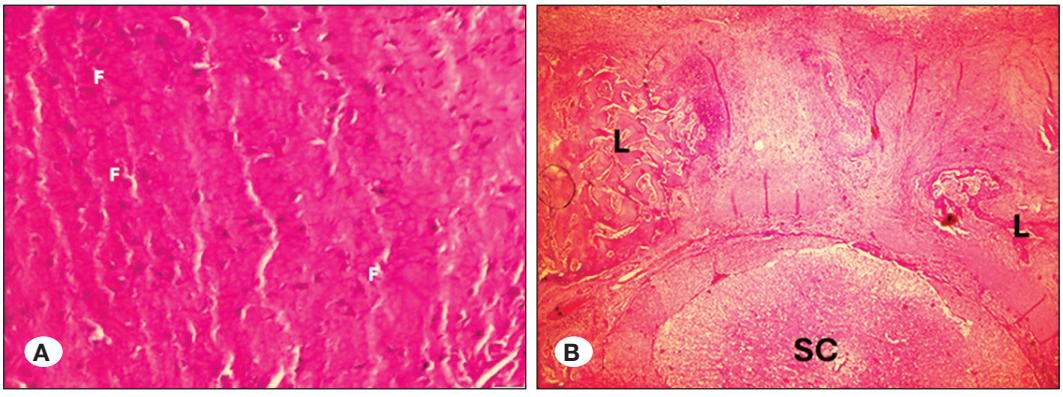


Figure 2: A) Control group section shows grade 1 fibroblast density. **F:** fibroblast; **B)** Dextrose group section shows scar tissue covered more than two-thirds of the laminectomy defect, Grade 3 healing [haematoxylin eosin, original magnification x 40 (Left) and x 5 (Right)]. **SC:** Spinal cord, **L:** Laminae.

Table I: Grades of Duramater Healing in Experimental and Control Groups

Groups	Grade 0	Grade 1	Grade 2	Grade 3
Week 3 control group	8 (80%)	2 (20%)	0	0
Week 3 dextrose group	4 (40%)	4 (40%)	2 (20%)	0
Week 6 control group	2 (20%)	5 (50%)	3 (30%)	0
Week 6 dextrose group	0	2 (20%)	6 (60%)	2 (20%)

Significantly difference was found between the dextrose and the control groups groups, p=0.003.

Table II: Fibroblast Density Grades of Experimental and Control Groups

Groups	Grade 1	Grade 2	Grade 3
Week 3 control group	10 (100%)	0	0
Week 3 dextrose group	5 (50%)	4 (40%)	1 (10%)
Week 6 control group	6 (60%)	3 (30%)	1 (10%)
Week 6 dextrose group	0	3 (30%)	7 (70%)

Significantly difference was found between the dextrose and the control groups, p=0.000.

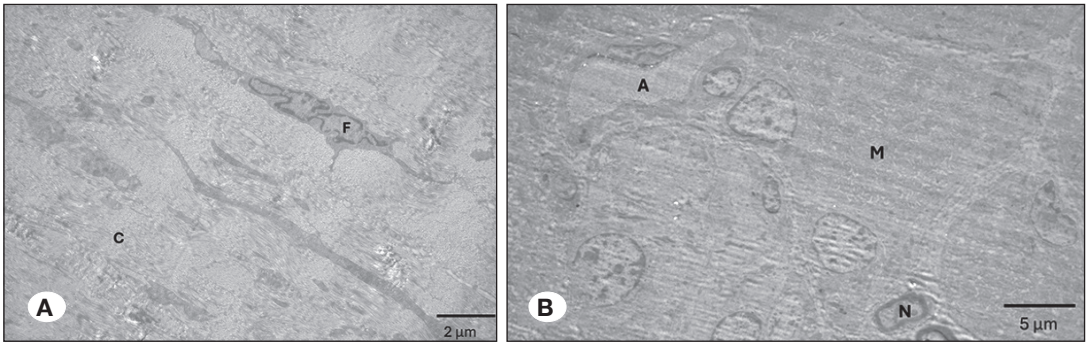


Figure 3: Transmission electron micrographs of control group samples: **A)** seldom fibroblasts are observed within regular collagen bundles (C). These fibroblasts (F) are less active with a narrow cytoplasm and few organelles; **B)** a capillary (A) and a motor axon (N) are seen among striated muscle fibers (M).

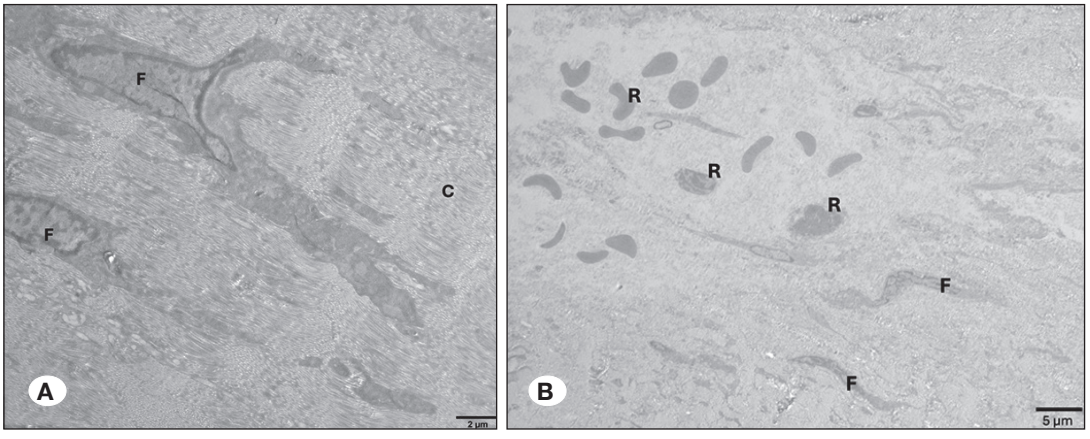


Figure 4: Transmission electron micrographs of dextrose group samples: **A)** active fibroblasts (F) with round nuclei, wide cytoplasm with active organelles. Collagen bundles in various directions are also observed (C); **B)** active fibroblasts (F) among blood cells (R) are observed.

to-reach areas—and can damage the dura mater, with needle holes complicating watertight sealing (7). Furthermore, it may cause secondary nerve/spinal cord stenosis and convert low dural defect pressure to high pressure, leading to persistent CSF leakage (5). Recent reports suggest that dural sealants offer superior long-term clinical outcomes for small defects (< 3 mm) compared to sutures or no treatment at all (24).

In recent years, tissue adhesives and sealants have gained significant attention for sutureless wound closure, hemostasis, and leakage-proof sealing due to their convenience, reduced tissue damage, and suitability for emergency and complex situations (5). For dural sealing, current clinical options include fibrin glue and polyethylene glycol-based hydrogel sealants. Fibrin glue, derived from animal fibrinogen and thrombin, forms a hydrogel via blood coagulation and is widely used (25). However, despite good biodegradability, its weak mechanical properties and risk of virus transmission tend to limit its application (13). DuraSeal® (Integra LifeSciences, Princeton, USA), a hydrogel sealant composed of trilysine and 4-armed polyethylene glycol with N-hydroxysuccinimide (NHS) ester end groups, aims for watertight dural repair. It forms a cross-linking network and achieves covalent tissue adhesion with tissue surface amine groups (35). A major issue with DuraSeal® (Integra LifeSciences, Princeton, USA) is excessive swelling under physiological conditions, which can be detrimental in confined spinal and intracranial spaces (10). Additionally, the NHS ester/amine coupling reaction's adhesion mechanism can lead to limited operating time and compromised tissue adhesion due to the hydrolytic instability of N -hydroxysuccinimide ester in aqueous solutions (3). However, despite these techniques, completely repairing the dura mater can be difficult (11).

To date, the literature contains no evaluations of hypertonic dextrose solution's effects on dura mater healing. The exact mechanism of dextrose prolotherapy remained incompletely understood for many years. Traditionally, the theory, which proposed that high osmolarity dextrose draws water from living cells, causing local tissue damage and subsequently triggering an inflammatory response that results in a net anabolic tissue effect, has been widely accepted. During progression of this cascade, it is presumed by some that cell death leads to the release of factors such as prostaglandins, thromboxanes, and leukotreines, which recruit inflammatory cells (1,9). Granulocytes and macrophages from the initial stage of inflammation may release factors that promotes the secretion of growth factors, recruits fibroblasts, and enhances collagen synthesis, collectively fostering tissue regeneration. Consequently, these biological changes may result in connective tissue strengthening, alleviation of pain, and functional restoration (17).

In our study, dextrose treatment was shown to positively affect tissue regeneration. Specifically, the application of 25% dextrose was linked to improved dural healing during both the initial and later phases of tissue mending. Animals that received the 25% dextrose treatment demonstrated superior healing outcomes compared to the control subjects at both the 3-week (early phase) and 6-week (late phase) time points. Nevertheless, the notable disparity in healing quality observed between the 3-week and 6-week dextrose-treated groups underscores that—consistent with typical wound recovery processes—the extent of healing was influenced by the duration of time elapsed.

Our findings from electron microscopy also supported the quantitative measurements of pathological data. On that count, administering dextrose seemingly recruited fibroblasts for scar formation and stimulated an inflammatory response in the epidural space. Zahid et al. investigated the effects of hypertonic dextrose solution pathologically in a chemically induced osteoarthritis knee model and found that prolotherapy significantly ameliorated the histomorphology of tibial articular cartilage (36). Our pathological quantitative measurements were compatible with the Zahid et al. results. In addition, Chen et al. also investigated the effects of dextrose prolotherapy in a rat model of interstitial cystitis/bladder pain syndrome and showed that dextrose prolotherapy improved bladder hyperactivity and damage by undergoing cell proliferation and differentiation (4). Our ultrastructural results (Table II; Figure 3), seen as compatible with the Chen et al. findings, demonstrate that fibroblasts exhibited active endoplasmic reticulum and mitochondria within an enlarged cytoplasm, suggesting enhanced collagen secretion. Treatment methods using dextrose present few side effects and few risks. Indeed, dextrose's safety is widely confirmed in the literature by physicians and medical authorities. Because dextrose is a normal component in blood chemistry, it is an ideal proliferant that can be safely injected in large amounts into various areas of the body. To fully understand the effects of applying 25% dextrose on the healing process of the dura mater, additional research, particularly studies conducted over extended periods, is necessary.

Limitations

It is important to recognize several limitations within this research. To begin, the investigation was conducted using a restricted number of subjects. Furthermore, the study exclusively assessed a single 25% dextrose dosage, which may limit the broader applicability of the findings. Subsequent research should explore a range of dosages to ascertain if the observed outcomes are dose-related. Another shortcoming of our study is the absence of parenteral administration of the 25% dextrose for comparative analysis. Additionally, the use of Wistar rats in this research, while a common model, might not entirely mirror the conditions of human surgical scenarios. Lastly, the inclusion of more extensive biochemical analyses focusing on inflammatory markers could enhance the pathological evaluation and offer a more thorough assessment of postoperative effectiveness.

CONCLUSION

In conclusion, this study shows that the topical use of a 25% hypertonic dextrose solution positively influences the repair of the dura mater by enhancing collagen formation in the traumatized region. This effect could potentially prevent cerebrospinal fluid leaks and subsequent complications. Further research with larger sample sizes and extended follow-up periods in animal and human models are required to validate these findings.

Declarations

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

Disclosure: The authors declare no competing interests.

AUTHORSHIP CONTRIBUTION

Study conception and design: OS, TT, DBC

Data collection: OS, TT, MC, AF, HSB

Analysis and interpretation of results: OS, TT, DBC

Draft manuscript preparation: OS, TT

Critical revision of the article: OS, DBC, TT, MC

Other (study supervision, fundings, materials, etc...): OS, TT, MC, AF, HSB, DBC

All authors (OS, TT, AF, HSS, MC, DBC) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Banks A: A rationale for prolotherapy. J Orthop Med 13:54–59, 1991. http://askdrlehman.com/UBDX612/prolo.pdf.
2. Bosacco SJ, Gardner MJ, Guille JT: Evaluation and treatment of dural tears in lumbar spine surgery: A review. Clin Orthop Relat Res 389:238–247, 2001. https://doi.org/10.1097/00003086-200108000-00033
3. Burks S, Spotnitz W: Safety and usability of hemostats, sealants, and adhesives. AORN J 100:160-176, 2014. https://doi.org/10.1016/j.aorn.2014.01.026
4. Chen CL, Kao CC, Yang MH, Fan GY, Cherng JH, Tsao CW, Wu ST, Cha TL, Meng E: A Novel intravesical dextrose injection improves lower urinary tract symptoms on interstitial cystitis/bladder pain syndrome. Front Pharmacol 12:755615, 2021. https://doi.org/10.3389/fphar.2021.755615
5. Cheng X, Zhang Z, Ren H, Zou Z, Zhang Y, Qu Y, Chen X, Zhao J, He C: A low-swelling hydrogel as a multirole sealant for efficient dural defect sealing and prevention of postoperative adhesion. Nat Sci Rev 11:nwae160, 2024. https://doi.org/10.1093/nsr/nwae160
6. Coucke B, Van Gerven L, De Vleeschouwer S, Van Calenbergh F, van Loon J, Theys T: The incidence of postoperative cerebrospinal fluid leakage after elective cranial surgery: A systematic review. Neurosur Rev 45:1827-1845, 2022. https://doi.org/10.1007/s10143-021-01641-y
7. d'Avella E, Fazzolari B, Schiariti M, Delitala A, Ferroli P, Cappabianca P, Servadei F: Common practice in the management of dural closure: An Italian questionnaire. World Neurosurg 129:e255-e263, 2019. https://doi.org/10.1016/j.wneu.2019.05.125
8. Di Paolo S, Gesualdo L, Ranieri E, Grandaliano G, Schena FP: High glucose concentration induces the overexpression of transforming growth factor-beta through activation of PDGF loop in human mesangial cells. Am J Pathol 149:2095-2106, 1996. https://pmc.ncbi.nlm.nih.gov/articles/PMC1865344/pdf/amjpathol00036-0301.pdf.
9. Ekwueme EC, Mohiuddin M, Yarborough JA, Brolinson PG, Docheva D, Fernandes HAM, Freeman JW: Prolotherapy induces an inflammatory response in human tenocytes in vitro. Clin Orthop Relat Res 475:2117-2127, 2017. https://doi.org/10.1007/s11999-017-5370-1
10. Epstein NE, Esq JL: Medicolegal corner (spine): Contraindicated use of DuraSeal in anterior cervical spine led to quadriplegia. Surg Neurol Intern 12:532, 2021. https://doi.org/10.25259/SNI_875_2021
11. Ergun E, Kurt G, Tonge M, Aytar H, Tas M, Baykaner K, Ceviker N: Effects of phenytoin sodium on dura mater healing in a rat model of CSF leakage. Turk Neurosurg 21:471-476, 2011. https://doi.org/10.5137/1019-5149.jtn.4165-11.2
12. Eser MT, Hanalioglu S, Cetiner MZ, Dinc S, Peker HO, Sorar M, Dolgun H, Turkoglu E: Identification of risk factors for postoperative cerebrospinal fluid leakage and comparison of two alternative dural augmentation techniques in posterior fossa and spinal surgeries. Turk Neurosurg 29:377-385, 2019. https://doi.org/10.5137/1019-5149.JTN.24432-18.0
13. Esposito F, Angileri FF, Kruse P, Cavallo LM, Solari D, Esposito V, Tomasello F, Cappabianca P: Fibrin sealants in dura sealing: A systematic literature review. PLoS One 11:e0151533, 2016. https://doi.org/10.1371/journal.pone.0151533
14. Fukuda K, Kawata S, Inui Y, Higashiyama S, Matsuda Y, Igura T, Tamura S, Taniguchi N, Matsuzawa Y: High concentration of glucose increases mitogenic responsiveness to HB-EGF in rat vascular smooth muscle cells. Arterioscler Thromb Vasc Biol 17:1962-1968, 1997. https://doi.org/10.1161/01.atv.17.10.1962
15. Gandhi J, DiMatteo A, Joshi G, Smith NL, Khan SA: Cerebrospinal fluid leaks secondary to dural tears: A review of etiology, clinical evaluation, and management. Intern J Neurosci 131:689-695, 2021. https://doi.org/10.1080/00207454.2020.1751625
16. Guo J, He S, Tu Y, Zhang Y, Wang Z, Wu S, Huang F, He W, Li X, Xie H: A stable large animal model for dural defect repair with biomaterials and regenerative medicine. Tissue Eng Part C Methods 25:315-323, 2019. https://doi.org/10.1089/ten.TEC.2019.0014
17. Hauser RA, Lackner JB, Steilen-Matias D, Harris DK: A systematic review of dextrose prolotherapy for chronic musculoskeletal pain. Clin Med Insights Arthritis Musculoskelet Disord 9:139-159, 2016. https://doi.org/10.4137/CMAMD.S39160
18. Hauser RA, Sprague IS: Outcomes of prolotherapy in chondromalacia patella patients: Improvements in pain level and function. Clin Med Insights Arthritis Musculoskelet Disord 7:13-20, 2014. https://doi.org/10.4137/CMAMD.S13098
19. He Y, Revel M, Loty B: A quantitative model of post-laminectomy scar formation. Effects of NSAID. Spine 20:557-580, 1995. https://doi.org/10.1097/00007632-199503010-00010
20. Hinton JL Jr, Warejcka DJ, Mei Y, McLendon RE, Laurencin C, Lucas PA, Robinson JS Jr: Inhibition of epidural scar formation after lumbar laminectomy in the rat. Spine 20:564-580, 1995. https://doi.org/10.1097/00007632-199503010-00011

21. Karkucak A, Turkoz D, Bayraktar B, Turkoz A, Cokluk C: Comparison of tachocomb and tissudura in terms of adverse effects and complications in duraplasty in rats. Turk Neurosurg 31:680-685, 2021. https://doi.org/10.5137/1019-5149.JTN.30444-20.2
22. Kaya SS, Yardımcı G, Göksu H, Genç H: Effects of splinting and three injection therapies on lateral epicondylitis. Turk J Phys Med Rehabil 68:205-213, 2022. https://doi.org/10.5606/tftrd.2022.8007
23. Kim KD, Wright NM: Polyethylene glycol hydrogel spinal sealant (DuraSeal Spinal Sealant) as an adjunct to sutured dural repair in the spine: results of a prospective, multicenter, randomized controlled study. Spine 36:1906-1912, 2011. https://doi.org/10.1097/BRS.0b013e3181fdb4db
24. Kinaci A, Van Doormaal TPC: Dural sealants for the management of cerebrospinal fluid leakage after intradural surgery: Current status and future perspectives. Expert Rev Med Devices 16:549–553, 2019. https://doi.org/10.1080/17434440.2019.1626232
25. Koopman JE, Duraku LS, de Jong T, de Vries RBM, Michiel Zuidam J, Hundepool CA: A systematic review and meta-analysis on the use of fibrin glue in peripheral nerve repair: Can we just glue it? J Plast Reconstr Aesthet Surg 75:1018-1033, 2022. https://doi.org/10.1016/j.bjps.2022.01.007
26. Nagata K, Kawamoto S, Sashida J, Abe T, Mukasa A, Imaizumi Y: Mesh-and-glue technique to prevent CSF leakage after ePTFE dura implantation. Neurol Med Chir 39:316-319, 1999. https://doi.org/10.2176/nmc.39.316
27. Oh JH, Ha H, Yu MR, Lee HB: Sequential effects of high glucose on TGF-β1 and fibronectin in mesangial cells. Kidney Int 54:1872-1878, 1998. https://doi.org/10.1046/j.1523-1755.1998.00193.x
28. Ohgi S, Johnson PW: Glucose modulates growth of gingival fibroblasts and PDL cells: Correlation with bFGF expression. J Periodontal Res 31:579-588, 1996. https://doi.org/10.1111/j.1600-0765.1996.tb00523.x
29. Pugliese G, Pricci F, Locuratolo N, Romeo G, Romano G, Giannini S, Cresci B, Galli G, Rotella CM, Di Mario U: Increased IGF activity in mesangial cells cultured in high glucose. Diabetologia 39:775-784, 1996. https://doi.org/10.1007/s001250050510
30. Rabago D, Best TM, Beamsley M, Patterson J: A systematic review of prolotherapy for chronic musculoskeletal pain. Clin J Sport Med 15:376-380, 2005. https://doi.org/10.1097/01.jsm.0000173268.05318.a4
31. Reeves KD, Atkins JR, Solso CR, Cheng CI, Thornell IM, Lam KHS, Wu YT, Motyka T, Rabago D: Rapid decrease in dextrose concentration after intra-articular injection. Biomedicines 13:350, 2025. https://doi.org/10.3390/biomedicines13020350
32. Reeves KD, Hassanein K: Randomized prospective double-blind placebo-controlled study of dextrose prolotherapy for knee osteoarthritis with or without ACL laxity. Altern Ther Health Med 6:68-80, 2000. https://www.prolotherapy.com/Reeves_Knee%20arthritis%20study_2000.pdf.
33. Sugawara T, Itoh Y, Hirano Y, Higashiyama N, Shimada Y, Kinouchi H, Mizoi K: Novel dural closure with polyglactin acid sheet prevents CSF leak after spinal surgery. Neurosurgery 57:290-294, 2005. https://doi.org/10.1227/01.neu.0000176410.65750.c0
34. Thomas KA: Fibroblast growth factors. FASEB J 1:434-440, 1987. https://doi.org/10.1096/fasebj.1.6.3315806
35. Tseng WL, Xiao F: Duraseal thecal sac compression after lumbar discectomy causing radiculopathy. Spine J 15:1892–1893, 2015. https://doi.org/10.1016/j.spinee.2015.03.048
36. Zahid A, Qamar K, Tabassum A, Abaid M, Bashir Kiani MR, Aslam M: Prolotherapy improves tibial cartilage in osteoarthritic rats. J Coll Physicians Surg Pak 33:836-841, 2023. https://doi.org/10.29271/jcpsp.2023.08.836