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Editor
Nancy E. Epstein, MD
Professor of Clinical Neurosurgery, School of Medicine, State U. of NY at Stony Brook

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Review Article

Perspective: Risks/adverse events for epidural spinal injections

Nancy E. Epstein[1], Marc A. Agulnick[2]

[1]Professor of Clinical Neurosurgery, School of Medicine, State University of NY at Stony Brook and Editor-in-Chief Surgical Neurology International NY, USA, and c/o Dr. Marc Agulnick, 1122 Franklin Avenue Suite 106, Garden City, NY, USA, [2]Assistant Clinical Professor of Orthopedics, NYU Langone Hospital, Long Island, NY, USA, 1122 Franklin Avenue Suite 106, Garden City, NY, USA.

E-mail: *Nancy E. Epstein - nancy.epsteinmd@gmail.com; Marc A. Agulnick - marc_agulnick@yahoo.com

***Corresponding author:**
Nancy E. Epstein, M.D., F.A.C.S., Professor of Clinical Neurosurgery, School of Medicine, State University of NY at Stony Brook, and Editor-in-Chief of Surgical Neurology International NY, USA, and c/o Dr. Marc Agulnick, 1122 Franklin Avenue Suite 106, Garden City, NY, USA

nancy.epsteinmd@gmail.com

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ABSTRACT

Background: Despite the lack of FDA (Food and Drug Administration) approval, cervical and lumbar epidural spinal injections are frequently performed in the US to address back pain and/or painful radiculopathy. The three major types of injections include; interlaminar/translaminar (ESI), transforaminal (TFESI), or caudal injections. Notably, most studies document little to no clear short-term, and no long-term benefits/efficacy for these injections vs. various placebos.

Methods: More adverse events (AE) occurred with cervical© rather than lumbar (L) injections, and more severe AE were attributed to C-TFESI vs. CESI injections.

Results: Acute post injection AE symptoms were observed immediately or within 72 post-injection hours. These symptoms included; hypotension, acute respiratory distress, chest pain, upper extremity numbness, weakness, paresthesias, paralysis, and fevers. More AE were attributed to cervical C-TFESI vs. cervical CESI. These AE included; intramedullary/cord injections, intravascular injections (i.e. vertebral artery) resulting in brain stem/cerebellar/cord strokes, epidural abscess/infection, confusion, epidural hematomas, intracranial hypotension, and/or 6th nerve cranial palsies. AE for lumbar LESI/L-TFESI included; infections/abscess, epidural hematomas/subdural hematomas, intravascular injections, cerebrospinal fluid (CSF) leaks/dural tears (DT), and intracranial/postural hypotension. Notably, the vast majority of studies showed little to no short-term, and no long-term benefits for cervical or lumbar ESI/TFESI vs placebos (i.e. mostly consisting of normal saline alone, or saline plus local anesthesia).

Conclusion: Epidural cervical and lumbar ESI or TFESI spinal injections demonstrated minimal to no short-term, and no long-term benefits for the treatment of cervical and/or lumbar pain/radiculopathy vs. placebos. Further, more AE were observed for cervical vs. lumbar epidural injections overall, with more AE usually seen with TFESI vs. ESI procedures.

Keywords: Spinal Epidural Injections: Interlaminar, Translaminar (ESI); Transforaminal (TFESI), Caudal: Cervical, Lumbar, Adverse Events, Cord Injections, Cerebrospinal Fluid (CSF) Leaks, Neurological Deficits, Paralysis, Vascular Injections

INTRODUCTION

Despite the lack of FDA (Food and Drug Administration) approval, Medicare reported that over 9 million cervical and lumbar epidural spinal injections were performed in 2012 [Table 1].[11] The three major type of epidural injections included; interlaminar/translaminar (ESI), transforaminal (TFESI), or caudal injections.[1-22] More adverse events (AE) were reported for cervical vs. lumbar injections overall, and most major cervical AE (i.e., including intramedullary/cord and/or intravascular

Table 1: Summary of articles regarding spinal epidural injections.

Author [Ref] Journal Year	Study Design	Diagnostic Studies	Procedures	Adverse Events	Outcomes
Carette[4] N Engl J Med 1997	No Doc Efficacy ESI for Sciatica RCT yo ti 3 ESI Methylprednisolone Acetate (80 mg8 ml NS) Vs. NS 1 mg 158 pts sciatic Due to Disc	ODI Pre Rx > 20 3 wk ODI Improved mean -8.0 Steroid vs. -5.5 NS Group (Not Sig)	6 wk only > Imp Leg P ESI Group 3 mos No Sig Diff Two Groups ODI -17.3 ESI vs. -15.4 NS Group	Prob Back Surgery 25.8% Steroids vs. 24.8% NS Group At 12 mos	ESI No Long Term Benefits Leg Pain Sensory deficits Due to Sciatica/ Disc Short-Term Only
Valat[22] Ann Rheum Dis 2003	Eval Efficacy ESI for Sciatica RCT 42 pts CG vs. 43 SG	3 ESI (2 day Intervals) 2 ml Prednisolone Acetate (50 mg) vs 1 ml NS to Pts With Sciatica 15-180 Days	Outcomes 20 d Meas P SLR and VAS Schober Test Dallas Pain Questionnaire Roland-Morris Index	Eval Outcomes Days 0, 5, 20, 35 Need for NSAID > 20 d Failures	Conclusion No Efficacy ESI or Epid NS for Sciatica
Arden[3] Rheumatology (Oxford) 2005	Multi RCT ESI for Sciatica WEST Study 228 pts Unilat Sciatica 1-18 mos	Test Efficacy/Response Lumbar ESI for Sciatica 12 months Multicenter DB Place-C Trial 4 Secondary Pain Clinics	Randomized **3 ESI: Triamcinolone Acetonide vs. Inj NS Q 3 wks**	Transient Benefit ESI vs. Placebo At 3 weeks ESI Not Improve Physical Fx RTW No Reduced Surgery	**Measured ODQ No Benefit 6-52 wks** No Benefit Repat ESI Over 1 Inj.
Abbasi[1] Spine 2007	Review Lit AE ICESI Review Medical Databases Major and Minor AE	Reported AE Rate ICESI Range 0-16.8%	Sig. Limitation Present Literature	Must Focus on AE	Need Standards for ICESI AE
Anderberg[2] Dur Spine J 2007	TFESI C Rad Prospective Randomized	40 Consecutive Pts Unilat Rad Below Elbow 1-2 Levels Same Side (MR-Based)	Randomized TFESI+Local Anes vs. NS/Local Anes	3 Week Follow-Up Clinical and Question	Follow-up SAME Results 2 Groups
Parr[19] Pain Physician 2009	L Int Epid Inj Chronic LBP LE P Review L Int Epid Inj =/- Steroids Applied to Discs Stenosis Rad	LBP/LE Pain Most Common P Disorder SEI One Most Common Procedures Chronic LBP	Techniques Int ESI Cauda TFESI Lit Rev 1966-2008 AHRQ USPSTF	Literature Short-Term Relief-Little Known Long-Term Relief Conclusion Limited Data Blind Int Epid-Short-Term Relief Disc/Rad	Primary :P Relief 6 mos Long-Term Relief > 6 mos Secondary : Fx, Psych, RTW, ROp
Karaman[15] Spine 2011	AE Lumbar TFESI Major and Minor AE Fluoro Injection Vascular Penetration	5 yr Data Under Fluoro Guidance Follow-up 3 wk 562 pts: 1305 L TFESI:	Vascular Penetration 7.4% NO Major AE Minor AE 11.5%	All Minor AE Transient Most Often Vasovagal 8.7%	Only Minor AE of L TFESI Conclude; Major AE Rare for L TFESI
McGrath[17] Pain Med 2011	AE from ESI Compare TFESI vs. ESI Interlaminar 4265 Injection 1857 pts over 7 yrs:	Interlaminar 161 C 123 L 17 Caudal Inj 3964 TFESI	103 Minor AE Overall AE Per Injection Rate 2.4%	Most AE Increase P 1.1% Pain Inj Site 0.33% Persistent Numbness 0.14% Other 0.8%	AE Less TFESI 2.1% AE 6% Interlaminar Conclude Fluoro ESI Safe C/L Rad Most AE Minor->P TFESI <AE

(Contd...)

Table 1: *(Continued).*

Author [Ref] Journal Year	Study Design	Diagnostic Studies	Procedures	Adverse Events	Outcomes
Epstein[6] Surg Neurol Int Mar 2013	Risks ESI and TFESI Epidural Translaminar Transforaminal Facet	Not FDA Approved Performed High Frequency Unnecessary Exposure to AE	Many pts No or Limited Spine Pathology Contam ESI-CDC 25 Died 337 Sickened 14000 Contam Steroids	AE: Inf. CSF Leak 0.4-6% Positional Headache 28%	AA 6-16%, HC, Allergy, **7.9-11.6%** IVI Stroke Blindness Neuro Deficits, Paralysis, Clots, Seizures Death
Epstein[7] Surg Neurol Int May 2013	Deliberate DT IDT, Shunts, Marsupialize Cysts Inadversent DT Trauma-Surgery-Revisions Scarring	Other Etiology DT, ESI OYL/OPLL Diagnosed: RIC, MR, CT, Myelo-CT Rec Direct Timely Repair	Direct Repair Interrupted 7-0 Gore-Tex Sutures-Suture Larger Than Needle-Occludes Holes	Adjuncts to DT Closure Muscle Graft, Dural Patches MC, Fibrin Sealant LD, WP, LP Shunts	DT/CSF Fistulas Primary Second Surgery Trauma ESI, OPLL/OYL, Others Timely Diagnosis and Treatment MR, CT/RIC
Epstein[8] Surg Neurol Int 2014	Preop ESI Result in Intraop CSF Leaks Older Pts Stenosis Multiple Unnec ESI 39 pts Lumbar Stenosis Multilevel Lam/Non-Instrumented Fusion	High Risks No Long-Term Benefits Risk 6 (18.2%) CSF Leak Due to Preop ESI in 33/39 patients who had preop ESI (performed Average 4.1 ESI Per Patient) (2 -5 wk. preop but Avg. 3.9 wk)	Intraop CSF Leaks Central/ Paracentral l45 Just Below OYL Size of Tuohy Needle	Repair CSF Fistulas 7-0 Gore-Tex Sutures/Fibrin Sealant/ Tisseel	33 of 30 pts having Lam/ Fusion With preop ESI Found CSF Leaks 6(18.2%)
Manchikanti [16] Curr Pain Headache rep 2015	Mult Case Reports AE Intraarterial Inj Steroids FDA Identified 131 Neuro AE 41 Cases AA	TFESI Cause Vast Majority AE/Most C-TFESI	Data C-TFESI Medicare 2.4% All ESI < 5% All TFESI	Causes Neuro Injury Particulate Steroid AIF	Causes Neuro Injury AD, Emb, AMS
Epstein[9] Surg Neurol Int Aug 2015	Unnec Multiple ESI Lumbar No Efficacy for Resolving Surgical Lesions	Case 54 yo Massive L23 Disc 3 Unnec ESI Delayed Surgery 4 mos Resulted CES	LBP=LLE Sciatica MR 2 mos Later Massive Central-Left Disc L23 Filling Canal	Pain Mngt 3 ESI Over 3 mos 2nd MR 4 mos Later Same Massive Disc	Lam L1-L3-Disc Removed Neuro Intact
Epstein[10] Surg Neurol Int Oct 2015	Varied Freq CSF Fistulas 336 Multilevel Lam Non-Instr Fusions Literature DT Lumbar Surgery 3-27%	2000-2015 Etiology CSF DT 336 Avg 4.7 Level Lam/Avg. 1.4 Level Non-Instr Fusions	Etiology DT OYL Postop Scar Iatrogenic-Traumatic, ESI, SC, IDT	Findings 7 ESI 6 SC 5 OYL 3 Postop Scar 3 IDT	Incidence DT 24 (7.14%) of 336 Pt Rec Direct Repair Incidence Reduced to 14 (4.16%)/336 No Preop ESI

(Contd...)

Table 1: *(Continued).*

Author [Ref] Journal Year	Study Design	Diagnostic Studies	Procedures	Adverse Events	Outcomes
Schreiber[20] Spine J 2016	C ESI vs. TFESI for P Incidence SCI Admitted to Rehab Center Due to Epidural Injections	2001-2008 SCI 1343 Pts Acute Rehab SCI 7 Due to C Inj	All Incomplete Mechanism 7 SCI: Onset Minutes to 72 hrs	7 SCI: 1 Cord Injection 2 Epid Abscess 1 Contusion 2 EDH 1 Unkown	Symptoms: Hypotension Resp Distress Chest Pain UE Numb Paresthesias Weakness Fever
Epstein[11] Surg Neurol Int 2017	AE of L + C ESI/TFESI + Dural Punctures (9 Million US yr Etiology: IPD Spont CSF Fistulas	Neuro AE ICHy SDH 6th CNP Cervical AE DT Cord Inj Strokes (Vascular or VA Injections)	8 Studies: Inadvertent Lumbar DT 5/6 studies During CESI Cord Inj Direct Intravascular VA Injection Monoplegia Quadriplegia	Inadvertant DT Multiple Neuro AE ICHY, SDH 6th CNP=Double Vision	CESI DT Cord Inj Cord Stroke Paralysis Vascular Inj
Smith [21] Oper Neurosurg 2017	NSGY AE ESI 1 Institution Database 14,247 NSGY Admitted 8 yrs Concluded: Majority AE Clot with Anticoag	AE 1182 C 4617 L Interlaminar ESI	13 AE Required NSGY Rx Rate 0.22% 0.51% C 0.15% L	Etiology Clot 7 Inf 3 (all L Inj) DT 3 Sig Assoc Anticoag with Clot	6 with EDH Stopped Anticoag 3 Taking ASA 3 All Prompt Rx/ Surgery Good Long-term Outcomes
Epstein[12] Surg Neurol Int 2018	Many Unnec CESI, including ICESI and TF-CESI Not FDA Approved No Long-Term Efficacy	Records of Morbidity Mortality CESIS AE Include EDH, Inf, (Abscess Meningitis) New Neuro deficits, (Cord Injections)	Intravasc Inj (Brain Stem, Cerebellar Particulate Steroids Embolize to Distal Artery Branches	Provide No Long-Term Benefit Perform For Minimal to No Indications	Sig Morbidity Sig Mortality May Delay Needed Surgery
Epstein[13] Surg Neurol Int 2019	39 Pts Lam 4.1 Levels/ Non Instrumented Fusion 1.3 Levels Mean 4.1 ESI per 33/39 pts Leak 6 (18%) due to Preop ESI	Cervical ESI Risk Cord Injections with Paralysis/ Intravascular Injections-Stroke Brain Stem Infarct	Pt mid 80's 1 year Neck P 2 yr ago -MI-5 Stents + Defib Rx Baby ASA	CT-No Pathology, But Rx 2 ESI Unnec Risk Stop ASA 5 d to Do ESI	No Need to Expose Pt to Risk Stopping Baby ASA- 5 Stents for Unnec ESI
Oliveira[18] Cochrane Database Syst Rev 2020	Lumbar Rad/Sciatica Safety/Efficacy ESI vs. Placebo Pain/Disability L Rad Databases Compared ESI vs. Placebo L Rad-All 3 ESI Interlaminar TFESI, Caudal	Placebo Inert Innocuous-NS Local Anes Location Epidural Space Sub Cut IM Interspinous	Eval 4 Times Immediate </= 2 wk Short >2 wk-3 mos Intermed >3 mos < 12 mos Long-Term >/= 12 mos	25 Clinical Trials ESI vs. Placebo LS Rad P 2470 pts Slightly More Effective Short Term Pain-	Limited Support ESI LS Rad-Rx Effects Small-Short-Term "may not be considered clinically important ...(Mean difference < 10%) No Long-Term Benefits

(Contd...)

Table 1: *(Continued).*

Author [Ref] Journal Year	Study Design	Diagnostic Studies	Procedures	Adverse Events	Outcomes
Chang[5] Curr Pain Headache Rep 2020	AE Lumbar TFESI for LBP/Rad TFESI One Most Used Rx Rad	Minor AE 2.4-9.6% Major AE Case Reports Spinal Abscess Cord Infarcts EDH	Most AE are Minor with TFESI	Case Studies of Major AE with TFESI	Early Diagnose and Treat AE of Lumbar TFESI
Epstein[14] Surg Neurol Int 2023	Advocate Early Direct DT Repair Recurrent Postop CSF Leaks EBP Doesn't Work 3 Studies-20 pts	Targeted Epid Blood Patch (EBP) Treat Focal DT Etiology DT ESI, LP, SA SICH	Identify DT US, Fluoro O-Arm Guidance To Perform Targeted EBP	3 Studies 20 Pts EBP Worked 1st 6/6 EBP 2nd 9/10 3rd 2/5 (Failed 60%)	Early Direct Repair Gold Standard 20% EBP Fail (Range 0-60%)

L=Lumbar, Int=Interlaminar Epid=Epidural, Inj=Injections CLBP=Chronic Low Back Pain, LBP=Low Back Pain, LE=Lower Extremity, P=Pain, SEI=Spinal epidural Injection, TFESI=Transforaminal ESI, Rad=Radiculopathy AHRQ= Agency for Healthcare Research and Quality, USPSTF=U.S. Preventive Services Task Force, mos=months, yr=year, wk=weeks Fx=Functional Status, Psych=Psychological Status, TRW=Return to Work, ROp=Reduction Opioid Use, RCT=Randomized Controlled Trial, Multi=Multicenter, DB=Double Blind, Pl-C=Placebo-Controlled, Pts=Patients NS=Normal Saline, q=Every, ODQ=Oswestry low back pain disability questionnaire,, Eval=Evaluate VAS=Visual Analog Scale, SLR=Straight Leg Raising Test, d=days,, NSAID=Non-Steroidal Anti-Inflammatory Drugs, CG=Control Group, SG-Steroid Group, Doc=Documented, OCI=Oswestry Disability Index, Sig=Significant, Prob=Probability Lit=Literature, ICESI=Interlaminar Cervical Epidural Steroid Injections, AE=Adverse Events, C=Cervical TFESI=Transforaminal Epidural Steroid Injection, Unilat=Unilateral, Anes=Anesthesia, Question=Questionnaire, Unnec=Unnecessary, FDA=Food and Drug Administration, TF=CESI=Transforaminal Cervical ESI, EDH=Epidural Hematoma, Inf=Infection, Intravasc=Intravascular, Strokes, Contam=Contaminated, CDC=Center for Disease Control, IVI=Intravascular Injections, HC=Hydrocephalus, AA=Adhesive Arachnoiditis, MI=Myocardial Infarction, Defib=Defibrillator, Rx = Medication or Treated, Preop=Preoperative, Intraop=Intraoperative, CSF=Cerebrospinal Fluid, Lam=Laminectomy, OYL=Ossification of the Yellow Ligament, EBP=Epidural Blood Patches, DT=Dural Tears, MR=Magnetic Resonance Imaging, CT=CAT Scan Studies Myelo=Myelogram, LP=Lumbar Puncture, SA=Spinal Anesthesia, SICH=Spontaneous Intracranial Hypotension, US=Ultrasound, Fluoro=Fluoroscopy , IPD= Intradural Pain Devices, Spont=Spontaneous, ICHy=Intracranial Hypotension, SDH, CNP=Cranial Nerve Palsy, VA=Vertebral Artery, CES=Cauda Equina Syndrome, Mngt=Management, Non-Instr=Non-Instrumented, Avg=Average, SC=Synovial Cysts, IDT=Intradural Tumors Rec=Recommended, RIC= Radioisotope Cisternography, LD=Lumbar Drain, LP Shunt=Lumboperitoneal Shunt, WP Shunt=Wound Peritoneal Shunt, MC=Microfibrillar Collagen (Duragen), AA=Adhesive Arachnoiditis, AIF=Arterial Intimal Flaps, AD Arterial Dissection, Emba=Dislodgement Plaque Causing Embolism, AMS=Arterial Muscle Spasm, Sub Cut=Subcutaneous, IM=Intramuscular, Intermed=Intermediate, NSGY=Neurosurgery, Anticoag=Anticoagulation, SCI=Spinal Cord Injuries

injections including stroke and death) were attributed to TFESI vs. ESI procedures. Further, many studies documented minimal/no short-term, and no long-term benefits for any of these injections (i.e. comparing epidural injections vs. placebos).

AE Attributed to ESI/TFESI That Are Not FDA (Food and Drug Administration) Approved

Two articles discussed the lack of FDA approval of cervical or lumbar spinal epidural injections.[6,16] In 2013, Epstein noted that both cervical and lumbar spinal ESI/TFESI were not FDA approved, and posed significant risks of AE [Table 1].[6] That article: "...cite(d) contaminated epidural steroid injections resulting in meningitis, stroke, paralysis, and death. The Center for Disease Control (CDC) specifically identified 25 deaths (many due to Aspergillosis), 337 patients sickened, and 14,000 exposed to contaminated steroids". Further, Manchikanti *et al.* in 2015 recounted the FDA warning regarding the greater risks observed for cervical TFESI that included 131 major neurological AE events, including death, and 41 instances of adhesive arachnoiditis.[16]

Time of Onset of Acute/Symptoms/Signs After Cervical/Lumbar ESI/TFESI Injections

Schreiber *et al.* in 2016 reported that adverse symptoms/signs occurred immediately to within 72 hours following epidural injections; these typically included hypotension, acute respiratory distress, chest pain, upper extremity numbness, weakness, paresthesias, and/or paralysis, and fever [Table 1].[20]

Minimal or No Short-Term and No Long-Term Benefits of Cervical ESI/TFESI

Two studies documented minimal/no short-term, and no long-term benefits of cervical ESI/TFESI vs. placebos [Table 1].[2,12] In Anderberg *et al.* (2007), 40 consecutive patients with unilateral 1-2 level cervical radiculopathy were randomized to receive either TFESI/local anesthesia vs. NS (Normal Saline)/local anesthesia; at 3 post-treatment weeks, both groups demonstrated comparable outcomes. [2] In 2018, Epstein noted that cervical C-TFESI demonstrated

minimal to no short-term, and no long-term benefits, but posed significant risks of AE.[12] These included; epidural hematomas, infections (abscess/meningitis), new neurological deficits (i.e. including intramedullary cord injections), intravascular injuries (brain stem, cerebellar), and strokes (i.e., largely attributed to particulate steroid emboli to distal arterial branches).[12]

Minimal to No Short-Term and No Long-Term Benefits of Lumbar ESI, TFESI, or Caudal Injections vs. Placebos

Five studies documented minimal/no short-term, and no long-term benefits of lumbar ESI/TFESI [Table 1].[3,4,18,19,22] Using Methylprednisolone Acetate/Normal Saline (NS) vs NS alone (placebo) to treat 158 patients with sciatica/lumbar disc disease, Carette *et al*. (1997) showed only transient short-term (i.e., </=6 weeks), but no long-term benefits of ESI (i.e., > 6 weeks to 3 mos. post-injection).[4] Further, 1 year later, both groups had similar requirements for surgery: 25.8% with ESI vs. 24.8% without ESI. Comparing 42 control group patients (CG without steroids) vs. 43 steroid group (SG) patients with sciatica, Valat *et al*. (2003) found no short or long term benefits utilizing ESI (i.e. SG employing 2 ml Prednisolone Acetate (50 mg) and performing 3 ESI at 2-day intervals) vs. 1 mg NS (CG); they both demonstrated comparable frequencies of treatment failures defined by the need to administer NSAIDS (non-steroidal anti-inflammatory agents) at 20 post-injection days.[22] In a randomized controlled study, Arden *et al*. (2005) utilized 3 ESI (Triamcinolone Acetonide) vs. 3 NS epidural injections given every 3 weeks to treat unilateral sciatica (i.e. patients followed for 1-18 months); those receiving ESI exhibited transient benefits up to 3 weeks following the 1st injection, but encountered no long-term benefits beyond 6-52 weeks after ESI.[3] Parr *et al*. (2009) also found no short (</= 6 mos.) or long-term benefits (> 6 mos.) for lumbar ESI (i.e. utilizing interlaminar, TFESI, or caudal injections) vs. placebo addressing stenosis/radiculopathy; their review of the literature yielded similar results.[19] In 2020, Oliveira *et al*. summarized data from 25 clinical trials comparing the efficacy of lumbar ESI (i.e. interlaminar TFESI or caudal injections) vs. subcutaneous, vs. intramuscular vs. interspinous steroid injections vs. placebo (i.e. inert, Normal Saline, local anesthesia) in the treatment of 2470 patients with lumbar radiculopathy/sciatica. [18] Over the 4 periods they reviewed (i.e. </= 2 weeks (intermediate); > 2 weeks to 3 mos. (short-term); > 3 mos.=< 12 mos (intermediate term); and >/= 12 mos. (long-term)), ESI vs. placebo showed only small short-term benefits that were "not... considered clinically important", and there were no long-term benefits.

More Minor vs. Major AE Reported for Cervical and/or Lumbar ESI, TFESI, or Caudal Lumbar Injections

Five studies documented more minor vs. major AE attributed to cervical and/or lumbar epidural injections; additionally some reports stated more AE occurred following TFESI vs. ESI [Table 1].[1,5,15,16,17] When Abbasi *et al.* (2007) reviewed the literature from multiple databases, they found a 0-16.8% incidence of AE for interlaminar CESI (0-16.8%); most AE were minor.[1] When McGrath *et al*. (2011) compared the incidence of AE in 1857 patients treated over 7 years with 3964 lumbar TFESI vs. 161 cervical ESI, 123 lumbar ESI, and 17 caudal injections, they observed 103 minor AE (2.4% incidence per injections).[17] These included; increases pain (1.1%), pain at injection sites (0.33%), persistent numbness 0.14%), and other factors (0.8%).[17] They concluded that fewer AE occurred following TFESI (2.1%) vs. ESI (6%). Over a 5-year period, Karaman *et al*. (2011) evaluated the frequency of minor vs. major AE for 1305 lumbar TFESI performed in 562 patients utilizing intraoperative fluoroscopy; patients followed for up to 3 weeks demonstrated a 7.4% incidence of vascular penetration that resulted in a 11.5% incidence of minor AE (i.e., including vasovagal events), but no major AE.[15] Manchikanti (2015) *et al*. stated that most AE were attributed to cervical TFESI (2.4% of total ESI) largely attributed to; "...particulate steroid (emboli), arterial intimal flaps, arterial dissection, dislodgement of plaque causing embolism, arterial muscle spasm, and embolism of a fresh thrombus following disruption of the intima."[16] Chang *et al*. (2020) found that most AE for lumbar TFESI were minor (2.4-9.6% incidence), and that major AE were only reported in individual case studies (i.e. including spinal abscesses, cord infarcts, or epidural hematomas).[5]

Variable Reporting of AE for Cervical and/or Lumbar ESI vs TFESI, with 2 of 3 Studies Emphasizing More AE with Cervical Injections

Three studies reported different frequencies for AE attributed to cervical and/or lumbar ESI vs. TFESI, with 2 citing greater AE for cervical injections (ESI/TFESI) [Table 1].[11,16,17] McGrath *et al*. (2011) compared the incidence of AE in 3964 lumbar TFESI vs. 161 cervical ESI, 123 lumbar ESI, and 17 caudal injections, and identified fewer AE (2.1%) for cervical/lumbar TFESI (2.1%) vs cervical/lumbar ESI (6%).[17] Manchikanti (2015) *et al*. found more AE attributed to cervical TFESI (2.4% of total ESI).[16] In 2017, Epstein also observed more AE for cervical injections that included both CESI and C-TFESI vs. lumbar injections (i.e., CESI/C-TFESI including DT/CSF leaks, intramedullary cord injections, intravascular injuries/strokes, and others).[11]

Various Symptoms/Signs of DT/CSF Leaks and Other AE Following Preoperative Spinal Epidural Injections

Multiple symptoms and signs may signal DT/CSF leaks or other AE following preoperative cervical and/or lumbar epidural injections [Table 1].[6,7,10] In 2013, Epstein quoted a 28% incidence of positional headaches, a 6-16% frequency of Adhesive Arachnoiditis, and a combined 7.9-11.6% risk for; intramedullary cord injections, intravascular injections/stroke, blindness, new neurological deficits/paralysis, clots/hematomas, seizures and death.[6] Also in 2013, Epstein discussed the varied etiologies of DT/CSF leaks encountered during spinal surgery, and/or documented with postoperative MR, CT, and Myelo-CT studies.[7] These included; preoperative epidural injections, intraoperative traumatic injuries due to lumbar resection of ossified yellow ligament, cervical removal of Ossification of the Posterior Longitudinal LIgament (OPLL), marsupialization of arachnoid cysts, revision surgeries, and postoperative scarring.[7] Out of a series of 336 patients undergoing average 4.7 level laminectomies/average 1.4 level non-instrumented fusions, Epstein (2015) found a total 7.14% (24 patients) incidence of DT/CSF fistulas; 7 were due to preoperative ESI. Other etiologies of these leaks included; 6 synovial cysts, 5 instances of ossification the yellow ligament (OYL), 3 cases of leaks due to postoperative scar, and 3 DT due to the resection of intradural tumors. Subtracting the 7 ESI and 3 patients with intradural tumors from the 24 overall incidence of DT/CSF leaks, reduced the frequency to 4.16% for the remaining 14 patients (6 synovial cysts, 5 OYL, 3 postoperative scar).

Frequency and Treatment/Repair of Traumatic Dural Tears (DT) Attributed to Preoperative Cervical/Lumbar Epidural Steroid Injections

Epstein documented in multiple studies that preoperative cervical and/or lumbar epidural injections resulted in intraoperatively documented DT that warranted direct repair [Table 1].[6-8,10,13] In 2013, Epstein reviewed the literature, citing a 0.4-6.0% incidence of intraoperative CSF leaks following spinal epidural injections.[6] Also in 2013, Epstein discussed the varied etiologies of DT/CSF leaks documented with MR, CT, and Myelo-CT studies. Emphasis was placed on performing timely direct dural repairs utilizing 7-0 Gore-Tex interrupted sutures (i.e. suture larger than the needle occludes needle holes), supplemented by adjunctive techniques (i.e. muscle/fascial patch grafts, microfibrillar collagen (suturable/non-suturable microfibrillar collagen, fibrin sealants, lumbar drains, wound-peritoneal, and lumboperitoneal shunts)). [7] In a 2014 study, Epstein observed that 33 of 39 patients undergoing multilevel lumbar laminectomies and non-instrumented fusions had preoperative lumbar epidural injections (i.e. average of 4.1 ESI/patient performed 2-5 weeks preoperatively (avg. 3.9 weeks); 6 (18.2%) patients had confirmed intraoperative DT/CSF leaks warranting direct repairs.[8] Epstein (2015) later documented that for 336 patients undergoing average 4.7 level laminectomies/average 1.4 level non instrumented fusions (2000-2015), 7 (29.2%) of 24 intraoperative DT/CSF fistulas were due to preoperative epidural steroid injections.[10]

High Failure Rate for Epidural Blood Patches (EBP) Utilized to Occlude Lumbar DT/CSF Leaks Largely Attributed to Preoperative ESi/TFESI and Other Factors

In 2023, Epstein emphasized the need for early direct repair of MR/Myelo-CT-documented sites of DT/CSF leaks encountered intraoperatively following preoperative ESI and other procedures/factors (i.e. lumbar punctures, spinal anesthesia (SA), and spontaneous intracranial hypotension (SICH)) rather than choosing to perform EBP [Table 1].[14] The efficacy of targeted EBP repair of DT/CSF leaks (i.e. typically utilizing intraoperative ultrasound, fluoroscopy, or the O-Arm) averaged 20%, with a range of from 0-60%.

Incidence of Acute Cervical Spinal Cord Injuries (SCI) Due to ESI/TFESI

Schreiber (2016) documented that 7 (0.52%) of 1343 patients admitted to an acute spinal cord injury (SCI) center sustained cervical injures attributed to ESI/TFESI (2001-2008) [Table 1].[20] All 7 patients had incomplete acute cervical neurological deficits attributed to; 1 cord injection, 2 epidural abscesses, 1 cord contusion, 2 epidural hematomas, and 1 of unknown etiology. Acute presenting symptoms for these patients included; hypotension, respiratory decompensation, chest pain, upper extremity numbness, paresthesias, weakness, and/or fever.

Frequency of Epidural Hematomas Due to Epidural Injections/ESI

Out of a total of 1182 (0.51%) cervical and 4617 (0.15%) lumbar interlaminar ESI performed over an 8-year period, Smith *et al.* (2017) observed that 13 patients required emergency neurosurgery for 3 DT/CSF leaks, 3 infections, and 7 hematomas [Table 1].[21] Interestingly, all 7 hematomas were lumbar cases; 3 patients had stopped anticoagulation, while 3 had continued on their Aspirin therapy.

Case Report: 3 Month Delay in L23 Laminectomy Due to Administration of 3 Lumbar ESI

In a 2015 case study, Epstein (2015) presented a 54-year-old-male with an MR-documented massive L23 disc herniation filling the spinal canal who was negligently treated for

3 months with ESI (i.e., 1 per month); when he finally presented paraplegic, he underwent a L23 laminectomy and fortunately recovered significant neurological function [Table 1].[9]

CONCLUSION

In this perspective/review of the literature, patients undergoing epidural cervical and lumbar ESI or TFESI spinal injections demonstrated minimal to no short-term, and no long-term benefits for the treatment of cervical and/or lumbar pain/radiculopathy vs. placebos. Further, more AE were observed for cervical vs. lumbar epidural injections, with more frequent and severe AE seen with TFESI vs. ESI procedures.

Ethical approval

Institutional Review Board approval is not required.

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.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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Commentary

Author: Jamie L. Baisden MD (Neurosurgery)

This article is a bit heavy on the risks of ESI and TFESI. What is this paper's overall purpose? To let people know the dangers of epidural steroid injections lacking FDA approval, or to save insurance companies money? As spine surgeons, we should not allow insurance companies that don't have a medical degree to act as gait-keepers to determine who should undergo multiple non-FDA-approved spinal epidural injections before being "disqualified" or "qualified" for spine surgery. Most oral steroids (i.e., oral steroids - Medrol Dose Packs, or Prednisone) or intramuscular steroid injections (i.e., especially trigger point injections) have minimal risks/minimal down-sides and may make people feel better, particularly in the short-term (i.e., weeks). Notably, the placebo effect of any injection (i.e., many studies typically compare epidural steroid vs Normal Saline epidural or intramuscular injections) is often around 30%; so, you may want to concede that 30% of patients may feel some transient improvement in the first 1-2 weeks. More critically, however, the "natural history" of spontaneous improvement kicks in at around 3-4 weeks, just around the time the "benefits" of steroids are actually waning or disappearing; patients may then mistakenly attribute their continued "improvement" to the steroids, rather than to the natural course of symptom resolution.

My primary concern, however, is what is left for patients if we can't offer narcotics or epidural steroid injections anymore, and the patient can't take NSAIDs (i.e., on blood thinners for cardiovascular disease, and/or a history of gastrointestinal, and/or chronic kidney disease)? We can certainly offer patient education and a multitude of medications (i.e., muscle relaxants, neuromodulators, non-opioid/non-NSAID medications) and/or other non-invasive modalities. It all remains a statistical balancing act of juggling potential risks versus benefits as we help patients navigate the cons/dangers posed by non-FDA-approved epidural spinal injections. Further, these unnecessary injections (i.e. well-documented minimal to no short-term (i.e. 3-6 weeks) and no long-term benefits) typically cost patients or their insurance carriers hundreds to over thousands of dollars per injection (i.e., varies by state, carrier, setting); certainly, these fees are lining pain management specialists' pockets. Lastly, in some instances, epidural steroid injections are being wrongly performed, negligently delaying "essential" spine surgery.

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