



Management of Pyogenic Spinal Infection, review of literature

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ABSTRACT

Objective: To evaluate the available evidence for the management of Pyogenic Spinal Infection (PSI).

Methods and results: A comprehensive search for the relevant literature published between 1990 and 2018 to evaluate the management of PSI was conducted.

Nonoperative management of carefully selected patients for an adequate duration of antibiotics can result in satisfactory outcomes with low recurrence rate. When there is an indication for surgery, posterior approach, with or without debridement of infected tissue reported to be associated with good outcomes.

Conclusion: Studies with larger sample sizes and longer duration of follow up are recommended to formulate more comprehensive evidence.

1. Introduction

Pyogenic Spinal Infection (PSI) is a rare, serious condition, and recent literature has suggested high rates of morbidity and mortality.^{1,2} PSI includes a wide spectrum of conditions, such as discitis, vertebral osteomyelitis, both discitis and vertebral osteomyelitis (spondylodiscitis), or Spinal Epidural Abscess (SEA).^{3,4} The annual incidence of PSI ranges from 0.5 to 2.2/100,000 people, and the infection commonly tends to affect elderly or chronically ill patients.^{1,5} However, in the past few decades, there has been an increase in the incidence of PSI⁶ attributed to an advancing population and increased numbers of immunocompromised patients.^{7,8}

Staphylococcus aureus is the most common causative micro-organism identified.⁹ Others include gram positive cocci such as; *Streptococcus viridans* or *Staphylococcus epidermis*, or gram negative bacteria such as; *Echerichia coli*.^{3,10} The most common site for spinal infection is the lumbar spine, followed by thoracic spine, cervical spine, and to a lesser extent sacral spine.⁴

Back or neck pain, which can be continuous and unremitting is the most common presentation of patients with PSI. Other symptoms include fever, chills, loss of weight, malaise or neurological symptoms.⁴ Delayed diagnosis can occur up to 3 months because of the non-specific initial symptoms, especially when pain and/or fever are the only presenting symptoms.^{11,12} Literature suggests that early diagnosis of PSI allows for early commencement of treatment, more effective response

and better prognosis.^{4,13}

PSI can be managed either by nonoperative measures, including intravenous or oral antibiotics and other supportive non-pharmacological measures, such as immobilisation/bracing or by surgical intervention.¹⁴ In general, conservative management can be considered when there is no indication for surgical intervention.¹² However, if there is any indication for surgery, or if conservative management has failed to control or eradicate the infection, then surgical intervention may be required.¹⁵

2. Method and results

A comprehensive search for the most relevant literature was performed using the following key words: spine, infection, management, surgery, posterior, spondylitis, discitis, spondylodiscitis, osteomyelitis and epidural abscess. The search for the relevant literature was performed using these search engines: PubMed, ScienceDirect, Ovid, Springer and Google Scholar. The search included the relevant studies published between 1990 and 2019 for the management of PSI.

With this search strategy, 58 studies were identified, 1 was randomised controlled trial, 5 of them were literature reviews, 49 were a retrospective cohort, and one was a prospective cohort study, and 2 were case reports.

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3. Literature review

3.1. Patients' presentations and pathology description

3.1.1. Presenting symptoms

The onset of symptoms in patients with PSI is usually insidious. Non-specific symptoms may cause a delay in the diagnosis and treatment.¹⁶ According to Arnold et al. 1997¹⁷ 94% of the patients with PSI included in their study presented initially with a site specific back pain, which was the most common presenting symptom. Lower limb weakness was a presenting problem in 84.9% in this series. Importantly, the mean time from the onset of symptoms till initiation of treatment was around 1 month, which reflected the difficulty in reaching early diagnosis, due to the non-specificity of the initial symptoms. More than 10 years later, Luzzati et al. 2009¹⁸ reported similar results regarding the occurrence of back or neck pain as a presenting symptom in patients with PSI. However, Luzzati et al. 2009¹⁸ stated that the rate of neurological deficit as a presenting symptom was only 7%, which is much lower than the rates reported by Arnold et al. 1997.¹⁷ In addition to that, Luzzati et al. 2009¹⁸ reported that fever (core body temperature > 37.5 °C) was a presenting sign in 96% of patients. Arnold et al. 1997¹⁷ did not mention whether fever was present or not in their patient sample. However, sample size could be considered as the main limitation in the previous two studies (33 and 55 patients, respectively). More recently, Patel et al. 2014¹⁹ conducted a study with a larger sample size (128 patients). All the included patients presented with back or neck pain. Neurological deficit was still a problem in 47% of the patients, while fever was reported in 50% of them. Overall, pain is a major feature of presentation therefore it is very important to keep a high index of suspicion of spinal infection when assessing an elderly or chronically ill patient presenting with back or neck pain.¹

3.1.2. Pathology location

PSI has a natural predilection to affect one specific area in the spine more than others.²⁰ According to Arnold et al., 1997¹⁷, the infection affected the lumbar spine in 52% of patients, while the thoracolumbar junction and the thoracic spine were affected in 27.8% and 21.2% of patients, respectively. Relatively similar results were reported by Hadjipavlou et al. 2000.³ Neurological deficit was more common in patients with cervical spine infection (15%) and thoracic spine infection (19%) than in patients with lumbar spine infection (9%).¹²

3.1.3. Causative micro-organisms

Arnold et al. 1997¹⁷ reported the operative tissue sample culture was positive in 15 patients (45%) with *Staphylococcus aureus* the most common causative micro-organism, isolated in 47% of the positive specimens. Similarly, McHenry et al. 2002²¹ reported *Staphylococcus aureus* as the most common causative microorganism isolated in 50% of their positive samples. The second most common pathogen was gram negative bacilli (mainly *Escherichia coli*). Relatively similar results were reported by Mann et al. 2004²² who performed a retrospective study which included 24 patients with PSI. Pathological sample culture was positive in 58% of patients, and *Staphylococcus aureus* was the most common causative micro-organism which was cultured in 33% of the cases. Other gram-positive cocci were isolated in 15% of the patients, while gram negative *Escherichia coli* was detected in only one patient (4%).

3.1.4. Co-morbidities

PSI usually tends to affect people with predisposing factors or with an extra-spinal focus of infection.⁸ Suspected extra-spinal source of infection seeding to the spine was detected in 33% of the patients with PSI who were included in one retrospective study.¹⁷ These focuses of infection were mainly cutaneous, pulmonary or renal infections. In addition to a third of the cohort having more than one site of infection, 47% of the study participants had at least one comorbidity. A history of

intravenous drug use or diabetes mellitus (DM) were the most common accounting for 42% of these. 6% of patients were on immunosuppressive therapy and 3% had a history of previous trauma to the spine. In support of these findings, Robinson et al. 2008² reported that 50% of the patients in their study were diagnosed with a different primary focus of infection. The study also concluded that end-stage renal failure and type 1 (insulin dependent) DM were additional comorbidities in 23% of the patients. Similar results were observed by Hempelmann et al. 2010²³, reporting that extra-spinal sources of infection were identified in 67% of the patients with skin infections being the most common (22%), followed by renal infections (11%). Also, all patients suffered with one (or more) comorbidities. Once again, the most common of these was DM (72%).

3.2. Conservative management of PSI

Traditionally, conservative management of PSI involved intravenous antibiotics with prolonged immobilisation (by bed rest or by using braces).²⁴ Conservative management can be considered in patients with PSI if there is no neurological deficit, no major instability or deformity, and there is no abscess or collection in the spine.¹ The antibiotic treatment should be guided by an accurate microbiological diagnosis (through obtaining infected tissue culture and/or blood culture) and by microbiologist advice.¹ During conservative management, the clinical and radiological state of the patients should be observed closely to monitor progress, and to detect the development of any possible complications of the infection as detailed above that may require surgical intervention.^{4,8}

The effectiveness of antibiotic therapy in the management of PSI was examined through a retrospective study conducted by Carragee 1997.²⁵ 72 patients were eligible for conservative management and had no indication for surgery. Conservative management of PSI was effective for the management of PSI in this carefully selected cohort. It is worth mentioning that the authors reported: the outcomes of conservative management can be affected by the patients' age, co-morbidities (such as DM) and Erythrocytes Sedimentation Rate (ESR) readings during the first month of treatment. Long-term outcomes were better in patients who were younger than 65 years old, in patients who had no co-morbidities and those who had more than 25% reduction in their ESR values during the first month of treatment. However, despite the clear methodology and clear inclusion and exclusion criteria of the study conducted by Carragee 1997²⁵, the age of the study may limit its utilisation whilst making a decision regarding effectiveness of antibiotics for the management of PSI.

A more recent retrospective study had added more evidence. Nasto et al. 2014¹ reported that in 15 patients who were eligible for conservative treatment, a total of 12 weeks of antibiotics (6–8 weeks parenteral antibiotics, followed by 4–6 weeks oral antibiotics) combined with brace immobilisation were effective and resulted in infection resolution in all of them. When this was compared to the 12 patients (in the same study) who were treated with surgery, although early outcomes were relatively similar, surgical management resulted in better pain improvement and better quality of life at three months of follow-up. However, the limitation of this study is its small sample size. Nonetheless, many of the studies that have assessed the management of PSI are of small sample sizes, which is somewhat inevitable when considering the rarity of cases of PSI. Patients were only followed-up for only 9 months, potentially an inadequate time to evaluate the long-term outcomes of treatment. Finally, it is not clear whether patients with a previous history of spinal pathology or surgery were excluded from the study, for example, post-surgical spinal infection may have different pathophysiology compared with de novo (first time) spinal infection.

An area of debate within the literature is the duration of antibiotic therapy. Jensen²⁶ et al., 1998 conducted a retrospective study to assess the management of PSI caused by *Staphylococcus aureus*. The results demonstrated that antibiotic therapy of less than 8 weeks may be

associated with a high recurrence rate (10%) during a mean follow-up period of 18 days after treatment cessation. The large patient sample (133 patients) enhances the validity of the study. However, given the fact that the causative micro-organism was *Staphylococcus aureus* in all patients, this may affect the study reliability when treating PSI as a whole. As, although *Staphylococcus aureus* was reported (in the literature) to be the most common causative micro-organism, other micro-organisms have been reported to cause PSI, and these micro-organisms may be more or less virulent than *Staphylococcus aureus*. Consequently, this study could be considered as good evidence to guide the duration of conservative management of PSI caused by *Staphylococcus aureus*, however, for other micro-organisms, this may not be the case.

Contrary to Jensen's findings, Roblot et al. 2007²⁷ conducted a retrospective study concluding that there was no significant difference in the risk of relapse between patients who were managed with ≤ 6 weeks of antibiotics, and those who were managed for > 6 weeks. The best available evidence on this however may come from the literature review conducted by Grados et al. 2007.²⁸ Their literature review provides good quality evidence compared to the retrospective studies, case reports or expert opinions alone. They suggested that a total duration of antibiotics of 12 weeks can decrease the risk of recurrence down from the 10% found with 8 weeks of antibiotics in Jensen's study to 3.9%. A very recent randomised controlled trial conducted by Li et al. 2019²⁹ suggested that oral antibiotics were not inferior to Intravenous antibiotics for the management of bone and joint infections if treatment started within 6 weeks of infection onset.

A note on conservative treatment in the presence of contraindications; Patel et al. 2014¹⁹ reported that, in the presence of SEA, conservative management was reported to be associated with a high risk of failure. The results showed that around 40% of patients who were managed with antibiotics failed conservative treatment and required late surgery. Treatment failure was defined as the worsening of the neurological state (measured by the American Spinal Injury Association "ASIA" score), or pain progression.

3.3. Surgical management

Surgery is generally indicated in cases of failed conservative treatment, when disease progression occurs in spite of adequate antibiotic treatment and in the presence of SEA, neurological dysfunction or spinal instability.³⁰ There are many surgical techniques that have been described in the literature regarding the surgical management of PSI with the majority of them involving debridement of the infected area with or without structural reconstruction.³¹ The approaches include a posterior approach, anterior approach, combined posterior and anterior approach, and lateral approach.³²

Fayazi et al. 2004³³ outlines the use of a combined anterior and posterior approach to assess the effectiveness of staged anterior debridement with a titanium mesh cage reconstruction followed by delayed posterior stabilisation in the management of active PSI. 11 patients with PSI of the thoraco-lumbar spine were managed with a two stage surgery. After a follow-up period of around 2 years, seven patients (64%) recovered completely and were pain free. Some pain was reported in 3 patients (27%), and one of them developed pseudo-arthrosis. One patient (9%) died during a revision surgery performed for hardware failure. Post-operative complications were reported in around 64% of the patients, including common iliac vein tear, upper respiratory airway problems, wound problems and deep venous thrombosis of the external jugular vein. The main limitation of this study was the small sample size. The authors did not comment whether the operations were performed by the same surgeon or by different surgeons. This is important as different surgeons may adopt different surgical techniques and will have different experience levels which could potentially introduce bias to the study.

There is debate within the literature with regard to whether staged surgery increases the risk of complications or poor outcomes for the

patient. One of the main disadvantages stated by Fayazi et al. 2004³³, is exposure to more analgesia, longer operative time and hospital stay increasing the risk of complications in debilitated or elderly patients.

Another factor for consideration is the approach used for surgical intervention. Arnold et al. 1997¹⁷ reported on combined anterior and posterior approach in the surgical management of PSI, this combined approach was not un-associated with increased morbidity and mortality. Despite being useful to allow easier access to the anterior column in patients with extensive infection, anterior access is associated with more complications compared to posterior access. Klöckner & Valencia 2003³⁴ stated that anterior access was associated with post-operative complications (mainly respiratory) in around 10% of patients. A recent study by Von Der Hoeh et al. 2018³⁵ compared the clinical, radiological and functional outcomes of surgical management of PSI using a two stage anterior and posterior approach (22 patients) to a single stage posterior approach surgery (25 patients). At the final follow up there was no significant difference in pain, quality of life or radiological outcomes. However, this study included only patients with single level PSI affecting thoracic spine only, thus, it may not be a good evidence to guide the management of PSI, as PSI most commonly affects Lumbar spine and can affect multiple levels.^{3,12,17}

Hempelmann et al. 2010²³ conducted a study to assess the outcome of posterior surgery only as management for PSI in patients who failed conservative management. Surgery included microsurgical debridement of the infected tissue concomitant with inter-body fusion using iliac crest bone graft, and posterior stabilisation. 18 patients were included in the study, however only 12 patients were available for long-term (1 year) follow-up. At the end of follow-up, 12 patients were cured of infection and their laboratory markers were normalised. Pain improved in 11 patients out of the 12 who were followed up. Neurological state improved in 5 out of 7 patients who had neurological symptoms before surgery. Three patients died during the follow-up time due to conditions unrelated to surgery. Surgery related morbidities were reported in 9 (50%) patients. Three patients had problems with the graft and 3 patients died because of multi-organ failure, pneumonia and endocarditis. As a result, the authors concluded that this treatment technique should not be considered as the first management option in the elderly, or high-risk patients with multiple comorbidities.

More recently Shiban et al. 2016³⁶ reported better outcomes compared to those reported by Hempelmann et al. 2010²³ following posterior approach for the management of PSI. 52 patients were included in this retrospective study conducted with minimal follow up of 12 months. The aim of project was to evaluate the efficacy of the posterior surgical approach with debridement, reconstruction with inter-body cage, and posterior stabilisation in the management of patients with PSI followed by antibiotics. All subjects were cleared of infection at final follow-up. Of patients who presented with neurological deficit before surgery, 21% had full recovery, and 36% had improved neurology at final follow-up. Pulmonary embolism (PE) reported in 1 patient and no mortalities reported.

Lin et al. 2012¹⁵; Mohamed et al. 2014³¹ suggested that as debridement was associated with increased complications, the patients with PSI may be managed without doing the formal debridement. The suggestion was to perform posterior stabilisation only and decompress neural tissue when it is compressed. Lin et al. 2012¹⁵ performed a retrospective study to evaluate the outcomes of posterior stabilisation and decompression (without debridement) in the management of PSI. 48 patients were included in the study and were followed up for a mean of 64 months. The results showed that Visual Analogue Score (VAS) improved by 5 scales on average, and the average improvement in the Frankel Grading System (FGS) was 1.03 grades and the average kyphotic angle improvement was 3°, no infection relapse was reported. Regarding complications, the authors did not mention clearly whether or not there were any complications or morbidities.

Mohamed et al. 2014³¹ also retrospectively reviewed the data of 15 patients with PSI who were managed with posterior surgery and

stabilisation (without debridement). After 1–2 years of follow-up, the results stated that 6 of the 9 patients (67%) who were non-ambulatory before surgery regained full ambulation after surgery, 2 patients (22%) were able to mobilise with assistance and one patient (11%) was still unable to mobilise. Furthermore, 3 patients required re-operation (due to epi-dural haematoma, superficial wound infection and loosening of fixation). The authors concluded that posterior stabilisation can be effective in management of patients with PSI, and it can improve neurological state significantly. Complications were reported in 20% of the patients (such as haematoma, superficial wound infection and hardware failure). The complication rate was less than Hempelmann's²³ posterior surgical findings but still more than Klöckner & Valencia 2003³⁴ study looking at the anterior approach. Importantly, Mohammed et al. 2014³¹ addressed clear inclusion and exclusion criteria, patients were followed up for an adequate time, and the surgeries were performed by only two surgeons, in order to decrease the risk of bias. All these previously mentioned three points help to improve the study's internal validity. Yet, the main limitation of this study is the small sample size, which may make it difficult to compare the results with the results of the previously mentioned papers. Consequently, more high-quality studies are required to assess the outcomes of posterior fixation without debridement for the management of PSI.

4. Conclusion

PSI is rare, serious condition that can be caused by many microorganisms. It is most commonly caused by *Staphylococcus Aureus*. PSI tends to affect elderly or patients with multiple comorbidities. Management of PSI can be either conservative or by surgical intervention.

Conservative management of PSI with adequate duration of antibiotics can result in successful infection resolution in carefully selected patients. There is no consensus about the duration of antibiotics treatment, but there was a relatively good evidence to suggest that 12 weeks or more is associated with the lowest recurrence rate. Interestingly, the patients' age, comorbidities and ESR values can help to predict the patients' outcome after conservative management.

With regards to surgical management the combined surgical approach by performing debridement of the infected tissue, anterior column support and posterior stabilisation seems to be associated with increased risk of complications (due to the anterior approaches association with higher post-operative morbidities and mortalities). Consequently, recent literature suggested that posterior approach only may be used as it may be associated with fewer complications. The most recent evidence showed that posterior approach was associated with good outcomes and fewer complications. Yet, there was no consensus in literature whether to debride the infected tissue during posterior approach. Papers have showed satisfactory outcomes after posterior stabilisation without debridement of infected tissue, with full resolution of infection.

Most of the reviewed literature had one or more limitations, with small sample size being the most common. A larger cohort with longer follow-up to assess the outcomes of posterior surgery in the treatment of PSI would be recommended.

Authors' contribution

Ahmed Aljawadi: Writing – review & editing, Formal analysis, Literature review, data Analysis, manuscript writing.

Noman Jahangir: Writing – review & editing, Formal analysis, Literature review & Analysis.

Ana Jeelani: Writing – review & editing, Formal analysis, Literature review & Analysis.

Zak Ferguson: Writing – review & editing, Formal analysis, Literature review & Analysis.

Noman Niazi: Writing – review & editing, Formal analysis,

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Frances Arnall: Writing – review & editing, Formal analysis, Literature review & Analysis.

Anand Pillai: Writing – review & editing, Formal analysis, Writing – original draft, Literature review & Analysis, Critical review & drafting.

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