original article

Effect of prophylactic intra-operative instillation of vancomycin powder on surgical site infections following spinal surgery: a retrospective case control study.

Saheel Maajid , Nadeem Ali , Senin , Ayaz Ali Mir , Tarsem Motten , Reyaz Ahmad Dar , Mudasir Ahmad Bhat

Abstract

Objectives: The aim of this study was to find effectiveness of intraoperative instillation of crystalline vancomycin powder in posterior spinal surgeries as a prophylaxis in preventing postoperative acute surgical site infections.

Background: Every surgical procedure is plagued with the risk of surgical site infection (SSI) despite use of parentral antimicrobial prophylaxis and same holds true for the spinal surgeries. SSI after spinal surgeries adds to patient morbidity and increases the burden on the health care system. Instillation of vancomycin powder in the wound before closure may decrease the incidence of SSI in spinal surgeries.

Methods:A retrospective analysis was done from the hospital medical record section about posterior spinal surgical procedures performed from January 2013 till May 2017. In patients operated from January 2015 onwards, intra-wound instillation of vancomycin powder before closure of the wound was done and these patients were allocated to vanco group. While as patients operated before January 2015, where no antibiotic was instilled in the wound, were allocated to non-vanco group. A total of 305 patients were included in this retrospective study with 153 patients belonging to vanco group and 150 to non-vanco group.

Results: The difference in the results between the two groups was compared.The two groups were statistically comparable with respect to age, gender, BMI, co-morbidities and surgical procedures. There was a significant reduction of SSI from 11.3% in non-vanco group to2.6% in the vanco group (p = 0.003). Bacteriologically this decrease was significant with respect to Staphylococcal infections from 6.7% to 0.65% (p = 0.005).

Conclusion: Intra operative use of vancomycin powder significantly reduces the incidence of SSI in posterior spinal surgeries, especially those caused by staphylococci. MRSA related SSI, which cannot be prevented by routine parentral antimicrobial prophylaxis, are also significantly reduced.

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Introduction

Surgical site infection (SSI) after spine surgery was first described as a clinical entity in 1953 by Turnbull[1]. Postoperative SSI after spine surgery is a common problem and a cause of morbidity which may require repeated surgical procedures, prolonged antibiotic use, prolonged hospital stay and even poor outcome of the surgical procedure. All this adds to the burden on the health care system[2,3].

Author Affiliations:

Saheel Maajid MS, **Ayaz Ali Mir** MS, **Tarsem Motten** MS, **Reyaz Ahmad Dar, Mudasir Ahmad Bhat** MBBS ;
Department of Orthopedics, SKIMS Medical College and Hospital, Bemina.

Nadeem Ali MS;
Bone and Joint Hospital Barzulla.
Srinagar ,Kashmir (India)

Senin MBBS;
Kasturba Medical College, Mangalore, Karnataka, India.

Correspondence:
Dr Saheel Maajid ,
Professor and Head Spine Unit
Department of Orthopaedics
SKIMS Medical College and Hospital, Bemina
Srinagar, Jammu and Kashmir
INDIA 190018
Mobile: 919419005107
Email: saheelmaajid@gmail.com

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Surgical site infection, Staphylococcus, Vancomycin

Despite proper antiseptic precautions in the pre-operative and intra-operative period and use of prophylactic intravenous antimicrobial therapy the incidence of SSI after spine surgery still remains high especially in high risk patients and patients undergoing posterior instrumentation with fusion for spinal deformities [4,5]. In the literature the incidence of SSI in spine surgery ranges from 0.5% to 18.8% [6]. Delivery of intravenously administered antibiotics to the wound bed may be hampered due to post-operative tissue ischemia and formation of local hematoma and seroma[7]. Direct application of antibiotic to the surgical wound has been used for treatment of chronic osteomyelitis as well as in open fractures with contamination in the form of a mixture with polymethylmethacrylate[8,9]. The purpose is to achieve a higher concentration of the antibiotic at the surgical site without any risk of systemic toxicity. The same principle applies to application of antibiotic in the wound bed after spine surgery with the purpose of reducing the rate of SSI[10].

Staphylococcus aureus remains the leading pathogen in spinal SSI. Coagulase negative Staphylococci, especially, Staphylococcus epidermidis is the other common organism isolated. Resistant organisms like methicillin resistant Staphylococcus aureus (MRSA) have emerged as a new threat in the recent years [6,11].

The purpose of this study was to evaluate the results of local application of vancomycin powder to the wound bed before wound closure in posterior spine surgeries in prevention of postoperative SSI at our institute.

Material and Methods

This retrospective study was conducted in the Orthopaedic Department of SKIMS Medical College and Hospital. Data was collected from the medical record department of the hospital and from the operating room registers about the patients that underwent posterior surgical procedures on thoracic, lumbar and lumbo-sacral spine for trauma, degenerative conditions and spinal deformities from January 2013 to May 2017. Patients who had at least a follow up of 3 months available after the operative procedure were included in the study. Patients with infective conditions of the spine or with previous history of infections of the spine were excluded from this study. All the cases included in the study had been operated by a single spine surgeon.

Patients that were operated from January 2015 had crystalline vancomycin powder instilled in the wound before closure of the wound routinely and these patients were retrospectively allocated to vanco group while as cases that were operated before January 2015 had no antibiotic instilled in the wound before closure and were allocated to non-vanco group. A total of 303 patients were included in the study with 153 patients belonging to Vanco Group and 150 to non-vanco group. All the patients had received routine intravenous antimicrobial prophylaxis (1 gram of cefazolin 30 minutes prior to surgical incision followed by 1 gram 12 hourly for three days or 1 gram vancomycin as slow intravenous infusion in case patient was allergic to cefazolin) as per hospital protocol. In addition to this Vanco Group patients received additional 1 gram of crystalline vancomycin powder that was smeared to muscle, fascia, subcutaneous tissue and skin edges before wound closure.

Data collected from the inpatient records and follow up was evaluated for age, gender, Body Mass Index, smoking, co-morbidities, anaemia, indication for surgery, duration of surgery, blood transfusions and any surgical site infection within 3 months of post-operative period. In cases of SSI, the organisms isolated on culture of pus or swab, if any, were recorded. Local complications associated with vancomycin application were also recorded. The data was analysed using statistical software MS (Microsoft) excel and SPSS (Statistical Package for Social Sciences) version 17 for windows. Student's t test, Chi-square test and Fisher Exact test were applied to evaluate statistical significance between the two groups. P-value of less than 0.05 was considered statistically significant. All the p-values reported are two-tailed.

Results

A total of 303 patients were included in this retrospective study. There were 153 patients in the vanco group and 150 in the non-vanco group. Demographic parameters, frequency of the associated co-morbidities and of obesity (BMI > 30 kg/m^2) of the patients of the two groups are listed in table I. The two groups were comparable with respect to age, gender distribution and frequency of co-morbidities (p-value > 0.05).

Spinal trauma was the most common indication of surgical intervention followed by degenerative disease of the spine including diskectomy in both the groups. Deformity correction in adolescent idiopathic scoliosis and adult scoliosis, and tumor surgeries were less common indications (Table 1). The two groups were statistically comparable with respect to indications for the surgery. Use of hardware was more common in the

Table 1: Demographic profile of the patients and frequency of co-morbidities.

Parameter	Vanco Group (n=153)	Non-vanco Group (n=150)	p-value
Total number of cases	153	150	
Age(years) Mean (Range)	48.2 (20-58)	46.7 (22-55)	0.63
Gender			
Male Female	89 64	80 70	0.41
Smoking history	31	28	0.77
Diabetes mellitus	08	06	0.78
Anaemia (Hb[(a)] <10 gm%)	15	11	0.53
Obesity (BMI[(b)] >30kg/m^2)	32	30	0.88
Hypertension	64	58	0.63

[(a)] Haemoglobin; [(b)] Body mass index

vanco group but it had no statistical significance (p = 0.06). Other operative parameters like previous surgery at same level, duration of surgery, and requirement for blood transfusion had no statistical significance between the two groups.

The incidence of SSI had significantly decreased from 11.3 % in non-vanco group to 2.6 % in the vanco group (p = 0.003). With respect to bacteriology, 87.2 % of SSI in non-vanco group yielded causative organism while as culture was positive in all cases of SSI in the vanco group. Staphyloccoci were the most common organisms isolated as a causative agent in the non-vanco group (n = 10; 58.8 %) with methicillin resistant Staphylococcus aureus (MRSA) accounting for 35.3 % (n = 6) of SSI. However, in vanco group Staphyloccoci were the causative agents of SSI in only one patient. This decrease in the Staphylococcal infections in the vanco group was statistically significant (p = 0.005). MRSA was not isolated from any SSI in the vanco group as compared to 6 SSI cases in the non-vanco group (p = 0.014). No infected case in any group had fungi or Mycobacteria as the causative agents. The bacteriological profile of the SSI of the two groups is summarized in Table 2. Escherichia coli and Psudomonas aeruginosa were the organisms isolated from Gram negative SSI in the vanco group while as Enterobacter cloacae, Acinetobacter baumannii and Proteus mirabilis were isolated from Gram negative SSI in the non-vanco group. Among poly-microbial SSI Enterococcus faecalis, Pseudomonas aeruginosa and Citobacter sp were isolated from the vanco group and Staphylococcus epidermidis, Staphylococcus aureus, Psedomonas aeruginosa, Enterococcus faecalis, Enterobacter sp, Serratia marcescens, Escherichia coli, Streptococcus viridians and Streptococci agalactiae were isolated from the non-vanco group.

Table 2: Bacteriological profile of SSI.

Isolated bacteria	Vanco Group (n = 4)	Non-Vanco Group (n = 17)	p-value (p = 0.003)
Staphylococcal	1	10	0.005
MRSA[(a)]	0	6	0.014
MSSA[(b)]	1	2	0.62
Cog Negative Staph	0	2	0.24
Gram negative bacteria	2	3	0.68
Polymicrobial	1	2	0.62
Negative culture	0	2	0.24

(a)Methicillin resistant Staph Aureus; (b)Methicillin sensitive Staph Aureus; Cog

None of the patients in the vanco group had any systemic or local side effects like red man syndrome, DRESS syndrome, anaphylaxis, nephrotoxicity, ototoxicity, aseptic wound discharge, local erythema or neurological complications attributed to local application of vancomycin powder.

Discussion

Surgical site infection (SSI) is a known complication of spine surgery and a nightmare for the surgeon and burden on the health care system[2,3]. Every attempt has been made to reduce the incidence of this complication by proper peri-operative precautions which include administration of prophylactic intravenous antimicrobial therapy, proper preparation of the part, improvised surgical techniques and copious saline irrigation before wound closure[4]. Despite these measures the incidence of SSI after spine surgeries continues to be high with reported incidence of 0.5 % to 18.8 % in the literature[6]. Various risk

factors have been described, pertaining to patient and the surgical procedure, which increase the risk for SSI in the spine surgeries. These include Diabetes Mellitus, smoking history, alcoholism, steroid intake, obesity, hypertention, advancing age, chronic obstructive pulmonary disease, anaemia, renal disease, nutritional deficiency, revision spine surgery, multiple level fusions, surgeries with instrumentation, prolonged duration of surgery, and transfusion of blood products[6,12-16]. SSI are more common in procedures on thoracic spine and for trauma surgery[6]. In our study, the various confounding factors in the two groups had been compared and there was no statistically significant difference between the vanco and non-vanco group. There are multitudes of studies which have demonstrated a significant decrease in the incidence of SSI in spine surgery with the use of vancomycin powder locally. The incidence of SSI in our study significantly decreased from 11.3 % in the non-vanco group (control group) to 2.6 % in the vanco group (intervention group). Caroom C et al in their study on posterior cervical spine fusion had infection rate reduced from 15 % to 0 % by intra-wound vancomycin powder[7]. Godil SS et al had the incidence reduced from 13 % to 0 % in instrumented posterior spine fusions in spine trauma with the application of vancomycin powder in the wound[17]. Sweet FA et al in their instrumented thoraco-lumbar fusions had the SSI rates reduced from 2.6 % to 0.2 % [18]. Strome RG et al reduced the SSI rate from 11% to 0 % with application of vancomycin powder in combined instrumented and non-instrumented lumbar spine surgeries[19]. In complex deformity reconstruction in adults, Theologis AA et al showed the infection rates decreased from 10.9 % to 2.6 % with local vancomycin [10]. Heller A et al had almost similar results of decrease in SSI from 8.8 % to 2.6 % in posterior instrumented spinal arthodesis [20]. These results are almost comparable with results of our study. Unlike our study, these studies have been performed on a particular spinal surgical procedure. Our study includes all the posterior spinal procedures that had been performed at our institute. Many of the above mentioned studies have 100 % SSI control with the use of local vancomycin, not seen in our study, which may be due to predominance of spine trauma cases in our study which carries maximum risk of developing SSI[6].

In the non-intervention group (non-vanco group), in our study, staphylococci were the predominant organisms isolated from the mono-microbial SSI, accounting for 58.8 % of the SSI. However, in the intervention group (vanco group), only 25 % of the mono-microbial SSI were attributed to Staphylococci. Overall the incidence of Staphylococci SSI decreased from 6.7 % in non-vanco group to 0.65 % in the vanco group. The incidence of MRSA had decreased from 4 % to 0 % by local application of vancomycin powder. Theologis AA et al also in their complex adult deformity correction had Staphylococcal infections decreased from 9.4 % in the control group to 0.66 % in the intervention group [10]. Caroom C et al in a study on posterior cervical fusion had incidence of methicillin resistant Staphylococci reduced from 9.7 % to 0 % by intra-wound application of vancomycin powder [7]. Chahoud J et al in their review on SSI in spine surgeries has Staphylococcus aureus as a causative agent in around 50 % cases with a range of 12 to 65 % in different studies, which is consistent with the results of our study (47 % in the non-vanco group) [6]. The rate of Gram negative infections and poly-microbial infections decreased from 2 % and 1.3 % to 1.3 % and 0.65 % respectively in our study which was statistically insignificant. Heller A et al did not find any difference in the incidence of non-staphylococcal infections between the two groups and concluded non-staphylococcal infections will continue to occur despite use of vancomycin powder in the wound in spinal surgeries[20]. Tomov M et al had an insignificant decrease in poly-microbial SSI from 0.88 % to 0.34 % with use of vancomycin powder locally. However, they noticed a decrease in culture of Gram positive organisms in the poly-microbial SSI as has been observed in our results of cultured bacteria from poly-microbial SSI [21].

Side effects are well known with systemic administration of vancomycin. These include a histamine release syndrome known as red man syndrome, immunoglobulin E mediated anaphylaxis, DRESS syndrome, nephrotoxicity, ototoxicity and others [22,23]. Systemic toxicity has not been reported with local application of vancomycin powder except for intra-peritoneal use in empirical treatment of peritoneal dialysis peritonitis where dosing is done every 3 to 5 days for 2 to 4 weeks [22]. We did not have any case of systemic side effects of vancomycin in our study. Sweet et al in their study on 2 grams of local vancomycin usage in spine surgery found vancomycin was not detectable in the blood in 80 % of the patients and in the remaining 20 % patients average serum level was 1.6 µg/ml at first post-operative day which is much less than the recommended safety level which is less than

15 µg/ml [18]. Like other studies on local vancomycin usage in spine surgery, our patients also did not encounter any local complications [7,11,24]. Theoretical concern regarding use of local vancomycin without a carrier is very high concentration of the drug locally which may interfere with function of osteoblasts and their osteogenic activity leading to pseudoarthosis of spine in spinal fusion procedures [25,26]. But, in vitro studies have demonstrated other antimicrobial agents are more toxic than vancomycin to the osteoblasts [27].

The limitations of our study are that it is a retrospective study with a single surgeon performing all the surgical procedures. Improvements in the surgical techniques of the surgeon over a period of time may be a source of bias. Besides, our study encompasses different spinal surgical procedures and it is a well known fact different procedures at different spinal levels have difference in the risk of developing SSI. Also, all the risk factors associated with SSI in spine surgery have not been taken into consideration in this study.

Conclusion

Use of prophylactic intra-wound vancomycin powder before closure of the wound, besides routine intravenous antimicrobial prophylaxis, significantly reduces the incidence of surgical site infections in spine surgeries, especially surgical site infections related to Staphylococci. Methicillin resistant Staphylococcal infection rates are also reduced but Gram negative bacterial infections and polymicrobial surgical site infection rates almost remain the same. Besides, local application of vancomycin is cheap, easy and safe method, without any risk of local and systemic adverse effects, of reducing the incidence of surgical site infections in spine surgery.

Further prospective case control studies with large cohorts and identification of surgical site infection risk factors are warranted in future to formulate the guidelines for use of intra-wound application of vancomycin in spine surgeries. Gram negative surgical site infections, not controlled by use of vancomycin, need an additional local antibiotic, besides vancomycin, to be applied to the wound bed and this needs to be investigated in the future studies.

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