European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 03, 2022

ORIGINAL RESEARCH

STUDY ON EFFECT OF LOCAL APPLICATION OF VANCOMYCIN POWDER ON SURGICAL SITE INFECTION RATE IN PATIENTS UNDERGOING INSTRUMENTED SPINAL FUSION SURGERIES

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ABSTRACT

Aim: To determine the effect of local application of vancomycin powder on surgical site infection rate in patients undergoing instrumented spinal fusion surgeries.

Methodolgy: This is a prospective, cohort study which was conducted at SVIMS, a tertiary care hospital. Informed consent was obtained from all the patients recruited in the study. The study conducted during July 2015 to July 2016 with follow up of patients for 1 year post operatively.The study cohort included consecutive patients undergoing posterior spinal fusion for various etiologies. All patients received standard systemic antibiotic prophylaxis consisting of 1 g IV ceftriaxone within 1 hour of surgical incision followed by 1 g IV ceftriaxone every 8 hours for 1 day. All patients underwent preoperative preparation with betadine solution.

Results: Total of 120 patients who underwent instrumented spinal fusion procedures were included in the study with or without topical application of vancomycin powder.Mean age of presentation in test group was 38.3 yrs whereas in control group it is 45.2 yrs.Most of the patients who underwent operation for listhesis in the present study were females with F:M ratio being 3.6:1.Only 4 of the patients from test group and 3 patients from control group gave history of smoking and alcoholism. SSI developed in only one of the patients with both smoking and alcoholism as risk factors.8 patients from test group and 9 patients from control group had comorbidities like diabetes, hypertension, rheumatoid arthritis, hepatitis B.None of the patients in the present study gave history of previous lumbar surgeryMost of the patients presented with symptoms of low back ache and the most common neurological deficit encountered was motor weakness related to respective spinal segment. In the test group 53 single level fusions and 7 two level fusions were done whereas in control group 55 single level fusions, 3 two level fusions and 2 three level fusions were done .Mean operative time in test group was 239.6 mts and mean estimated blood loss was 87.4 ml whereas in control group it is 221.25 mts and 88.08 ml respectively.Two patients in the test group had deep SSI of which one required implant removal on readmission and the other patient was managed conservatively when he was diagnosed to have spondylodiscitis post operatively with appropriate antibiotics.

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Conclusion: In the present study topical application of vancomycin powder did not reduce the incidence of SSI and therefore we propose that further large volume studies are needed to authenticate the liberal use of its application in instrumented spinal fusion surgeries.
Keywords: Vancomycin, spondylodiscitis; spinal fusion surgeries; comorbidities

INTRODUCTION

Wound infections are a common and preventable source of morbidity and healthcare expenditure in patients undergoing spine surgery. Postoperative spinal wound infection is a potentially devastating complication after spine procedures. Despite the development of prophylactic antibiotics and advances in operative technique and postoperative care, wound infection continues to compromise patients outcome after spinal surgery. This kind of infection places the patient at risk for pseudoarthrosis, adverse neurologic sequalae, chronic pain, deformity and even death.[1]

The incidence of Surgical site infections (SSI) varies according to several factors and it is estimated that between 0.5% and 18.8% of patients undergoing spinal surgery will suffer SSI, despite the application of conventional prevention strategies. [1-2]

Surgical site infections are categorised into superficial and deep infections as per CDC- centre for disease control and prevention.[2]

Besides the higher invasiveness, the use of instrumentation has an important role in the development of postoperative infections. Furthermore, it can cause local soft tissue irritation leading to inflammation and seroma formation that subsequently provides a fertile breeding ground for microorganisms to grow. Adherence of bacteria to the surface of implants is promoted by a polysaccharide biofilm called glycocalyx that acts as barrier against host defense mechanisms and antibiotics. Finally, metallosis from micromotion of the instrumentation leads to granuloma formation and provides yet another medium for bacterial colonization.[3]

Risks factors for infection after spinal surgery have been well-defined in numerous studies. Advanced patient age, obesity, malnutrition, prolonged surgical time, revision surgery, increased blood loss, smoking, use of instrumentation, and revision surgery are among the reported risk factors for increasing rates of deep infection.[4]

The effectiveness of additional intraoperative measures to reduce infection remains unclear. While perioperative antibiotic prophylaxis as a means of lowering infection rates after spinal surgery has been well described, there is a paucity of literature with respect to other adjunct measures to prevent spinal surgery postoperative infection.[5]

Diluted povidone–iodine has been demonstrated in two separate case-controlled studies to reduce the rate of postoperative spine infections when used for wound irrigation.[6]There is no currently compelling evidence in the literature to support the role of antibiotic solutions used as wound irrigation substitutes.

The local delivery of antibiotics to surgical wounds remains attractive as these wounds may be difficult to penetrate with systemic antibiotic therapy because of local tissue ischemia, seroma and hematoma. The application of vancomycin in the form of unreconstituted powder within the surgical site represents an innovative trend for the prevention of SSI and is increasingly gaining supporters among spinal surgeons due to its low cost, extensive availability, ease of application, good safety profile.

Therefore the present study aims to determine the effect of local application of vancomycin powder on reducing the infection rate among patients undergoing instrumented spinal fusion

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surgeries by comparing patients who did and did not receive local application of vancomycin powder at the surgical site,in addition to standard intravenous (IV) antibiotic prophylaxis.

AIMS AND OBJECTIVES

1. To determine the effect of local application of vancomycin powder on surgical site infection rate in patients undergoing instrumented spinal fusion surgeries.

INCLUSION CRITERIA:

1. Hemodynamically stable
2. Age > 18 yrs
3. Patients undergoing instrumented spinal fusion surgeries.

EXCLUSION CRITERIA:

Patients with presence of

1. Sepsis
2. Active infection
3. Open or penetrating spinal injury
4. Known allergy to vancomycin
5. Previous surgery in operative site
6. History of radiation therapy at surgical site
7. Immunocompromised status

MATERIALS AND METHODS

This is a prospective, cohort study which was conducted at SVIMS, a tertiary care hospital. Informed consent was obtained from all the patients recruited in the study.

Duration of the study:

July 2015 to July 2016 with follow up of patients for 1 year post operatively.

The study cohort included consecutive patients undergoing posterior spinal fusion for various etiologies. All patients received standard systemic antibiotic prophylaxis consisting of 1 g IV ceftriaxone within 1 hour of surgical incision followed by 1 g IV ceftriaxone every 8 hours for 1 day. All patients underwent preoperative preparation with betadine solution.

All the patients recruited in the study were randomized into test and control groups. The patients under test group received local vancomycin before closing the wound 50% dose above the deep lumbar fascia and 50% dose below the fascia after ensuring that the bone graft or dura mater was not exposed in addition to standard intravenous antibiotic prophylaxis.

For surgeries involving 3 contiguous segments or less 500mg of vancomycin was applied whereas for more than 3 contiguous segments 1gm was applied. The patients in control group received standard intravenous (IV) antibiotic prophylaxis only.

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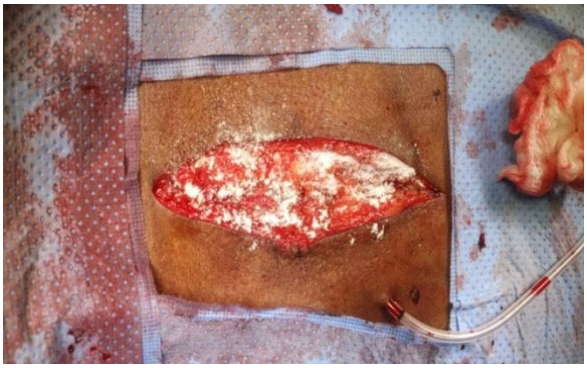

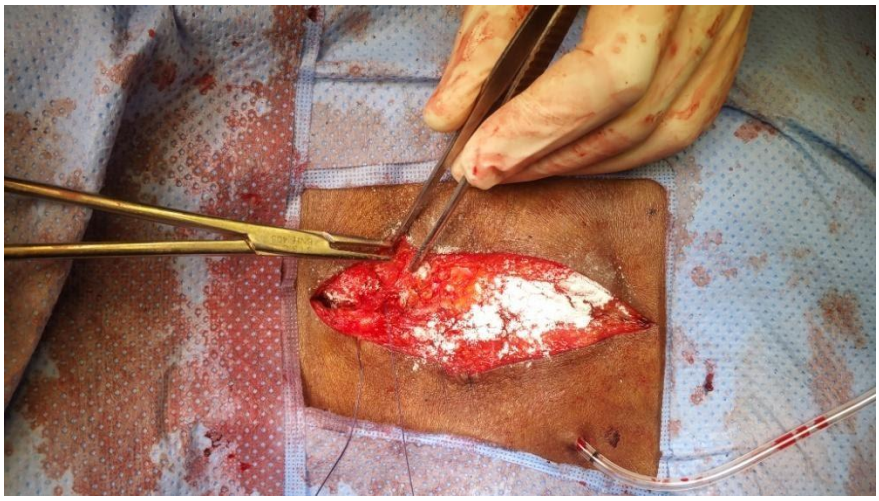

Figure 2: Application of vancomycin powder at the surgical site (subcutaneous and subfascial) before the wound closure

The wounds were closed with absorbable sutures for the fascia, subcutaneous layers and with staples for the skin. After skin closure, the incision was cleaned with betadine solution, and a sterile dressing will be applied.

Surgical drain was kept and maintained until the drainage volume less than 30 cc, and regular dressings were done until the stitches were removed.

The clinical demographics (age and gender), data on coexisting chronic diseases (diabetes, hypertension, and tuberculosis), history of tobacco use, and operative time for each patient are obtained from clinical data and the estimated blood loss, number of levels fused, were obtained from the operative data respectively.

All the patients were followed post operatively for 3 months and the frequency of follow up is for every 4 weeks. Clinical examination of surgical site wound is done for all patients on follow up visits. The patients who were found to have surgical site infections are adviced for complete hemogram including inflammatory markers (ESR,CRP),culture sensitivity of discharge, diagnostic imaging (MRI/contrast CT) and were treated accordingly by regular wound dressings and wound debridement.

Randomization sequence was generated before the start of the study by a computer generated set of random numbers. Treatment allocation was done by “opaque sealed envelope method”. Randomization was done in block of 20 (10 each in test and control groups respectively).

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SAMPLE SIZE CALCULATION:
Using 95% confidence interval and 5% margin of error, the sample size required was 118 (n) (www.calculator.net/sample size calculator). For logistic reasons sample size taken was 120 with 60 in arm A and 60 in arm B.

STATISTICAL ANALYSIS:
All continuous variables were described as means +/- SD and categorical variables were described as percentages.
Statistical analysis was performed using SPSS-20 for windows.
Fischers exact chi square test was used for comparing categorical variables.
Relationship between quantitative variables was assessed with Pearsons correlation and wherever appropriate students t test was used.

ETHICAL ISSUES:
The identity of the patient and his/her family was not revealed and an informed written consent was taken from each of them. The intraoperative administration of vancomycin powder is not a standard practice and the cost for vancomycin powder will not be paid by the patient and is availed from SBAVP scheme.

RESULTS

I. AGE DISTRIBUTION:

Mean age of presentation in test group was 38.3 yrs (range : 29-65 yrs) and in control group was 45.2 yrs (range : 25-69 yrs).

Table 4: Age Distribution

AGE	VANCOMYCIN GROUP	CONTROL GROUP
21-30	1	2
31-40	14	18
41-50	24	24
51-60	19	14
>60	2	2

In the present study , the female to male ratio was 3.6:1 (94 females, 26 males).

Table 5: Sex Distribution

SEX DISTRIBUTION	VANCOMYCIN GROUP	CONTROL GROUP
Male	12	14
Female	48	46

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RISK FACTORS:

1. TOBACCO USE:

Table 6: Tobacco Use

TOBACCO USE	VANCOMYCIN GROUP	CONTROL GROUP
Yes	4	3
No	56	57

- Seven out of one hundred and twenty patients had tobacco use in form of smoking as a modifiable risk factor.

2. ALCOHOLISM:

Only 5 of the patients were habituated to alcohol in the present study ,three from test group and two from control group.

Table 7: Alcoholism

ALCOHOL USE	VANCOMYCIN GROUP	CONTROL GROUP
Yes	3	2
No	57	58

HYPERTENSION:

10 out of 120 patients had hypertension, 5 each in test and control groups and the blood pressures were well normalised before operation in all the patients.

Table 8: Hypertension

HYPERTENSION	VANCOMYCIN GROUP	CONTROL GROUP
Yes	5	5
No	55	55

DIABETES MELLITUS (DM):

Only 5 out of 120 patients had DM and the blood sugars were normalised in all the patients before taking up for surgery.

Table 9: Diabetes mellitus (DM)

DM	VANCOMYCIN GROUP	CONTROL GROUP
Yes	2	3
No	58	57

PREVIOUS LUMBAR SURGERY:
None of the patients underwent prior lumbar surgery and so reoperation as the risk factor for SSI was not considered in the present study.

6. OTHER RISK FACTORS:

The following table gives information about non modifiable risk factors like tuberculosis, rheumatoid arthritis and hepatitis B .
One each in the control group had tuberculosis and rheumatoid arthritis respectively whereas one patient in the treatment group was found to be having hepatitis B.
None of the patients with these risk factors developed SSI.

Table 10: Non Modifiable Risk Factors

RISK FACTOR	VANCOMYCIN GROUP	CONTROL GROUP
TB	0	1
HBSAG	1	0
RA	0	1

CLINICAL FEATURES :

Most of the patients in the present study complained of low back ache and the most common neurological deficit encountered was motor weakness related to respective spinal segment.

Table 11: SYMPTOMS

SYMPTOMS	VANCOMYCIN GROUP	CONTROL GROUP
PAIN	60	60
WEAKNESS	20	25
SENSORY	25	47
BLADDER AND BOWEL	0	0

Table 12: SIGNS

SIGNS	VANCOMYCIN GROUP	CONTROL GROUP
MOTOR DEFICIT	32	28
SENSORY DEFICIT	0	0
MOTOR + SENSORY	25	30
NO DEFICIT	3	1

The results related to the neuronal deficits were not statistically significant as the p value obtained was 0.4418 with chi square test.

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V. Levels of fusion:

In the test group 53 single level fusions and 7 two level fusions were done whereas in control group 55 single level fusions, 3 two level fusions and 2 three level fusions were done.
Number of levels of fusion did not influence the development of SSI as they were all noticed in single level fusion surgeries.

Tab 13: LEVELS OF FUSION

NUMBER	VANCOMYCIN GROUP	CONTROL GROUP
SINGLE LEVEL	53	55
TWO LEVEL	7	3
THREE LEVEL	0	2

TABLE 14 : LEVEL OF FUSION

Level of fusion	VANCOMYCIN GROUP	CONTROL GROUP
L3-4	4	5
L4-5	31	36
L5-S1	18	14
L3-4,L4-5	5	3
L4-5,L5-S1	2	0
L3-4,L4-5,L5-S1	0	2

P value obtained for the above factor was not significant statistically (P=0.3782) as the number of levels of fusion were not related to the development of SSI.

VI. ESR AND CRP LEVELS:

Post-operative ESR and CRP levels showed a wide range i.e, 4-120 mm/1st hr and <6 ->24 mg/l in both the groups but the increase and decrease in these values were not clinically and statistically significant.

TABLE 15 : TOTAL WBC COUNTS, ESR AND CRP VALUES:

Factor (Mean)	Present study	P value
TOTAL COUNT (WBC)	TEST CONTROL	
PREOPERATIVE	10745 12303	0.872 (NS)
POD 3	11191 12820	0.535 (NS)
ESR (MM/HR)		
PREOPERATIVE	26.39 19.96	0.682 (NS)
POD 3	20.49 22.07	0.564 (NS)
CRP (MG/L)		
PREOPERATIVE	11.01 11.68	0.467 (NS)
POD 3	12.98 12.82	0.382 (NS)

The patients who developed SSI in the present study had elevated ESR and CRP levels at the time of their presentation which were normalised after appropriate treatment.

Table 16: Mean operative time and EBL:

RESULT	VANCOMYCIN GROUP	CONTROL GROUP	p VALUE
Surgical site infection, n (%)	2	1	-
Mean operation time, min	239.6 ±24.71	221.25±26.31	0.0002(NS)
Estimated blood loss (EBL) mL	87.4	88.08	0.8762(NS)

Mean operative time for both the groups were found to be insignificant by paired t test.
There was no significant correlation between mean operative time, EBL and development of SSI in the present study.

VII. FOLLOW UP :
The mean duration of follow up was 1 year 3 months (range : 1 year – 1.6 yrs)

Table 17 : SSI RATE

SSI	VANCOMYCIN GROUP	CONTROL GROUP
SUPERFICIAL SSI	0	1
DEEP SSI	2	0

The p value for SSI incidence in this study was 0.5620 by Z test for proportion.
This implies that the incidence of SSI in test group might be an incidental finding due to low sample size and further large volume studies are needed to know the efficacy of topical vancomycin powder in reducing the SSI**.**
During follow up two of the patients in test group presented with recurrence of low back ache 8 months and 1 month after operation respectively.
The first patient presented with severe low back ache with numbness of both lower limbs. He was diagnosed to have deep SSI and implant removal was done by reoperation The organisms isolated from the surgical cultures (pus) on reoperation in the first case was staphylococcus aureus and staphylococcus hemolyticus both being sensitive to antibiotic Linezolid which was administered in time. Post operatively patient gradually improved by his symptoms and he was on regular follow up till date with no further complications.
The other patient who developed SSI in test group presented with severe low back ache one month after surgery and his ESR levels were elevated .Patient was started on empirical antibiotic therapy (Linezolid) for which pain was subsided and patient was on regular follow up till date without other complications.
One of the patients from control group presented with surgical site discharge one month after operation . This patient was diagnosed to have superficial SSI and was managed by regular dressings with appropriate antibiotics.

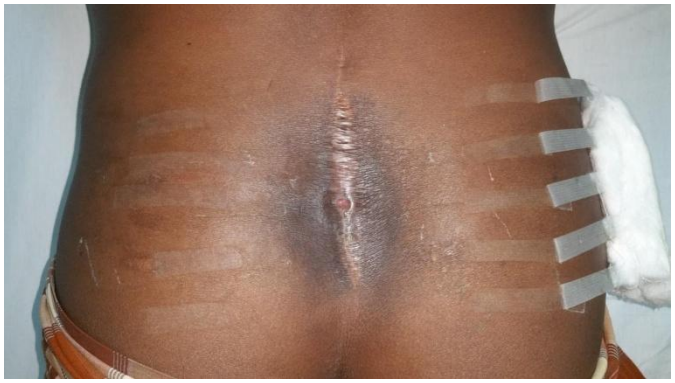
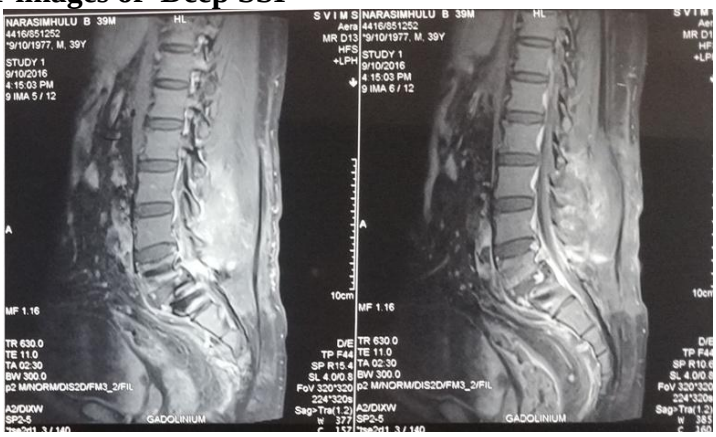


Figure 1 : Clinical picture of deep SSI

Fig 2 : MRI and CT images of Deep SSI



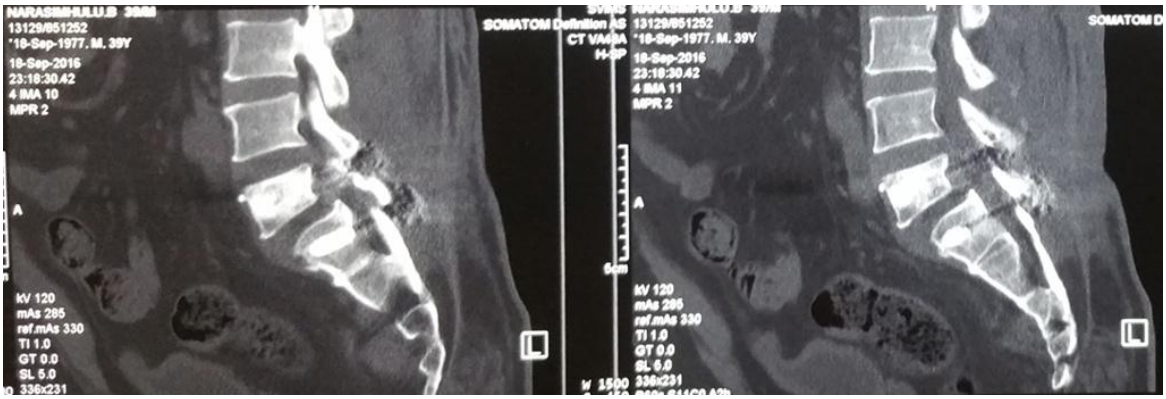


Fig 13: Intraoperative picture of deep SSI showing implant removal

Fig 4: Postoperative picture showing healed wound

DISCUSSIONS

Our study was intended to evaluate the use of topical application of vancomycin powder in reducing SSI in instrumented spinal fusion surgeries.

Number of patients enrolled in the present study was 120 which was near similar to the study conducted byMolinari et al[8]

The present study showed a female predominance with a ratio of 3.6:1.A similar predominance was observed in the study conducted by Heller et al.[6]

In the present study mean age of the patient in the present study was 41.7 yrs which was less when compared to studies conducted by Caroom et al (57.6 yrs)[12]In the present study the association of preoperative risk factors (DM, HTN,smoking,alcohol) in development of SSI doesn't seem to be significant as most of the patients with these risk factors did not develop SSI and only one patient with such infection had both smoking and alcoholism as risk factors.

Similar finding was noted in the study conducted by Strom et al[11] and Caroomet al [12]wherein patients without these risk factors developed SSI.

None of the patients in the present study had history of prior lumbar surgery .In the study conducted by Strom et al [11][53]only one patient (total 110) was documented with such history and there was no correlation of this factor to the development of SSI in this patient.

In the present study, motor deficits were seen in 32 patients of test group and 28 patients of control group whereas both motor and sensory deficits were seen in 25 and 30 of test and control groups respectively.

Table: 18 Comparision of deficits:

Deficit	Strom et al [11](Test,control)	Present study (Test,control)
SENSORY	5,8	0,0
MOTOR	6,11	32,28
MOTOR+SENSORY	11,9	25,30
None	34,26	3,1

Mean number of levels of fusion in both test and control groups (1.13,1.11) were less in the present study relative to studies conducted Strom et al [11], caroom[59] et al.[12] This difference is due to more number of single level fusions in the present study.

Table :19Comparision of mean levels of fusion:

Study	Test	Control
Strom et al [11]	**4.8**	**4**
Caroom et al [12]	**5.2**	**4.6**
Present study	**1.13**	**1.11**

The following table gives information about Mean operative time and EBL when compared to other studies.

Table 20: Comparision of mean operative time :

Mean operative time (mts)	Test	Control
Caroom et al [12]	**267**	**275**
Strom et al [11]	**257**	**185**
Present study	**238.6**	**221.2**

The Mean operative time and EBL in studies conducted by Caroom and Brain et al were relatively more compared to the present study which might be attributed to more number of spinal fusions done in these studies.(5.2,4.8)

The organism that was isolated from patients with SSI in the present study are staphylococcus aureus and staphylococcus hemolyticus which were very similar to the studies conducted by Heller et al [6](1992) and Abhijeet et al [7] (2016).[8]

SSI:

The following table gives information that the incidence of SSI was low in test group in the studies conducted by, Nicolas et al [9] whereas in the recent study of Bo-Kyung et al [10]the incidence of SSI was more in test group which was similar to the present study.

In the present study, the incidence of SSI in the test group were more when compared to control group and the risk factors like diabetes, hypertension, smoking, alcoholism ,prior lumbar surgery, duration of surgery were not significant in development of these infections and topical vancomycin application did not reduce infections in two of these patients.

Major limitations in the present study were low sample size and short follow up periods and so further large volume studies with longer follow up periods are needed to know the efficacy of topical application of vancomycin powder in spinal fusion surgeries.

CONCLUSIONS

In the present study topical application of vancomycin powder did not reduce the incidence of SSI and therefore we propose that further large volume studies are needed to authenticate the liberal use of its application in instrumented spinal fusion surgeries.

ACKNOWLEDGMENT

The author is thankful to Department of Neurosurgery for providing all the facilities to carry out this work.

Conflict of Interest

The authors declare that they have no conflict of Interest

Funding Support

Nil

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