**Table**. Previous reports of hypertonic saline administration for pain management

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| Authors (year) | Study Design | Patient Population | Route | Solution | Results | Comments |
| *Epidural* | | | | | | |
| Kanayama *et al.* (1969)1 | Case series | 29 patients with persistent pain from various conditions, including 19 with cancer | Epidural (interlaminar) | Hypertonic saline, ranging from 7 to 30% | Pain relief in all cases, lasting from several hours to several months. More than 60% of cases reported >2 weeks of pain relief. | Post-injection discomfort (heaviness) after initial 2 injections relieved with intrathecal injection of 1% local anesthesia prior to treatment. No side effects noted with concentrations <=15%. |
| Koh *et al.* (2013)2 | Randomised controlled trial | 68 patients with persistent low back pain from spinal stenosis | Epidural (transforaminal) | Hypertonic group: 2 mL of 10% saline mixed with 20 mg triamcinolone  Control group: 2 mL of 0.9% saline mixed with 20 mg triamcinolone | Hypertonic group with greater reduction in NRS radicular pain intensity from baseline and patient satisfaction compared to control at 3 months. Otherwise reductions in NRS radicular pain and ODI ratings similar between two groups up to 6 months. | Dropouts (15 patients, 22%) excluded from analysis making study underpowered. All patients received 0.5-2.0 ml contrast and 2 mL of 1% lidocaine with hyaluronidase 1500 units. One patient experienced burning during injection of hypertonic saline. |
| Heavner *et al*. (1999)3 | Randomised controlled trial | 83 patients with persistent low back pain | Epidural (lysis of adhesions) | Group A: 10% saline and hyaluronidase  Group B: 10% saline  Group C: 0.9% saline  Group D: 0.9% saline and hyaluronidase  Volume not reported. | No differences among Short Form McGill Pain Questionnaire, VAS for back pain, or VAS for leg pain at discharge or 1-, 3-, 6-, or 12-months after treatment. | Dropouts (24 patients, 29%), gender imbalance among groups, and statistical analysis limit findings. |
| Manchikanti *et al.* (2001)4 | Retrospective review | 18 patients with persistent low back pain from spinal stenosis | Epidural (lysis of adhesions) | 6 mL of 10% saline with betamethasone 6 mg, 5 mL of 2% lidocaine, and 0 to 10 mL 0.9% saline | Improvements in average NRS pain score and functional status following injection. | Multiple injections (up to 10) permitted. |
| Manchikanti *et al.* (2001)5 | Randomised clinical trial | 45 patients with persistent low back pain and post-lumbar laminectomy syndrome | Epidural (lysis of adhesions) | Group II: 6 mL of 10% saline, preceded by 5 mL of 1% lidocaine with betamethasone 6 mg  Group I: physical therapy, exercise, medication, and no injection | Group II with improvements in average NRS pain score and functional status compared to Group I. | Multiple injections (up to 10) permitted. |
| Manchikanti *et al.* (2004)6 | Randomised clinical trial | 75 patients with persistent low back pain for >= 2 years | Epidural (lysis of adhesions) | Group III (lysis): 6 mL of 10% saline  Group II (lysis): 6 mL of 0.9% saline  Group I (no lysis): 6 mL of 0.9% saline  In all groups, 5 mL of 2% lidocaine, 80 mg methylprednisolone or 12 mg betamethasone, 1 mL 0.9% saline used. | Similar, significant improvement in VAS pain scores and ODI at 3-, 6-, and 12-months in Groups II/III compared to Group I. Non-significant trend of enhanced improvement in Group III compared to Group II. Fewer injections required in Group III compared to Group II. | Multiple injections permitted. Unintentional intrathecal injection noted in 1 patient in Group II. |
| Manchikanti *et al.* (2013)7 | Prospective cohort | 70 patients with persistent low back pain from spinal stenosis | Epidural (lysis of adhesions) | 6 mL of 10% saline with betamethasone 6 mg, 1 mL of 0.9% saline, 5 mL of 2% lidocaine | Significant improvement in NRS pain scores and ODI at 3-, 6-, 12-, 18-, and 24-month intervals, with 71% sustaining >=50% improvement in both outcomes at 24 months. | Initial randomised study comparing lysis of adhesions to caudal epidural injection changed to cohort study due to recruitment problems. All patients received 3-5 mL contrast. Multiple injections permitted. Dural puncture in 1.5% (6/397) of procedures |
| *Intrathecal* | | | | | | |
| Thompson (1971)8 | Case report | 1 patient with rectal and sacral pain from colon cancer status post anterior sigmoid resection and radiation | Intrathecal at L3-L4 | 40 mL of 5% saline | Pain relief described as ‘minimal pain.’ Complication of pulmonary edema immediately following procedure, which resolved after 48 hours. | Prior to injection, Injectate was at 0oC. 40 mL cerebrospinal fluid was withdrawn. |
| Hitchcock *et al*. (1973)9 | Retrospective review | 108 patients with persistent pain from various conditions | Intrathecal | 10 mL of hypertonic saline, ranging from 10 to 15% | Pain relief noted in 50% of cancer patients and >40% in non-cancer patients at 3 months. | Side effects of bladder/bowel incontinence (8%) and muscle weakness (3%) reported. |
| Booth (1974)10 | Case series | Unknown number of patients with persistent pain from various conditions | Intrathecal | Hypertonic saline. Concentration and volume not reported. | Reports of ‘good control’ or ‘abolished pain’ in ‘about 45% of those treated’ | Side effects of sacral anesthesia and fecal incontinence noted in two patients. |
| Squire *et al*. (1974)11 | Case series | 9 patients with persistent pain of the trunk and lower extremities | Intrathecal | 15 mL of a mixture of 20 mL 8% saline with 1 mL 0.4% lidocaine | Pain relief lasting from 50 to 90 minutes in 8 patients to complete pain relief in 1 patient. | Prior to injection, 15 mL cerebrospinal fluid was withdrawn. Side effects of backache noted in 6 patients. |
| Patel *et al*. (1974)12 | Prospective cohort | 35 patients with persistent pain of various types | Intrathecal | 5 mL of 5% saline. If unsuccessful, then repeat injection with 5 mL of 8% saline. | Pain relief described as ‘complete’ in 80% of patients, with 74% after 1 injection and 6% after 2 injections. Duration ranging from 3-6 weeks to ‘permanent.’ | Prior to injection, 10 mL cerebrospinal fluid was withdrawn. All non-responding patients had malignancy. Side effects of hyperpnoea, hypertension, bradycardia, and muscle twitching noted. One patient died from meningitis. One patient developed paraplegia after administration of 15% saline. |
| Lucas *et al.* (1975)13 | Retrospective cohort | 2105 patients with persistent pain from various conditions | Intrathecal | Hypertonic saline. Concentration and volume varied. | Temporary adverse reactions noted in 11% of cases. Serious complications noted in 1% of cases, including paraplegia/quadriplegia (n = 16), partial paralysis (n = 1), myocardial infarction (n = 3), and hearing loss (n = 2). | 32.4% survey participation rate. Study included 136 patients with hypothermic isotonic saline, 40 patients with hypertonic hypothermic saline, and 26 patients with hypotonic saline. |
| Kim *et al.* (1988)14 | Case report | 1 patient with history of pancreatitis, surgery for pancreatic duct obstruction, and narcotic dependence | Intrathecal at L4-L5 | 10 mL of 15% saline | Pain relief, followed at 1 day by paraplegia and loss of sensation below umbilicus | Prior to injection, 25 mL cerebrospinal fluid was withdrawn, and 10 mL mixed with hypertonic saline prior to injection. Morphine 10 mg given intrathecally prior to injection. |
| *Other* | | | | | | |
| Hitchcock (1969)15 | Case series | 7 patients with persistent facial pain from carcinoma | Perineural via cisternal route | 6 to 20 mL of hypertonic saline, ranging from <2 to >9% concentration at 4 to 36OC | Pain relief in all cases, lasting from 3 to 105 days. | Side effects of vertigo, vomiting, and facial weakness. |
| Pinto *et al.* (2006)16 | Randomised controlled trial | 60 patients after endoscopic sinus surgery | Intranasal | HS: 3% saline buffered spray  NS: 0.9% saline spray  NI: no spray | No differences in overall pain/pressure via 5-day sum of scores among 3 groups. Higher pain scores on day 2 and 3 for hypertonic group compared to other 2 groups. | Pain outcome measure combined with pressure in assessment using a categorical 5-item measurement. |

ODI – Oswestry disability index; NRS – numeric rating scale; VAS – visual analogue scale

Note: articles were selected by searches of the PubMed and CINAHL databases from inception to April 2015 using combinations of the search terms “epidural,” “intrathecal,” “pain management,” and “hypertonic saline.” Case reports, review articles, abstracts, and controlled trials which reported pain outcomes from administration of hypertonic saline adjacent to nerves or the intrathecal/epidural space were all considered for inclusion with English language restriction.

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