Preventing and treating surgical site infection in patients with spinal metastatic disease

KEY WORDS
- Infection
- Spinal metastases
- Surgical site infection

Surgery to remove secondary spinal tumours is often necessary to relieve symptoms associated with metastatic spinal cord compression (MSCC). However, such individuals are at high risk of surgical site infection (SSI). This article aims to summarise published literature reporting interventions used to prevent or treat SSI in people with MSCC. A systematic review of the literature was undertaken with randomised controlled trials (RCTs) and non-RCTs of any intervention to prevent or treat SSI eligible for inclusion if a MSCC patient group was reported. Seven reports were included, of which only one was an RCT. Preventative interventions included intraoperative wound irrigation with dilute povidone-iodine solution, postoperative prostaglandin E1 administration, use of a specific intraoperative antibiotic regimen, and soft-tissue reconstruction strategies following surgery. Methods to treat SSI involved the use of soft-tissue reconstructive strategies. Several methods to prevent and treat SSI in MSCC patients are highlighted. However, further high-level research is needed to determine the efficacy of such interventions.

ROSS ATKINSON
Spinal Research Coordinator, Greater Manchester Neurosciences Centre, Salford Royal NHS Foundation Trust, Salford, UK; Honorary Research Associate, Manchester Academic Health Science Centre, University of Manchester, Manchester

STEVE LUI
Senior Lecturer, School of Human and Health Sciences, University of Huddersfield, Huddersfield

KAREN OUSEY
Reader Advancing Clinical Practice, School of Human and Health Sciences, University of Huddersfield, Huddersfield

The surgical removal of metastatic (secondary) tumours from the spine is considered palliative treatment to relieve symptoms of pain, and impaired physical and neurological function associated with compression of the spinal cord (metastatic spinal cord compression [MSCC]; Quan et al, 2011).

Healing of the surgical wound in these patients is difficult as they are often malnourished, catabolic, and immunosuppressed due to the malignant process. A number of risk factors for poor wound healing have previously been identified (McPhee et al, 1998; Olsen et al, 2003; Omeis et al, 2011). Therefore, it is not surprising that surgical site infection (SSI) occurs more frequently in spinal tumour patients, with reported rates being as high as 20%, as opposed to 1–5% in non-instrumented spinal fusion (McPhee et al, 1998).

Highlighting interventions that may be effective in treating or preventing SSI will, therefore, improve practice and enhance quality of life for these patients, and will provide a focus for future research.

The aim of this article is to provide an overview of the published literature where interventions aimed at preventing or treating SSI in patients undergoing surgery to relieve MSCC have been reported.

METHODS

A systematic review of the literature based on search strategies recommended by the Cochrane back and wounds review groups was undertaken using the Cochrane Library, MEDLINE, EMBASE, CINAHL, and Web of Knowledge databases.

Any publications between 1900 and 2012 (randomised controlled trials [RCTs] and non-RCTs, including case studies and evaluative studies) were eligible for inclusion if they included patients (of any sex, age or background) undergoing surgical treatment for spinal metastatic tumours, with any type of primary tumour. Any type of intervention aimed at preventing or treating SSI was deemed suitable for inclusion. Studies were assessed for outcomes relating to the presence/rate of SSI.

Two of the authors of this article (Ross Atkinson and Karen Ousey) reviewed the title and abstract of all results initially retrieved. Those deemed suitable for initial inclusion were reviewed in full. Articles that satisfied the inclusion criteria were then selected for analysis in this review.

RESULTS

The original search yielded 199 records. After removing duplicates and initial screening,

37 publications were considered eligible and were reviewed in full. Thirty were excluded and seven fulfilled the inclusion criteria:

- One was a prospective, single-blinded RCT (Cheng et al, 2005).
- One was a retrospective and prospective study (Demura et al, 2009).
- Five were retrospective studies (Disa et al, 2001; Vitaz et al, 2004; Mastronardi and Tatta, 2004; Chang et al, 2007; Garvey et al, 2010).

Preventative methods

A number of methods aimed at preventing SSI were identified. These included intraoperative irrigation of the wound with dilute povidone-iodine solution (Cheng et al, 2005), twice-daily postoperative prostaglandin E1 (PGE1) administration for 7 days (Demura et al, 2009), the use of a specific, intraoperative antibiotic regimen (Mastronardi and Tatta, 2004), and soft-tissue reconstruction strategies following surgery for spinal metastases (Chang et al, 2007; Garvey et al, 2010).

None of the seven patients who contracted SSI in the RCT investigating povidone-iodine irrigation were spinal tumour patients (Cheng et al, 2005). Therefore, no further data from that study are reported in this review.

Postoperative PGE1 administration appeared to reduce SSI rate only in patients who had undergone pre-operative irradiation (SSI rate of 1/22 [5%] procedures with PGE1 vs 7/22 [32%] in the retrospective phase; Demura et al, 2009).

The specific intraoperative antibiotic regimen employed by Mastronardi and Tatta (2004) was safe and efficacious, but a significantly higher rate of SSI was observed in the tumour group (9.1% vs 0.9% in the entire cohort).

The rate of SSI was not reduced by the use of immediate soft-tissue reconstruction when the studies by Garvey et al (2010) and Chang et al (2007) are compared (8/52 cases vs 4/92 cases; 15% vs 4%, respectively).

Methods of treating SSI

Both publications describing methods to treat SSI and poor wound healing in MSCC patients involved the use of soft-tissue reconstructive strategies (Disa et al, 2001; Vitaz et al, 2004). These surgical techniques involved the use of muscle turnover and paraspinous advancement flaps.

Out of the six patients included in their study, Disa et al (2001) reported two patients with infected open wounds who were treated with trapezius muscle turnover flaps. All muscle flaps survived, and primary wound healing was achieved.

Vitaz et al (2004) included 18 tumour patients in their study, 14 of which were treated effectively using muscle flaps because of infection, and four for dehiscence without infection.

Definition of SSI

Only one report (Mastronardi and Tatta, 2004) provided a definition of SSI that was based on recognised classification criteria (Horan et al, 1992). Five studies did not include adequate information regarding the way SSI was defined or diagnosed (Disa et al, 2001; Vitaz et al, 2004; Chang et al, 2007; Demura et al, 2009; Garvey et al, 2010).

Micro-organisms reported

Staphylococci were the most frequently reported bacteria. These were: coagulase-negative *Staphylococcus* (Mastronardi and Tatta, 2004; Demura et al, 2009), *S aureus* (Vitaz et al, 2004; Demura et al, 2009), Meticillin-resistance *S aureus* (MRSA; Demura et al, 2009), and *S epidermidis* (Mastronardi and Tatta, 2004; Vitaz et al, 2004).

Other organisms included *Pseudomonas* (Mastronardi and Tatta, 2004; Demura et al, 2009), *Enterococcus faecalis* (Vitaz et al, 2004; Demura et al, 2009), *Escherichia coli* (Vitaz et al, 2004; Demura et al, 2009), *Klebsiella* (Mastronardi and Tatta, 2004), *Candida albicans* (Demura et al, 2009), *Proprionibacterium acnes* (Vitaz et al, 2004), and *Serratia* (Vitaz et al, 2004).

Despite reporting on people with SSI, several studies failed to report any details on the types of micro-organism that may have been present (Disa et al, 2001; Chang et al, 2007; Garvey et al, 2010).

DISCUSSION

This systematic review highlights a number of published reports of interventions that may be useful in either preventing or treating SSI in a very specific high-risk group of patients. Unfortunately,

"A number of methods aimed at preventing surgical site infection were identified."

"The recent rise of resistant strains of bacteria due to persistent over-use of antibiotics means that stewardship of these valuable treatments is paramount now more than ever."

the quality of these studies varied, with no high-level evidence available to decisively conclude whether any of the interventions described are effective. Nevertheless, it should be recognised that dissemination of clinical experience and the use of somewhat unconventional methods can often lead to further research where there is adequate theory to support such interventions.

Prevention of infection in the first instance is of utmost importance to the patient, clinician, and society in general for a number of reasons. SSI can be a devastating consequence of any surgical procedure. In operations involving the implantation of prostheses (as in the majority of spinal tumour cases), wound infection could result in removal of instrumentation and severely compromises surgical outcome. Furthermore, longer in-patient stay, severe pain, a number of diagnostic tests, treatments (including antibiotic therapy), and often further surgery, all adversely affect an individual's quality of life.

The recent rise of resistant strains of bacteria due to persistent over-use of antibiotics means that stewardship of these valuable treatments is paramount now more than ever. All of these factors exacerbate the already high costs associated with complex surgical procedures and impose a huge financial burden on budgets and compromises the capacity of health systems to provide appropriate standards of care.

It is interesting that interventions aimed at three important areas of practice have been identified in the literature pertaining to MSCC patients undergoing surgery. The use of pharmacological interventions, antiseptics, and variations in surgical techniques highlights that a multi-faceted approach is needed to reduce the likelihood of infection and optimise outcomes. This is certainly advocated in the UK by the SSI prevention and treatment guidelines set out by the NICE, which brings together evidence on a host of interventions that can be employed at the pre-, intra-, and postoperative stages (NICE, 2008). Care bundles have been shown to be effective in reducing the incidence of SSI in some areas (Acklin et al, 2011) and have been incorporated into advice of the National Patient Safety Agency (NPSA) since the introduction of the World Health Organization (WHO) surgical safety checklist (National Patient Safety Agency [NPSA], 2009).

Appropriate antibiotic prophylaxis in spinal surgery is an important step in the pre-operative phase. Despite showing a relatively low SSI rate with the use of their specific antibiotic regimen, Mastronardi and Tatta (2004) also highlight that infection may be more common in tumour patients. This is in agreement with previous studies which have shown that surgery for spinal tumours is a risk factor for SSI (Olsen et al, 2003).

The North American Spine Society (NASS) states that existing literature is sufficient to recommend the use of prophylactic antibiotics for spinal surgery (NASS, 2007). Similarly, NICE recommends that antibiotic prophylaxis be administered in all cases involving placement of an implant (NICE, 2008). It has been suggested that future research should utilise existing datasets to investigate the efficacy of various antibiotic protocols, identify populations at high risk of infection, and evaluate the utility of broad spectrum antibiotic coverage in reducing SSI rates in high-risk populations treated with instrumented fusion (NASS, 2007). Patients with spinal metastases constitute one such high-risk group.

Use of pharmacological interventions as prophylactic measures – other than antibiotic prophylaxis alone – is also an area which may deserve further attention. PGE1 is a potent vasodilator and acts to increase peripheral blood flow, which has been cited as one possible way it may act to reduce SSI in people with diabetes (Demura et al, 2009).

Previously, Shiga et al, 2002 conducted a small retrospective study of people undergoing laryngectomy procedures and found that a lower complication rate was associated with those administered PGE1 after surgery. Despite this, a higher rate of infection has been observed in neonates undergoing cardiac surgery who were treated pre-operatively with PGE1 (Fleming et al, 1984). Erez et al also reported pre-operative administration of PGE1 in children undergoing cardiac surgery, but no explanation was given as to the reason for its usage, or the effect on preventing or treating infection (Erez et al, 2000). Given that the majority of complex spinal procedures are

undertaken in non-infants, administration of PGE1 in the postoperative phase may be feasible and worthy of further investigation.

The use of antiseptics is an area which may potentially benefit from further research. Skin preparation using chlorhexidine in alcohol has been shown to be superior to povidone-iodine (Darouiche et al, 2010), and has subsequently been adopted as standard by a number of surgical areas. However, current NICE guidance advises against the use of wound irrigation (including with antiseptics) to prevent SSI. This is despite evidence suggesting that irrigation with povidone-iodine solutions prior to closure may be effective in reducing SSI rate (Chundamala and Wright, 2007; Fournel et al, 2010). Further work to assess the utility of antiseptics as wound irrigants to prevent SSI may be warranted, but the benefits and risks of their use at certain concentrations in orthopaedic surgery should be carefully considered (Kaysinger et al, 1995).

A number of studies described less conventional surgical strategies to aid wound closure. These involved the use of muscle flaps, both prophylactically to prevent SSI, and to treat poorly healing or infected wounds. These techniques aim to rebuild anatomy and preserve external appearance, restore function, and achieve optimal quality of life for the patient (Dolan et al, 2012). It is understandable that such methods may be less favourable aesthetically. However, in cases where life expectancy is limited (for example, those treated palliatively for spinal metastases), patients and clinicians must assess the advantages and disadvantages of such techniques that may offer superior surgical outcomes over desired aesthetic appearance, bearing in mind that a poor aesthetic outcome may also impact negatively on quality of life (Dolan et al, 2012). While evidence exists to suggest that the rate of major complications (i.e. those requiring further surgical treatment) may be reduced by employing alternative soft-tissue reconstruction strategies (Garvey et al, 2010), further research may be needed to ascertain whether these methods are also associated with lower rates of SSI.

Few studies reporting SSI in this review described the way this outcome was defined. While some reported the types of micro-organism cultured, insufficient detail regarding the criteria for determining SSI was evident in most. This leaves the reader to assume that microbiological results were perhaps the only criterion for the diagnosis of infection.

Since positive cultures have the potential to result from contaminated samples obtained from the wound, or may simply be an indication of bacterial colonisation, it is imprudent to diagnose SSI on microbiology alone. Therefore, it is important that studies reporting SSI take great care in defining how this was classified and diagnosed, with the recommendation that clinical signs of infection are considered in conjunction with results of microbiological examination where appropriate (Bowler et al, 2001; Patel, 2007).

In particular, authors should use and cite recognised SSI classification systems such as the Centers for Disease Control and Prevention definition (Horan et al, 1992) where possible, and be aware of alternative ways to classify SSI which generate interval data to determine the severity of SSI (Williams et al, 2011). Examples of such systems include the ASEPSIS (Wilson et al, 1986) and Southampton (Bailey et al, 1992) scores. Investigators should also ensure that the personnel diagnosing SSI are appropriately qualified to do so and that surveillance is undertaken rigorously. Such standardisation measures will ensure accurate reporting of SSI rates and enable valid comparison between centres and studies (Tanner et al, 2012).

CONCLUSION

This review highlights the limited number of reports that have investigated methods to prevent and treat SSI in patients undergoing surgery for spinal metastatic tumours. Appropriate antibiotic prophylaxis is an extremely important factor in preventing against SSI in these procedures that involve the implantation of instrumentation. Other pharmacological interventions such as the use of PGE1 in the Postoperative phase may also contribute towards reducing the rate of wound infection and may deserve further investigation. Furthermore, unconventional surgical approaches to wound closure may provide good outcomes in patients where wound healing is severely impaired, with or without infection, or where tissue coverage is insufficient.

"It is important that studies reporting surgical site infection take great care in defining how this was classified and diagnosed."

"Current NICE guidance encourages the adoption of a rigorous, multifaceted approach to the prevention of surgical site infection (SSI), which can be promoted through an SSI care bundle approach."

While there is currently no published evidence determining the efficacy of the use of antiseptics specifically in patients with spinal metastases, their successful employment in other areas of surgery indicate that they too play an important role in reducing the risk of infection. Current NICE guidance encourages the adoption of a rigorous, multifaceted approach to the prevention of SSI, which can be promoted through an SSI care bundle approach. WUK

Declaration of interest

This work was funded by a competitive grant from the 2011 Foundation Urgo Award. A poster entitled "A Systematic Review of Ways to Prevent and Treat Surgical Site Infection (SSI) in Patients Undergoing Surgery for Spinal Metastases" was presented at the *Wounds UK* conference in 2012, winning first place in the "Hard-to-Heal" award category. The Woundcare4Heroes charity is gratefully acknowledged for its sponsorship of this award and the authors would also like to thank Valerie Haigh (Library Manager) for her assistance in conducting the literature search, Brad Williamson (Consultant in Spinal Surgery), and Anna Fletcher (SSI Surveillance Nurse) for their support with this project.

REFERENCES

Acklin YP, Widmer AF, Renner RM et al (2011) Unexpectedly increased rate of surgical site infections following implant surgery for hip fractures: problem solution with the bundle approach. *Injury* 42(2): 209–16

Bailey IS, Karran SE, Toyn K et al (1992) Community surveillance of complications after hernia surgery. *BMJ* (6825): 304, 469–71

Bowler PG, Duerden BI, Armstrong DG (2001) Wound microbiology and associated approaches to wound management. *Clin Microbiol Rev* 14(2): 244–69

Chang DW, Friel MT, Youssef AA (2007) Reconstructive strategies in soft tissue reconstruction after resection of spinal neoplasms. *Spine* 32(10): 1101–6

Cheng MT, Chang MC, Wang ST et al (2005) Efficacy of dilute betadine solution irrigation in the prevention of postoperative infection of spinal surgery. *Spine* 30(15): 1689–93

Chundamala J, Wright JG (2007) The efficacy and risks of using povidone-iodine to prevent surgical site infection: an evidence-based review. *Can J Surg* 50(6): 473–81

Darouiche RO, Wall MJ jr, Itani KM et al (2010) Chlorhexidine-Alcohol versus Povidone-Iodine for Surgical-Site Antisepsis. *N Engl J Med* 362(1): 18–26

Demura S, Kawahara N, Murakami H et al (2009) Surgical site infection in spinal metastasis: risk factors and countermeasures. *Spine* 34(6): 635–9

Disa JJ, Smith AW, Bilsky MH (2001) Management of radiated reoperative wounds of the cervicothoracic spine: the role of the trapezius turnover flap. *Ann Plast Surg* 47(4): 394–7

Dolan RT, Butler JS, Murphy SM, Cronin KJ (2012) Health-related quality of life, surgical and aesthetic outcomes following microvascular free flap reconstructions: an 8-year institutional review. *Ann R Coll Surg Engl* 94(1): 43–51

Erez E, Katz M, Sharoni E et al (2000) Pectoralis major muscle flap for deep sternal wound infection in neonates. *Ann Thorac Surg* 69(2): 572–7

Fleming WH, Sarafian LB, Kobayashi RH (1984) Prostaglandin E1 therapy. Is it associated with a higher incidence of wound infection in the cyanotic neonate? *Chest* 85(2): 241–3

Fournel I, Tiv M, Soulias M et al (2010) Meta-analysis of intraoperative povidone-iodine application to prevent surgical-site infection. *Br J Surg* 97(11): 1603–13

Garvey PB, Rhines LD, Dong W, Chang DW (2010) Immediate soft-tissue reconstruction for complex defects of the spine following surgery for spinal neoplasms. *Plast Reconstr Surg* 125(5): 1460–6

Horan TC, Gaynes RP, Martone WJ et al (1992) CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol* 13(10): 606–8

Kaysinger KK, Nicholson NC, Ramp WK, Kellam JF (1995) Toxic effects of wound irrigation solutions on cultured tibiae and osteoblasts. *J Orthop Trauma* 9(4): 303–11

Mastronardi L, Tatta C (2004) Intraoperative antibiotic prophylaxis in clean spinal surgery: a retrospective analysis in a consecutive series of 973 cases. *Surg Neurol* 61(2): 129–35

McPhee IB, Williams RP, Swanson CE (1998) Factors influencing wound healing after surgery for metastatic disease of the spine. *Spine* 23(6): 726–32

NICE (2008) *Surgical Site Infection: Prevention and Treatment of Surgical Site Infection* (CG74). NICE, London

National Patient Safety Agency (2009) *WHO Surgical Safety Checklist*. National Patient Safety Agency, London

North American Spine Society (2007) *Evidence-based Clinical Guidelines for Multidisciplinary Spine Care: Antibiotic Prophylaxis in Spine Surgery*. North American Spine Society, Burr Ridge, IL

Olsen MA, Mayfield J, Lauryssen C et al (2003) Risk factors for surgical site infection in spinal surgery. *J Neurosurg* 98(Suppl 2): 149–55

Omeis IA, Dhir M, Sciubba DM et al (2011) Postoperative surgical site infections in patients undergoing spinal tumor surgery: incidence and risk factors. *Spine* 36(7): 1410–9

Patel S (2007) Understanding wound infection and colonisation. *Wound Essentials* 2: 132–42

Quan GM, Vital JM, Aurouer N et al (2011) Surgery improves pain, function and quality of life in patients with spinal metastases: a prospective study on 118 patients. *Eur Spine J* 20(11): 1970–8

Shiga K, Tateda M, Saijo S (2002) Complication-free laryngeal surgery after irradiation failure with prostaglandin E1 administration. *Ann Otol Rhinol Laryngol* 111(9): 783–8

Tanner J, Padley W, Kiernan M et al (2012) A benchmark too far: findings from a national survey of surgical site infection surveillance. *J Hospital Infection* 83(2): 87–91

Vitaz TW, Oishi M, Welch WC et al (2004) Rotational and transpositional flaps for the treatment of spinal wound dehiscence and infections in patient populations with degenerative and oncological disease. *J Neurosurg* 100(1 Suppl Spine): 46–51

Williams N, Sweetland H, Goyal S et al (2011) Randomized trial of antimicrobial-coated sutures to prevent surgical site infection after breast cancer surgery. *Surg Infect (Larchmt)* 12(6): 469–74

Wilson AP, Treasure T, Sturridge MF, Grüneberg RN (1986) A scoring method (ASEPSIS) for postoperative wound infections for use in clinical trials of antibiotic prophylaxis. *Lancet* 1(8476): 311–3