ROLE OF ADHESIOLYSIS IN THE MANAGEMENT OF CHRONIC SPINAL PAIN: A SYSTEMATIC REVIEW OF EFFECTIVENESS AND COMPLICATIONS

Pradeep Chopra, MD, Howard S. Smith, MD, PhD, Timothy R. Deer, MD, and Richard C. Bowman, MD

Background: Percutaneous epidural adhesiolysis and spinal endoscopic adhesiolysis are interventional pain management techniques that play an active role in managing chronic intractable low back pain. There have not been any systematic reviews performed on this subject.

Objective: To evaluate the effect of percutaneous adhesiolysis and spinal endoscopic adhesiolysis in managing chronic low back and lower extremity pain.

Study Design: A systematic review utilizing the methodologic quality criteria of the Cochrane Musculoskeletal Review Group for randomized trials and the criteria established by the Agency for Healthcare Research and Quality (AHRQ) for evaluation of randomized and non-randomized trials.

Methods: Search identified the relevant literature, through searches of MEDLINE and EMBASE (January 1966 to November 2004), BioMed Central and Cochrane Review database. Manual searches of bibliographies of known primary and review articles, and abstracts from scientific meetings within the last 2 years, in English language. Randomized and non-randomized studies were included in the review based on the criteria established.

Three reviewers independently assessed the trials for the quality of their methods. Percutaneous adhesiolysis and endoscopic adhesiolysis were analyzed separately.

Outcome Measures: Primary outcome measure was significant pain relief (50% or greater). Other outcome measures were functional improvement, improvement of psychological status, and return to work. Short-term relief was defined as less than 3 months, and long-term relief was defined as 3 months or longer.

Results: There was strong evidence to indicate effectiveness of percutaneous epidural adhesiolysis with administration of epidural steroids for short term and long term in chronic, refractory low back pain and radicular pain. There was moderate evidence of effectiveness of addition of hypertonic saline. The evidence of effectiveness of hyaluronidase was negative.

There was strong evidence to indicate effectiveness of spinal endoscopic adhesiolysis and epidural steroid administration for short-term improvement, and moderate evidence for long-term improvement in managing chronic, refractory, low back and lower extremity pain.

Conclusion: The evidence of effectiveness of percutaneous adhesiolysis with administration of hypertonic sodium chloride administration, and spinal endoscopic adhesiolysis with epidural steroid administration in managing chronic, refractory low back and lower extremity pain of post lumbar laminectomy syndrome or epidural fibrosis was moderate to strong.

Keywords: Spinal pain, chronic low back pain, percutaneous adhesiolysis, spinal endoscopic adhesiolysis, spinal stenosis, post lumbar laminectomy syndrome, epidural fibrosis.

Chronic low back pain has a prevalence ranging from 35% to 75% at 12 months after the initial attack (1-6). Kuslich et al (7) were able to identify different tissue such as intervertebral discs, nerve root dura, facet joints, ligaments and muscles that were potentially capable of transmitting pain. Post lumbar laminectomy syndrome, vascular compromise, spinal stenosis and inflammatory response have also been implicated in chronic low back pain. Post operative epidural fibrosis may contribute from 5% to 60% of poor surgical outcome following decompressive surgery (1, 8-12). The prevalence of pain following surgery for the lumbar spine, also known as post lumbar laminectomy syndrome is estimated in approximately 5% to 40% of patients after surgical intervention (13-16). Ross et al (10) and other authors have reported a correlation between peridural scarring and radicular pain (11, 17), and poor clinical outcomes (13, 14), while others have questioned the role of epidural fibrosis as a cause of chronic pain (15, 16, 18).

Hematoma formation in the epidural space during the post operative period is invaded by dense fibrous tissue from the peristemeum and the deep surface of the paravertebral musculature (19, 20). Fibrous tissue in the epidural space may adhere to the dura mater and nerve roots; this causes a mechanical tethering of the nerve roots or the dura. This mechanical tethering may contribute to chronic low back pain and lower extremity pain following lumbar laminectomy in significant subset of patients. LaRocca and McNab (19) have demonstrated the presence of fibrous connective tissue causing epidural fibrosis into a postoperative hematoma. Fibrosis in the spinal canal may also develop without any surgical intervention as in infection, hematoma, annular tear or intrathecal contrast media (20-22). McCarron et al (20) reported an inflammatory reaction in spinal cord sections taken from dogs sacrificed after an initial injection of homogenized nucleus pulposus. Cooper et al (21) were able to identify peridural fibrosis and vascular abnormalities occurring with herniated intervertebral discs. Parke and Watanabe (22) demonstrated epidural adhesions in...
40% of cadavers with lumbar disc herniation at L4-L5 level, 36% at L5-S1 level and in 16% at L3-L4 level. Perineural fibrosis can interfere with cerebrospinal fluid mediated nutrition, which can render the nerve roots to be hyperesthetic and hypersensitive to compression (11, 23, 24). Ross et al (10), in a study of the relationship between epidural fibrosis and radicular pain, showed that subjects with extensive scarring were 3.2 times more likely to experience radicular pain, as evaluated by magnetic resonance imaging after lumbar laminectomy.

Traditionally, fluoroscopically directed lumbar epidural corticosteroid injections have been used in intervention-related pain management to treat chronic low back pain and lumbar radiculopathy. Philips and Cunningham in 2002 (25) in describing the role of decompressive surgery in managing chronic pain of spinal origin after lumbar surgery, noted that no forms of surgical treatment or adhesion lysis procedure for this diagnosis has proven to be safe and effective.

Percutaneous and endoscopic adhesiolysis have been employed in interventional pain management in management of chronic, refractory low back and lower extremity pain. The purpose of percutaneous epidural lysis of adhesions is to eliminate deleterious effects of scar formation, which can physically prevent direct application of drugs (steroids, hypertonic saline, hyaluronidase) to nerves or other tissues to treat chronic back and extremity pain. The goal of percutaneous lysis of epidural adhesions is to assure delivery of high concentrations of injected drugs to the target areas (1, 26-30). Epidural lysis of adhesions and direct deposition of corticosteroids in the spinal canal are also achieved with a 3-dimensional view provided by epiduroscopy or spinal endoscopy (1, 26-30).

This systematic review was undertaken to determine the evidence pertaining to effectiveness of percutaneous and endoscopic adhesiolysis in the management of chronic low back and lower extremity pain. We sought to answer the following questions:

1. Is percutaneous adhesiolysis an effective treatment?
2. Is percutaneous adhesiolysis superior to epidural steroid injections?
3. Does the addition of hypertonic sodium chloride solution improve outcomes?
4. Does the addition of hyaluronidase improve outcomes?
5. Is percutaneous adhesiolysis a safe procedure?
6. Is spinal endoscopic adhesiolysis an effective treatment?
7. Is spinal endoscopic adhesiolysis superior to percutaneous adhesiolysis?
8. Is spinal endoscopic adhesiolysis a safe procedure?

**METHODS**

**Literature Search**

The strategy utilized for evidence synthesis was comprehensive and included a detailed literature search of EMBASE, MEDLINE (Jan 1966 – Nov 2004), BioMed Central and Cochrane Reviews. All systematic and narrative reviews; all relevant and published peer-reviewed indexed and non-indexed journals; cross-references to the reviews; scientific meeting proceedings, scientific newsletters; various published trials. The search strategy consisted of interventional techniques, lysis of epidural adhesions, percutaneous adhesiolysis, endoscopic adhesiolysis, with

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Table 1. Domains and elements for randomized controlled trials

<table>
<thead>
<tr>
<th>Domain</th>
<th>Elements</th>
</tr>
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<tbody>
<tr>
<td>Study Question</td>
<td>• Clearly focused and appropriate question</td>
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<tr>
<td>Study Population</td>
<td>• Description of study population</td>
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<tr>
<td></td>
<td>• Specific inclusion and exclusion criteria</td>
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<tr>
<td></td>
<td>• Sample size justification</td>
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<tr>
<td>Randomization</td>
<td>• Adequate approach to sequence generation</td>
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<tr>
<td></td>
<td>• Adequate concealment method used</td>
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<td></td>
<td>• Similarity of groups at baseline</td>
</tr>
<tr>
<td>Blinding</td>
<td>• Double-blinding (e.g., of investigators, caregivers, subjects, assessors, and other key study personnel as appropriate) to treatment allocation</td>
</tr>
<tr>
<td>Interventions</td>
<td>• Intervention(s) clearly detailed for all study groups (e.g., dose, route, timing for drugs, and details sufficient for assessment and reproducibility for other types of interventions)</td>
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<tr>
<td></td>
<td>• Compliance with intervention</td>
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<tr>
<td></td>
<td>• Equal treatment of groups except for intervention</td>
</tr>
<tr>
<td>Outcomes</td>
<td>• Primary and secondary outcome measures specified</td>
</tr>
<tr>
<td></td>
<td>• Assessment method standard, valid, and reliable</td>
</tr>
<tr>
<td>Statistical Analysis</td>
<td>• Appropriate analytic techniques that address study withdrawals, loss to follow-up, missing data, and intention to treat</td>
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<tr>
<td></td>
<td>• Power calculation</td>
</tr>
<tr>
<td></td>
<td>• Assessment of confounding</td>
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<td></td>
<td>• Assessment of heterogeneity, if applicable</td>
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<tr>
<td>Results</td>
<td>• Measure of effect for outcomes and appropriate measure of precision</td>
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<td></td>
<td>• Proportion of eligible subjects recruited into study and followed up at each assessment</td>
</tr>
<tr>
<td>Discussion</td>
<td>• Conclusions supported by results with possible biases and limitations taken into consideration</td>
</tr>
<tr>
<td>Funding or Sponsorship</td>
<td>• Type and sources of support for study</td>
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</table>

*Key domains are in italics

*Elements appearing in italics are those with an empirical basis. Elements appearing in bold are those considered essential to give a system a Yes rating for the domain.

†Domain for which a Yes rating required that a majority of elements be considered.

Adapted from ref 31

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emphasis on chronic pain, low back pain and lumbar radicular pain.

Selection Criteria

All randomized clinical trials, observational studies, and abstracts presented in the last 2 years published in English language were considered for inclusion. The population of interest was patients suffering with chronic lumbar and sacral spinal pain with or without lower extremity pain for at least 6 months.

Outcome Measures

The primary outcome measure was percentage of patients with pain relief. The secondary outcome measures were functional or psychological improvement, return to work, and complications. Pain relief was evaluated on a short-term (less than 3 months) and long-term (3 months or longer) basis.

Review Methods

The quality of individual articles was evaluated using the criteria from the Agency for Healthcare Research and Quality (AHRQ) publication (31). Important domains and elements for randomized and non-randomized trials are shown in Tables 1 and 2. For evaluation of randomized trials, criteria described by Cochrane Review Group for musculoskeletal disorders (32) was also utilized (Table 3).

A study was regarded as relevant if at least one of the questions sought to be answered, and at least one of the outcome measures concerned pain intensity, overall improvement, or functional status were evaluated. A study was considered for inclusion only if the methodological score was 50% or more. Randomized trials not meeting the 50% criteria were also considered for inclusion as observational studies.

Inclusion and Exclusion Criteria

Only studies that met an inclusion algorithmic criterion (Figure 1) and criteria as listed in Table 4 were included (33).

Prior Treatment Criteria

The patients should have been tried either one or multiples of non-interventional techniques or should have undergone surgical intervention. Non-interventional techniques must have included exercises, physical therapy with activity improvement, chiropractic management, and drug therapy with non-steroidal anti-inflammatory agents.

For percutaneous adhesiolysis, prior treatments included fluoroscopically directed epidural steroids.

For endoscopic adhesiolysis, prior treatments included fluoroscopically directed epidural steroids and percutaneous adhesiolysis.

Data Extraction

Study evaluation, inclusion and exclusion algorithmic approach is shown in Figure 1 and Table 4. Methodologic quality assessment was performed as described in “review methods” section.

Analysis of Evidence

A qualitative analysis was conducted, using five levels of evidence for effectiveness of adhesiolysis as illustrated in Table 5. Duration of pain relief was considered for both short-term and long-term. Short-term relief was considered as less than 3 months and long-term was considered as 3 months or longer. A study was judged to be positive if the authors concluded that the adhesiolysis was more effective than the reference treatment in randomized trials or simply concluded that it was effective in other studies. All other conclusions were considered negative. If, in the opinion of reviewers, there was conflict with the conclusion, the con-
Table 3. Methodologic quality criteria list (key items of internal validity) of Cochrane Musculoskeletal Review Group

Table 4. Inclusion/exclusion criteria

Our search strategy yielded a total of 236 results. Relevant reports included a total of 11 articles. Of the reports evaluated for lumbar percutaneous adhesiolysis (34-44), there were 4 randomized controlled trials (34-37), and 7 retrospective evaluations (38-44).

Methodological Quality
A study of ventral epidural adhesiolysis (42), an inappropriate procedure (43), a retrospective evaluation of spinal stenosis (40), a publication from non peer-reviewed literature (41), and an abstract (44) published in 1993 were not included due to multiple deficiencies, leading to exclusion due to inability to meet inclusion/exclusion criteria, or inability to meet at least 50% of the methodological quality criteria.

Detailed review of reports revealed the two publications by Heavner et al (34) and Racz et al (35) were of the same study, they were considered as one study (34). Thus, a total of 3 studies by Heavner et al (34), Manchikanti et al (36, 37) were included.

The observational reports included 3 retrospective reports (38-40). Of these 2 were included (38, 39).

Methodological criteria are shown in Tables 6 and 7.

Descriptive Characteristics
All the studies included in the evidence synthesis described the baseline characteristics (34, 36-39). Three randomized trials (34, 36, 37) had similar patient characteristics. Manchikanti et al
(36, 37) also reported proportion of the patients included with history of previous surgery, which ranged from 64% to 72% in all intervention groups. Patients in all 3 studies have failed multiple conservative modalities of treatments including fluoroscopically directed epidural steroid injections.

Among the 2 observational reports included (38, 39), patient demographics were described in both studies. However, the proportion of patients in Group II was 37% compared to 65% in Group I. In addition, in this study (38), patients following work-related injury were also lower in Group II with 30% whereas it was 50% in Group I. Duration of pain was also longer in Group II compared to Group I. Patients in this study in Group I received adhesiolysis and hypertonic saline neurolysis on two consecutive days with catheter in place for the second day. In contrast, Group II patients received a single day procedure with percutaneous adhesiolysis, as well as hypertonic saline neurolysis. In another retrospective evaluation, only patients with post lumbar laminectomy were included (39).

The number of patients also varied with a total of 59 subjects in one study with patients divided into 4 groups of 17, 15, 17, 10 (34) receiving 4 separate types of interventions; a total of 75 patients with 25 patients in each group (36); a total of 45 patients with 15 patients in Group I receiving conservative management, and 30 patients in Group II receiving intervention with percutaneous adhesiolysis and hypertonic saline neurolysis. Among the observational studies, one study compared a 1-day procedure to a 2-day procedure (38), whereas a second study compared percutaneous adhesiolysis to spinal endoscopic adhesiolysis (39).

Heavner et al (34) compared various types of solutions after the adhesiolysis was performed. Group A consisted of patients receiving a combination of hyaluronidase and hypertonic saline, Group B consisted of patients hypertonic sodium chloride solution, Group C consisted of patients receiving isotonic saline solution, whereas, Group D consisted of patients receiving hyaluronidase and isotonic saline solution. Manchikanti et al (36) divided 100 patients randomly into 4 groups, with Group I consisting of a control group without adhesiolysis, with injection of local anesthetic, steroid, and normal saline; Group II consisting of pa-

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**Table 5. Designation of levels of evidence**

<table>
<thead>
<tr>
<th>Level</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>Level I</td>
<td>Conclusive: Research-based evidence with multiple relevant and high-quality scientific studies or consistent reviews of meta-analyses</td>
</tr>
<tr>
<td>Level II</td>
<td>Strong: Research-based evidence from at least one properly designed randomized, controlled trial; or research-based evidence from multiple properly designed studies of smaller size; or multiple low quality trials.</td>
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<tr>
<td>Level III</td>
<td>Moderate:</td>
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<tr>
<td></td>
<td>a) Evidence obtained from well-designed pseudorandomized controlled trials (alternate allocation or some other method);</td>
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<td></td>
<td>b) evidence obtained from comparative studies with concurrent controls and allocation not randomized (cohort studies, case-controlled studies, or interrupted time series with a control group);</td>
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<td>c) evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group.</td>
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<tr>
<td>Level IV</td>
<td>Limited: Evidence from well-designed nonexperimental studies from more than one center or research group; or conflicting evidence with inconsistent findings in multiple trials</td>
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<tr>
<td>Level V</td>
<td>Indeterminate: Opinions of respected authorities, based on clinical evidence, descriptive studies, or reports of expert committees.</td>
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Adapted and modified from ref 1
Table 6. Results of randomized trials of percutaneous adhesiolysis and hypertonic saline neurolysis

<table>
<thead>
<tr>
<th>Study/Methods</th>
<th>Participants</th>
<th>Intervention(s)</th>
<th>Outcome(s)</th>
<th>Result(s)</th>
<th>Conclusion(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manchikanti et al (36)</td>
<td>75 patients</td>
<td>Experimental group:</td>
<td>Timing: 3 months, 6 months</td>
<td>72% of patients in Group III (adhesiolysis and hypertonic saline neurolysis)</td>
<td>Positive short and long term relief</td>
</tr>
<tr>
<td>A randomized, double blind</td>
<td>were evaluated</td>
<td>Adhesiolysis, hypertonic saline neurolysis, steroid and local anesthetic and adhesiolysis, normal saline, and steroid.</td>
<td>and 12 months</td>
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</tr>
<tr>
<td>trial AHRQ criteria 10/10</td>
<td>25 patients</td>
<td>Control group: Catheterization and no adhesiolysis.</td>
<td>Outcome measures: VAS pain scale, Oswestry Disability Index 2.0, work status, opioid intake, range of motion measurements and psychological evaluation by P-3</td>
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</tr>
<tr>
<td>Cochrane review criteria 10/10</td>
<td>in Group I</td>
<td></td>
<td>72% of patients in Group III (adhesiolysis and hypertonic saline neurolysis), 60% of patients in Group II (adhesiolysis only), compared to 0% in Group I (control) showed significant improvement at 12-month follow-up.</td>
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<tr>
<td></td>
<td>served as controls and were with catheterization but no adhesiolysis.</td>
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<td></td>
<td>25 patients</td>
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<td></td>
<td>in Group II</td>
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<td></td>
<td>were treated with catheterization, adhesiolysis, followed by injection of local anesthetic, normal saline, and steroid.</td>
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<td></td>
<td>25 patients</td>
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<td></td>
<td>in Group III</td>
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<tr>
<td></td>
<td>consisted of adhesiolysis followed by injection of local anesthetic, hypertonic saline, and steroid.</td>
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<tr>
<td>Heavner et al (34)</td>
<td>39 patients</td>
<td>Experimental group:</td>
<td>Timing: 4 weeks, 3 months</td>
<td>Initially 83% of the patients showed significant improvement compared to 49% of the patients at 3 months, 43% of the patients at 6 months, and 49% of the patients at 12 months.</td>
<td>Positive short and long term relief</td>
</tr>
<tr>
<td>A randomized, double blind</td>
<td>with chronic intractable low back pain. All the patients failed conservative management, along with fluoroscopically directed epidural steroid injections.</td>
<td></td>
<td>and 12 months</td>
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<tr>
<td>trial AHRQ criteria 7/10</td>
<td>were treated</td>
<td>Group I: hypertonic saline plus hyaluronidase</td>
<td>Outcome measures: Pain relief</td>
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<td></td>
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<tr>
<td>Cochrane review criteria 7/10</td>
<td>with percutaneous epidural adhesiolysis and hypertonic saline neurolysis,</td>
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<tr>
<td>Manchikanti et al (37)</td>
<td>45 patients</td>
<td>Experimental group:</td>
<td>Timing: 1 month, 3 months</td>
<td>Experimental group showed improvement with pain relief in 97% at 3 months, 93% at 6 months, and 47% of the patients at 1 year. Generalized anxiety disorder, somatization disorder, average pain, and functional status improved significantly in Group II.</td>
<td>Positive short and long term relief</td>
</tr>
<tr>
<td>A randomized, controlled trial</td>
<td>were evaluated. 15 patients in group I were treated conservatively; 30 patients in group II were treated with percutaneous epidural adhesiolysis and hypertonic saline neurolysis.</td>
<td></td>
<td>and 12 months</td>
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<tr>
<td>Cochrane review criteria 5/10</td>
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<tr>
<td>AHRQ criteria 6/10</td>
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</table>

Tons undergoing adhesiolysis, with injection of local anesthetic, steroid, and normal saline; and Group III consisting of patients undergoing adhesiolysis, as well as injection of 10% sodium chloride solution, in addition to local anesthetic and steroid. Heavner et al (34) evaluated a procedure lasting for 3 days where the catheter was inserted on the first day and the drugs were injected on the second and third day. Manchikanti et al (34, 37) evaluated one-day adhesiolysis.

Outcome parameters by Heavner et al (34) included short-form McGill Pain Questionnaire and Visual Analog Scale for back pain and leg pain. Manchikanti et al (36) utilized VAS pain scale, Oswestry Disability Index 2.0, work status, opioid intake, range of motion measurement, and psychological evaluation by Pain Patient Profile.

Outcome measures included in the third randomized clinical trial (37) were significant pain relief (≥50%) cumulative pain relief, physical health, mental health, functional status, narcotic intake, psychological status, and return to employment. In the observational reports (38, 39), authors evaluated significant pain relief, cumulative pain relief with multiple procedures, and cost effectiveness.

Manchikanti et al (37), included 45 patients with 15 patients in the control group, who were treated with conservative modalities of treatments, and 30 patients in Group II, who were treated with percutaneous epidural adhesiolysis and hypertonic saline neurolysis.

Both the observational studies (38, 39) evaluated patients with 1-day adhesiolysis and hypertonic saline neurolysis, whereas, one study (38) evaluated patients...
also with a 2-day adhesiolysis.

Randomization was adequate in all 3 studies. Blinding was adequate in 2 studies (34, 36).

Statistical analysis included Fisher’s Exact Test (2-by-2 tables) and the generalized Fisher’s Exact Test (4-by-2 tables) by Heavner et al (34); chi-squared test, Fisher’s Exact Test, student’s t test, paired t test, and intent-to-treat analysis were utilized by Manchikanti et al (36); and chi-squared statistic, student’s t test, and paired t test were utilized by Manchikanti et al (37). Appropriate statistical evaluations were utilized by 2-by-2 chi-squared tests and student’s t test in observational reports (38, 39).

Description of results of published studies of percutaneous adhesiolysis and hypertonic saline neurolysis are shown in Table 6.

**Effectiveness**

Effectiveness was evaluated based on the questions sought to be answered.

1) Is percutaneous adhesiolysis an effective treatment?

All three randomized studies (34, 36, 37) evaluated the effectiveness of percutaneous adhesiolysis. Subsequently 2 retrospective evaluations (38, 39) also evaluated percutaneous adhesiolysis. Heavner et al (34) had no control group. However, they assessed effectiveness of adhesiolysis by means of each patient being their own control, as all the patients failed previously fluoroscopically directed epidural steroid injections, including other conservative modalities of treatments. Manchikanti et al (36) evaluated the role of adhesiolysis, specifically with a control group receiving epidural steroid injection only where the catheter was inserted without adhesiolysis, followed by injection of epidural steroid and local anesthetic injection with sodium chloride solution injection with catheter in place in the sacral region (S2 or S3), with Group II and Group III undergoing adhesiolysis. The third study (37) had no control group and intervention group consisted of adhesiolysis and hypertonic saline neurolysis. All three studies showed positive results for short-term improvement and long-term improvement with adhesiolysis. All three studies showed significant improvement, either over the control group (36, 37), or patients as their own controls (34).

Among the observational reports, both (38, 39) were positive for short-term relief, whereas, only one (39) was positive for long-term relief.

2) Is percutaneous adhesiolysis superior to epidural steroid injections?

Heavner et al (34) and Manchikanti et al (37) demonstrated that percutaneous adhesiolysis was superior to epidural steroid injections and provided both short-term and long-term improvement in managing chronic low back and lower extremity pain. Manchikanti et al (36) evaluated the issue specifically with a control group where patients only received epidural steroid injection in a random and blinded manner. These studies showed the clear superiority of adhesiolysis alone and with hypertonic saline neurolysis, over epidural steroid injections. Other studies (37-39) also reveal evidence of successful pain relief with adhesiolysis with inclusion of patients after failure of fluoroscopically directed epidural steroid injections.

3) Does the addition of hypertonic sodium chloride solution improve outcomes?

Heavner et al (34) evaluated the effect of hypertonic sodium chloride solution and compared it with isotonic sodium chloride solution and hyaluronidase. They noted lack of significant differences among the groups. Manchikanti et al (36) evaluated the effectiveness of adhesiolysis alone or with hypertonic saline injection. In this study, authors demonstrated significant improvement with addition of hypertonic sodium chloride solution following adhesiolysis compared to adhesiolysis alone when they compared only the successful patients. When all the patients, utilizing intent-to-treat analysis was utilized, the differences were not significant.

4) Does the addition of hyaluronidase improve outcomes?

Heavner et al (34) evaluated the effectiveness of hyaluronidase with
comparison to isotonic sodium chloride solution or mixed with hypertonic sodium chloride solution. However, they noted no significant differences among the groups.

5) Is percutaneous adhesiolysis a safe procedure?

Heavner et al (34) reported no adverse effects. Manchikanti et al (36-39) reported one subarachnoid block in Group II of 25 patients in this particular group and 75 patients in the study (36), suspicion of infection in one case (37), subarachnoid blockade in 2% or 5 patients, serious infection in one patient with development of an abscess, suspicion of infection in 2% of the patients or 4 cases in a retrospective evaluation (38); subarachnoid puncture in 4 out of 178 procedures, infection in one of 178 procedures and suspicion of infection in 8 of 178 procedures (39). Manchikanti et al (37-39) also reported minor complications such as rash, itching, etc. However, none of the studies have reported any incidents of arachnoiditis, paralysis, weakness, bladder disturbances, or other serious complications.

Level of Evidence

All randomized trials (34, 36, 37) showed positive short-term and long-term relief. Of the two retrospective evaluations, both (38, 39) showed short-term improvement, whereas long-term improvement was seen only in one study (39). The level of evidence was designated as described in Table 5. Based on this illustration there was research-based evidence from three properly designed randomized controlled trials. Strong or level 2 evidence consisted of research-based evidence from at least one properly designed randomized, controlled trial; or research-based evidence from multiple properly designed studies of smaller size; or multiple low quality trials.

The evidence for percutaneous adhesiolysis is strong for short-term and long-term relief with repeat interventions, in chronic refractory low back and lower extremity pain secondary to post lumbar laminectomy syndrome or lumbar epidural fibrosis. The evidence for percutaneous adhesiolysis as a better treatment than epidural steroid injections is also strong for short-term and long-term improvement. However, the evidence for addition of hypertonic sodium chloride solution providing better outcomes, is moderate for short-term and long-term improvement. Finally, the evidence for improved outcomes following addition of hyaluronidase is negative.

Spinal Endoscopic Adhesiolysis

Our search strategy yielded a total of 112 articles. Relevant reports studying spinal endoscopic adhesiolysis were eight. Two randomized, double blind evaluations (45, 46), 3 prospective evaluations (47-49), and 3 retrospective evaluations (39, 50, 51), and multiple case reports were available for review.

Methodological Quality

Of the two randomized, double-blind evaluations one of them was a preliminary report (45), whereas the second study (46) described one year follow-up. Hence, they were considered as a single randomized double-blind trial (46).

The 3 of 3 prospective evaluations, met the criteria for inclusion (47-49). Among the retrospective evaluations, two reports (39, 50) were included as they met the inclusion criteria. One report (51) due to insufficient data and failure to meet inclusion criteria was excluded. Table 8 shows details of studies included.

Descriptive Characteristics

Demographic characteristics were described in all the studies. There were no significant differences noted in any of the studies among the demographic characteristics. Patients with previous surgery were 73% in Group I and 84% in Group II in the study by Manchikanti et al (46). Igarashi et al (48) evaluated patients with spinal stenosis. All other studies included post lumbar laminectomy patients, whereas, one retrospective evaluation (39) included only post lumbar laminectomy patients who also have failed percutaneous adhesiolysis.

Inclusion criteria was uniform across all the reports with failure to respond to conservative modalities of treatments, as well as fluoroscopically directed epidural steroid injections. Manchikanti et al (39, 46, 50) used inclusion criteria as of patients to have failed percutaneous adhesiolysis prior to performing spinal endoscopic adhesiolysis. Manchikanti et al (46) also identified proportion of patients with epidural fibrosis as 73% in Group I receiving epidural steroid injection and 84% in Group II undergoing spinal endoscopic adhesiolysis.

Interventions included spinal endoscopic adhesiolysis with administration of local anesthetic and steroids in all the studies. In the randomized, double-blind trial by Manchikanti et al (46), the control group received advancement of the scope into sacral region (S2 or S3) followed by injection of steroid and local anesthetic, whereas, intervention group received spinal endoscopic adhesiolysis in the target area along with targeted delivery of local anesthetic and steroids.

Outcomes included Visual Analogue Scale, Oswestry Disability Index 2.0, range of motion evaluation, psychological evaluation by Pain Patient Profile, opioid intake, and return to work by Manchikanti et al (46); whereas, pain relief was the major outcome measurement in all the other reports. Geurts et al (47) also measured changes in employment status. Further, they utilized an independent evaluator.

Statistical methods included student’s “t” test, chi-squared test, Fisher’s Exact Test, paired “t” test, and Wilcoxon Signed-Rank Test (46); Man-Whitney-U tests (48); paired “t” tests and an adapted last-observation-carried-forward (LOCF) analysis (47); and 2 x 2 chi-squared test and student “t” test (39).

Effectiveness

The randomized trial (46) showed significant improvement in pain relief, as well as multiple other parameters including return to work at 3 months, 6 months, and 1 year. The prospective evaluations (47-49) also showed improvement. Both the retrospective evaluations (39, 50) included in the analysis showed positive short-term and long-term results. Details of the included studies are illustrated in Table 8.

Safety

Complications of endoscopic adhesiolysis were described as one subarachnoid puncture and block in endoscopy group (46) of 50 patients; post dural puncture headache in 3 of 21 patients (47); no deterioration of motor or sensory deficits (48); subarachnoid puncture of 7 of 77 procedures; suspicion of infection in 8 of 77 procedures (39); subarachnoid puncture in 8 of 112 procedures; infection in 2 of 112 procedures; and suspected infection in 6 of 112 patients (50). Minor complications such as rash, itching, in-
Table 8. Description of randomized and observational studies of spinal endoscopy

<table>
<thead>
<tr>
<th>Study/Methods</th>
<th>Participants</th>
<th>Intervention(s)</th>
<th>Outcome(s)</th>
<th>Result(s)</th>
<th>Conclusion(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manchikanti et al (46)</td>
<td>A prospective, randomized, double-blind trial</td>
<td>A total of 83 patients were evaluated, with 33 patients in Group I and 50 patients in Group II. Group I served as the control with endoscopy into the sacral canal without adhesiolysis, followed by injection of local anesthetic and steroid. Group II consisted of spinal endoscopic adhesiolysis, followed by injection of local anesthetic and steroid. 73% of the patients in Group I and 84% of the patients in Group II were of post lumbar laminectomy syndrome and had MRI evidence of epidural fibrosis.</td>
<td>In Group I, guide wire and a 0.8 mm fiberoptic spinal endoscopic video guided system was introduced and advanced until the tip was positioned S3. Injections included 10 ml of 1% lidocaine and 6 mg to 12 mg of Celestone or 40 mg to 80 mg of methylprednisolone. In Group II, spinal endoscopy was advanced to the level of suspected pathology. Adhesiolysis was carried out. Injections included 10 ml of lidocaine 1%, preservative free, mixed with 6 mg to 12 mg of betamethasone acetate or 40 mg to 80 mg of methylprednisolone.</td>
<td>Timing: 1 month, 3 months, 6 months, and 12 months</td>
<td>Intention to treat analysis was performed. Among the 50 patients in the treatment group with spinal endoscopic adhesiolysis 80% at 3 months, 56% at 6 months, and 48% at 12 months showed significant improvement without adverse events. In control group improvement was noted only at one month. Group II patients showed improvement in Oswestry Disability Scores, psychological status, reduced opioid intake, and increased employment.</td>
</tr>
<tr>
<td>Igarashi et al (48)</td>
<td>A retrospective</td>
<td>58 patients with degenerative lumbar spinal stenosis divided into monosegmental (34) and multisegmental (24) groups.</td>
<td>Epiduroscopy including adhesiolysis by injection of saline, and injection of steroids/local anesthetics.</td>
<td>Timing: up to 12 months</td>
<td>Outcome measures: Pain relief by visual analog scale Significant pain relief 50% or greater Oswestry Disability Index 2.0 Work status Opioid intake Range of motion measurement Psychological evaluation Return to work</td>
</tr>
<tr>
<td>Geurts et al (47)</td>
<td>A prospective observational study</td>
<td>20 chronic low back pain patients, the majority of them with post lumbar laminectomy syndrome failing to respond to other modalities of treatments.</td>
<td>Epiduroscopy with adhesiolysis and target delivery of 120 mg of methylprednisolone acetate, 600 IU of hyaluronidase, and 150 mcg of Clonidine.</td>
<td>Timing: 3, 6, 9 and 12 months.</td>
<td>Outcome measures: Adhesiolysis and pain relief</td>
</tr>
<tr>
<td>Richardson et al (49)</td>
<td>A prospective case series</td>
<td>34 patients suffering with chronic, severe low back pain with 50% of the patients having failed back surgery syndrome.</td>
<td>Epidural adhesiolysis and target delivery of steroid. Adhesiolysis followed by injection of bupivacaine, Depo-Medrol, and Clonidine.</td>
<td>Timing: 1, 2, 6, and 12 months</td>
<td>Outcome measures: Pain relief</td>
</tr>
<tr>
<td>Manchikanti et al (39)</td>
<td>A retrospective evaluation in post lumbar laminectomy syndrome</td>
<td>60 patients with post lumbar laminectomy syndrome</td>
<td>Spinal endoscopy with targeted delivery of steroid.</td>
<td>Timing: 1, 3, 6, and 12 months</td>
<td>Outcome measures: Pain relief</td>
</tr>
<tr>
<td>Manchikanti et al (50)</td>
<td>A retrospective evaluation of spinal endoscopy</td>
<td>85 consecutive patients underwent 112 epidural endoscopic procedures.</td>
<td>Spinal endoscopy with targeted delivery of steroid.</td>
<td>Timing: 1, 3, 6, and 12 months</td>
<td>Outcome measures: Pain relief</td>
</tr>
</tbody>
</table>
creased discomfort, and neck pain were reported in some studies.

Level of Evidence

One randomized trial (46), 3 prospective trials (47-49) and 2 retrospective evaluations (39, 50) showed positive short-term and long-term results. The evidence synthesis for spinal endoscopy showed strong evidence for short-term relief and moderate evidence for long-term improvement. The evidence of effectiveness of spinal endoscopic adhesiolysis compared to epidural steroid injections is strong for short-term and long-term improvement. The evidence of spinal endoscopic adhesiolysis in patients after they have failed percutaneous adhesiolysis is strong. The evidence of effectiveness of spinal endoscopic adhesiolysis in lumbar spinal stenosis is moderate for short-term and limited for long-term improvement.

Complications

Our search strategy yielded a total of 358 articles. Only some relevant articles are included here. The complications related to percutaneous adhesiolysis and spinal endoscopy in the included reports are described in the results section.

The most common and worrisome complications of adhesiolysis and spinal endoscopy with lysis of adhesions are related to dural puncture, spinal cord compression, catheter shearing, intravascular injection, vascular injury, cerebral vascular or pulmonary embolus, infection, steroids, hypertonic saline, hyalurondase, instrumentation with endoscope, and administration of high volumes of fluids potentially resulting in excessive epidural hydrostatic pressures, death and brain damage (26-30, 34-101). This may cause spinal cord compression, excessive intraspinal and intracranial pressures, epidural hematoma, bleeding, infection, increased intracranial pressures with resultant visual deficiencies, and even blindness and dural puncture. Unintended subarachnoid or subdural puncture with injection of local anesthetic or hypertonic saline is one of the major complications of the procedure with catheter adhesiolysis. Hypertonic saline injected into the subarachnoid space has been reported to cause cardiac arrhythmias, myelopathy, paralysis, and loss of sphincter control (27, 34, 52). One report attributed arachnoiditis following epidural adhesiolysis with hypertonic saline, due to subarachnoid leakage of hypertonic saline (72). However, there were multiple variations in the technique and injection of hypertonic saline, (intrathecally or injecting in spite of subarachnoid blockade), which may be responsible for these complications. While there are multiple reports with experience of hypertonic saline solution, there are no controlled reports of potential adverse effects (26, 27, 34-42, 44). Another specific complication of percutaneous epidural adhesiolysis is related to catheter shearing and its retention in the epidural space (78). Additionally, a troublesome complication is that of excessive intraspinal pressure development with its potential to affect both local and distant profusion, and resulting in visual changes and even blindness. Even though the incidence is rare, it appears that this would be much higher with spinal endoscopic procedures with a combination of high volumes of fluid and generation of high hydrostatic pressures (79). It is also possible with catheter based adhesiolysis if excessive amounts of fluids are injected rapidly. Spinal cord trauma or spinal cord or epidural hematoma formation is a catastrophic complication possible with both catheter based or endoscopic adhesiolysis; however, more so with endoscopic adhesiolysis. But, there are no such case reports in the literature. Understanding fluoroscopic imaging is crucial to avoid significant complications (80).

Discussion

The literature identified in this systematic review clearly documents the role of epidural adhesions as a cause of many chronic pain disease states of the spine. It is not surprising that methods to disrupt the scarring can lead to improved outcomes particularly when this change in the anatomical relationships leads to improved access to the neural elements for depositing drugs. This access can be provided by adhesiolysis of the epidural space by the percutaneous route or by spinal endoscopic visualization. These methods are interventional pain management techniques that have a role in the treatment paradigm of the physician treating interventional pain.

In reviewing the studies in this review that have met the stringent criteria set forth by the authors, it appears that current techniques are valuable in cases of epidural scarring, resulting in chronic pain problems. The results must be looked at somewhat cautiously because of the variability in physician technique and procedural ability. More extensive work is needed to determine the characteristics of patients who may have the best outcomes with these techniques.

This systematic review provided strong evidence describing the role of percutaneous adhesiolysis, moderate evidence for injection of hypertonic sodium chloride solution, and negative evidence for injection of hyaluronidase in managing chronic, refractory, low back pain and radicular pain. This systematic review also showed moderate to strong evidence to indicate effectiveness of spinal endoscopic adhesiolysis in managing chronic, refractory, low back and lower extremity pain. This study showed limited to moderate evidence in managing lumbar spinal stenosis with spinal endoscopic adhesiolysis. However, this study showed no evidence of effectiveness of hyaluronidase. In addition, this study showed, percutaneous adhesiolysis and spinal endoscopic adhesiolysis are clearly superior to fluoroscopically directed epidural steroid injections. Further, this also demonstrates review modalities of an effective management of chronic, refractory low back and lower extremity pain, specifically secondary to post lumbar laminectomy syndrome and epidural fibrosis.

This systematic review with stringent inclusion and exclusion criteria as well as methodological quality, demonstrated that the technique of adhesiolysis overcomes the obstacle of being able to get various medications to a lesion specific site by placing the tip of a soft spring catheter within the scar or tip of the fiberoptic endoscope by opening the perineural space. Thus, the steroid and other solutions reach the appropriate site and provide anti-inflammatory effect, and neural blockade. This systematic evaluation showed three appropriately performed randomized trials (34, 36, 37) of percutaneous adhesiolysis, and one well performed, randomized, double-blind trial of spinal endoscopic adhesiolysis (46). Further there were multiple prospective and retrospective evaluations. Majority of the studies met the stringent inclusion criteria and also methodological criteria. Majority of the publications showed positive short-term (less than 3 months) and long-term (3 months or longer) improvement in pain status and multiple other parameters. The variations in results may be ex-
plained on various factors including technical expertise and the drugs injected.

The methodological quality and number of patients included in the studies may be criticized in the randomized trials of percutaneous adhesiolysis. Heavern et al (34) included 59 patients with chronic intractable low back pain. All the patients failed conservative management, along with fluoroscopically directed epidural steroid injections. Consequently these authors studied effect of isotonic saline, hypertonic saline plus hyaluronidase, and finally isotonic saline plus hyaluronidase. The patients functioned as their own controls for the purposes of adhesiolysis. They measured various outcomes at 4 weeks, 3 months, 6 months and 12 months. Their outcome measures included pain relief by visual analog scale. Of the 83 patients 24 patients were removed from the study before the injection series was completed. In addition authors also have not performed intention-to-treat analysis. The results showed, 49% of the patients with significant improvement at 3 months, 43% at 6 months, and 49% at 12 months. However the study has been misinterpreted in the past due to lack of differences between various groups (102, 103). In this study (34), all the patients prior to being enrolled in the randomized, double-blind study failed to respond to many types of conservative modalities of treatment including fluoroscopically directed epidural steroid injections. Thus, this study provided evidence for effectiveness of adhesiolysis, but not for injection of hypertonic saline or hyaluronidase.

The second randomized trial of percutaneous adhesiolysis by Manchikanti et al (36) evaluated one day lumbar epidural adhesiolysis and hypertonic saline neuromyelisation in treatment of chronic low back pain with randomized, double-blind design. These authors studied a total of 75 patients with 25 patients in each group with 3 types of interventions. Group I served as controls with catheterization without adhesiolysis, followed by injection of local anesthetic, normal saline, and steroid. Group II consisted of catheterization and adhesiolysis followed by injection of local anesthetic, normal saline, and steroid. Group III consisted of adhesiolysis followed by injection of local anesthetic, hypertonic saline, and steroid. These authors also incorporated statistical analysis which included intention-to-treat analysis. They included extensive outcome measures with visual analog pain scores, Oswestry Disability Index, work status, opioid intake, range of motion measurement, and psychological status. They defined significant pain relief as average relief of 50% or greater. Their results showed that significant improvement was seen in patients in Group II and Group III at 3 months, 6 months and 12 months, compared to baseline measurements, as well as compared to Group I without adhesiolysis. In this study, 72% of patients in Group III with adhesiolysis and hypertonic saline neurolysis 60% of patients in Group II with adhesiolysis only compared to 0% in Group I without adhesiolysis however with steroid injection showed significant improvement at 12 month follow-up. These authors also showed that the average number of treatments for one year were 2.76 in Group II and 2.16 in Group III. Duration of significant relief with the first procedure was 2.8 ± 1.9 months in Group II and 3.8 ± 3.37 months in Group III. Consequently, authors of this review concur with the authors of the study which concluded that percutaneous adhesiolysis, with or without hypertonic saline neurolysis is an effective treatment for chronic low back pain.

The third randomized trial by Manchikanti et al (37) also showed positive results. In this study, forty-five patients were randomly assigned, with fifteen patients in the control group, or Group I, who were treated with conservative modalities of treatments, including medication, physical therapy, and an exercise program; and, thirty patients in Group II, who were treated with percutaneous epidural adhesiolysis and hypertonic saline neurolysis. The results of this study showed that cumulative relief, defined as relief greater than 50% with one to three injections, in the treatment group was 97% at 3 months, 93% at 6 months, and 47% at 1 year. They also demonstrated improvement in multiple parameters and cost-effectiveness of adhesiolysis.

Further, 2 of the 3 retrospective evaluations showed positive results for long-term improvement. Consequently the evidence is strong for short-term and long-term improvement in patients with chronic refractory lower extremity pain with percutaneous adhesiolysis.

For spinal endoscopic adhesiolysis, one randomized, double-blind evaluation (46) provided strong evidence for short-term improvement and moderate evidence for long-term improvement. This prospective, randomized, double-blind trial (46) was conducted to determine the outcome of spinal endoscopic adhesiolysis to reduce pain and improve function and psychological status in patients with chronic refractory low back and lower extremity pain. Authors evaluated a total of 83 patients, with 33 patients in Group I and 50 patients in Group II. Group I served as the control with endoscope advanced to S1 or S2, without adhesiolysis followed by injection of local anesthetic and steroid. Group II consisted of spinal endoscopic adhesiolysis, followed by injection of local anesthetic and steroid. The results demonstrated significant improvement without adverse events in 80% of the patients at 3 months, 56% at 6 months and 48% at 12 months among the 50 patients in the treatment group. In contrast, control group failed to provide any significant improvement. These authors also showed that the average significant relief was 0.7 ± 0.73 months in the control group, whereas it was 7.6 ± 4.7 months in the spinal endoscopy group. Significant improvements were seen in functional status as evaluated by Oswestry Disability Index, range of motion evaluation, psychological outcomes of depression, anxiety, and somatization, opioid intake with reduction in dosages, and finally return to employment.

In prospective trials of spinal endoscopic adhesiolysis, Igarashi et al (48) showed its effectiveness on low back and lower extremity pain specifically in patients with mono-segmental spinal stenosis, whereas multiple other authors also have shown consistently positive short-term and long-term relief.

Even though there is a possibility of severe complications, reported complications were rare. Thus, moderate to strong evidence exists in favor of adhesiolysis as an interventional pain management technique, in managing chronic low back and lower extremity pain, refractory to conservative modalities of treatments including interventional techniques.

In current clinical practice spinal endoscopic fiberoptics allows for nerve root visualization, however this view is often hindered by haziness or scope fogging. Advancement of this technology to match that seen in laparoscopic abdominal would be very helpful in improving outcomes. Additional technological advanc-
es would assist in reducing complications such as stroke, retinal bleeding and blindness. Additional advances are needed to reduce the incidence of dural leakage and nerve root injury. These changes could be achieved with improved visualization and improved catheter maneuverability and material. One of the major drawbacks of this review includes our inability to find diverse studies meeting inclusion criteria. The majority have been conducted by one or two groups of investigators. Thus, replication of these studies is essential.

A registry of patients undergoing these techniques could be beneficial in following long-term outcomes. In the studies we have noted in this review, three months is considered a good long-term outcome, but we do not find a credible amount of evidence based research to suggest the results of these patients over time in regard for the need of repeat procedures and additional spinal surgery.

CONCLUSION

Both percutaneous and spinal endoscopy assisted adhesiolysis appear to have reasonable basis for utilization based on a summary of the evidence. Based on the present systematic review there is strong evidence for percutaneous adhesiolysis and moderate to strong evidence for spinal endoscopic adhesiolysis in managing chronic refractory low back and lower extremity pain specifically of post-lumbar laminectomy origin with epidural fibrosis.

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