

# The Treatment and Prophylaxis Usage Profile of Intravenous Vancomycin Medication in Orthopedics

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## Research article

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# Abstract

**Background:** Despite vancomycin has been widely used in orthopedics, the details of vancomycin usage in orthopedics remains unknown. The purpose of the study was to evaluate the usage profile of intravenous vancomycin medication in orthopedics.

**Methods:** The medical records of inpatients receiving intravenous vancomycin medication from January 2015 to December 2019 in a single center of orthopedics department were retrospectively reviewed. The gender, age, diagnosis, surgical information, microbiological data, duration of vancomycin medication were collected. The related data were analyzed and compared between subgroups.

**Results:** A total of 258 cases receiving intravenous vancomycin medication ( $\geq 3$  days) were enrolled. The mean age was 57.3 years. There were 141 cases in treatment and 117 in Prophylaxis group. The mean duration of vancomycin medication was 11.2 days. The duration was longer in Treatment than Prophylaxis group (14.8 versus 6.9 days,  $P < 0.05$ ). The main reasons for treatment were PJI after TKA (46.7%) and THA (18.2%) in Joint subgroup and SSI after spine surgery (51.5%) for Spine subgroup. For prophylaxis usage, the main reasons were postoperative clinical suspicious infection. The bacteria responsible for infections in Treatment group were *S. epidermidis* (34.6%), *S. aureus* (31.8%), other *Staphylococcus* (12.1%), MRSA (7.5%), *Streptococcus* (7.5%), *Enterococcus faecalis* (3.7%) and *Bacillus* (2.8%).

**Conclusion:** Taken together, our research firstly revealed the treatment and prophylaxis usage profile of intravenous vancomycin medication in orthopedics. It provides the different purposes, main causes, bacteriological data and medication duration for treatment and prophylaxis vancomycin usage in orthopedics.

## Background

Vancomycin is a glycopeptide antibiotic with bacteriostatic activity that has been used since the mid-1950s to treat Gram-positive bacterial infections [1]. Most clinicians use vancomycin for both empiric and definitive therapy of serious infections as outlined in Infectious Diseases Society of America treatment guidelines [2]. Vancomycin has been regarded as the first-line antibiotic in the treatment of *S. aureus* strains that produce penicillinase, especially for methicillin-resistant *Staphylococcus aureus* (MRSA) [3].

Vancomycin has been widely used in orthopedics because of the high incidence of device-associated infections and surgical site infection (SSI), which are especially difficult to treat since bacteria attach to the implant surface and form so-called biofilm colonies [4]. For the osteoarticular infections, Gram-positive bacteria are much more frequently isolated than Gram-negative bacteria, and among Gram-positive bacteria the proportion of staphylococcal strains was 74.2% [5], most of which are sensitive to vancomycin.

In order to prevent or treat the infection in orthopedics, vancomycin has often been the priority due to its wide coverage of the microbes most prevalent in SSI following spine and joint surgery [6]. However, the details of vancomycin use related with treatment and prophylaxis in orthopedic remain unknown. To evaluate the usage profile of intravenous vancomycin medication in orthopedics, including the duration, bacteriological relevance, the current retrospective study was conducted.

## Methods

We retrospectively reviewed the records of the inpatient population received intravenous vancomycin medication between January 2015 and December 2019 in orthopedics center.

Patients who received successive intravenous vancomycin medication for at least 3 days in the wards of orthopedic department were included. The following available information was collected retrospectively from medical records: gender, age, diagnosis, surgical information, microbiological data, duration of vancomycin medication. According to the purpose of vancomycin use and microbiological data, the cases was divided into Treatment and Prophylaxis subgroups. Treatment refers to medication for the cases of proven infection with positive bacteria culture or clinical definite infectious disease without bacteria culture test or with negative bacteria culture. Prophylaxis refers to medication for cases of suspicious infection without bacteria culture test or with negative bacteria culture.

All the cases suffered from either joint or spine diseases in a single orthopedic department. According to the localization and type of the infection and disease, the cases were divided into Joint and Spine subgroups. According to whether there was bacteria (BAC) culture test, the cases were divided into BAC culture (+) and (-) subgroups. If the result of BAC culture was positive, it was defined as BAC (+), otherwise BAC (-).

## Statistical Analysis

Means and standard deviations were calculated for age, duration of vancomycin mediation. Differences between subgroups parameters were determined by the independent-sample T test.  $P \leq 0.05$  was considered as statistically significant. Statistical measures were performed using Statistical Package for Social Science (SPSS, 19.0).

## Results

### Patients Population

The present study was composed of a group of 258 patients receiving intravenous vancomycin medication in a single orthopedic center (123 male and 135 female). The patients' characteristics are summarized in Table 1. The mean age was 56.3 years. There were 141 cases in Treatment group and 117 cases in Prophylaxis group. The mean age was 58.0 and 54.2 years for Treatment and Prophylaxis subgroups respectively. There were 137 cases in Joint group and 121 cases in Spine group. For all the

258 cases, duration of vancomycin medication was 11.2 days. The mean duration of vancomycin medication was longer in Treatment than Prophylaxis group (14.8 versus 6.9 days,  $P < 0.05$ ).

Table 1  
Demographic for all the cases

	All the cases	Treatment Group	Prophylaxis Group
<b>Number of cases (n)</b>	258	141	117
<b>Sex (M/F) (n)</b>	123 / 135	74 / 67	49 / 68
<b>Age (yr)</b>	56.3 ± 13.8	58.0 ± 13.9	54.2 ± 13.5
<b>Joint/Spine subgroups (n)</b>	137 / 121	76 / 65	61 / 56
<b>Duration of medication (d)</b>	11.2 ± 8.4	14.8 ± 9.6 *	6.9 ± 3.1*
* significant statistical difference ( $P < 0.05$ )			

## Reasons for vancomycin use

In Treatment group, the main reasons for the cases receiving intravenous vancomycin treatment were postoperative SSI. For Joint subgroup, the main reasons were PJI (periprosthetic joint infection) after TKA (total knee arthroplasty) (36/77, 46.7%), PJI after THA (total hip arthroplasty) (14/77, 18.2%), SSI after other joint surgery (14/77, 18.2%) and other bone and joint infection (13/77, 16.9%). For Spine subgroup, the main reasons were superficial and deep SSI after spine surgery (34/66, 51.5%), followed by intervertebral space and paraspinal tissue infection (32/66, 48.5%) (Fig. 1).

For Prophylaxis group, the main reasons for vancomycin use were clinical signs of postoperative suspicious infection, including incision extravasating, pyrexia, extreme increase of blood inflammatory index, including WBC, CRP and ESR.

## Bacteriological data for treatment vancomycin use

In Treatment group, there were 132 cases with BAC culture (+) and 9 cases with BAC culture (-). The pathogenic detection rate was 93.6%. Out of 132 patients with BAC culture (+), 107 (81.1%) turned out to have a bacteriological proof of infection as BAC (+). The mean duration of vancomycin treatment was 13.8, 14.9, 15.5, 12.2 days for BAC culture (-), BAC culture (+), BAC (+) and BAC (-) subgroups and there was no statistically significant difference ( $P > 0.05$ ).

For Treatment group, there were 76 and 65 cases in Joint and Spine subgroups. There was no significant difference of duration between Joint and Spine subgroup (15.6 versus 13.8 days,  $P > 0.05$ ). When comparing the Joint and Spine subgroups, the treatment duration for the cases of BAC culture (-), BAC culture (+), BAC (+) and BAC (-) subgroups were also similar without no significant difference ( $P > 0.05$ ).

All the 107 patients with BAC (+) in Treatment group were infected with Gram-positive bacteria, including *S. epidermidis* (n = 37, 34.6%), *S. aureus* (n = 34, 31.8%), other *Staphylococcus* (n = 13, 12.1%), MRSA (n =

8, 7.5%), Streptococcus (n = 8, 7.5%), Enterococcus faecalis (n = 4, 3.7%) and Bacillus (n = 3, 2.8%). All the bacteria for infections were sensitive to vancomycin. The detailed bacteriological data was shown in Fig. 2.

## Vancomycin treatment for infections of *S. epidermidis*, *S. aureus* and MRSA

For all cases in Treatment group, the duration of vancomycin treatment was longer for MRSA than *S. epidermidis* (22.9 versus 14.7 days, P = 0.03) and *S. aureus* (22.9 versus 16.5 days, P = 0.14).

For Joint subgroup, out of 61 cases with BAC (+), the infection was mostly due to *S. aureus* (n = 24, 39.3%), *S. epidermidis* (n = 20, 32.8%) and MRSA (n = 4, 6.6%). The duration was also longer for MRSA than *S. epidermidis* (23.8 versus 13.4 days, P = 0.03) and *S. aureus* (23.8 versus 17.1 days, P = 0.26) in Joint subgroup.

For Spine subgroup, out of 46 cases with BAC (+), the infection was mostly due to *S. epidermidis* (n = 17, 37.0%), *S. aureus* (n = 10, 21.7%), and MRSA (n = 4, 8.7%). There was no statistically significant difference of duration between MRSA and *Staphylococcus epidermidis* and *S. aureus* (P>0.05) in Spine subgroup. The data of vancomycin medication duration for cases of Treatment group were shown in Table 2.

Table 2  
Duration of vancomycin medication for the cases in Treatment group

	All the cases		Joint		Spine	
	No. (n)	Duration (d)	No. (n)	Duration (d)	No. (n)	Duration (d)
<b>Average</b>	141	14.8 ± 9.6	76	15.6 ± 9.8	65	13.8 ± 9.4
<b>Male</b>	74	14.5 ± 9.1	34	16.3 ± 10.2	40	13.1 ± 8.0
<b>Female</b>	67	14.9 ± 10.2	42	15.1 ± 9.6	25	15.0 ± 13.4
<b>BAC culture (-)</b>	9	13.8 ± 9.9	4	13.8 ± 9.0	5	13.8 ± 11.7
<b>BAC culture (+)</b>	132	14.9 ± 9.6	72	15.7 ± 9.9	60	13.8 ± 9.3
<b>BAC (+)</b>	107	15.5 ± 10.4	61	16.4 ± 10.3	46	14.2 ± 10.3
<b>BAC (-)</b>	25	12.2 ± 4.8	11	11.8 ± 6.1	14	12.6 ± 3.5
<b><i>S. epidermidis</i></b>	37	14.7 ± 9.8 *	20	13.4 ± 7.4 #	17	16.2 ± 12.1
<b><i>S. aureus</i></b>	34	16.5 ± 11.2	24	17.1 ± 10.5	10	15.2 ± 13.2
<b>MRSA</b>	8	22.9 ± 9.1 *	4	23.8 ± 12.3 #	4	22.0 ± 6.2
* # significant statistical difference (P<0.05)						

# Vancomycin use in Prophylaxis group

In Prophylaxis group, there were 39 cases with BAC culture (+) and 78 cases with BAC culture (-). The pathogenic detection rate was 33.3%. Out of 39 patients with BAC culture (+), only 2 (5.1%) turned out to have a bacteriological proof of infection as BAC (+), which were both in Spine subgroups and infected with Escherichia coli. The mean duration of vancomycin medication was longer for cases with BAC culture (+) than BAC culture (-) (8.2 versus 6.2 days, P = 0.0011). There was no significant difference of duration between BAC(+) and (-) (P>0.05).

For Prophylaxis group, there were 61 and 56 cases in Joint and Spine subgroups. There was no significant difference of duration between Joint and Spine subgroups (6.5 versus 7.3 days, P = 0.16). The mean duration of vancomycin medication was longer for cases with BAC culture (+) than BAC culture (-) in both Joint (7.9 versus 5.8 days, P = 0.0011) and Spine subgroups (8.4 versus 6.7 days, P = 0.0332). The data of vancomycin medication duration for cases of Prophylaxis group were shown in Table 3.

Table 3  
Duration of vancomycin medication for the cases in Prophylaxis group

	All the cases		Joint		Spine	
	No. (n)	Duration (d)	No. (n)	Duration (d)	No. (n)	Duration (d)
<b>Average</b>	117	6.9 ± 3.1	61	6.5 ± 3.3	56	7.3 ± 2.9
<b>Male</b>	49	7.0 ± 3.5	28	6.8 ± 3.9	21	7.3 ± 3.0
<b>Female</b>	68	6.8 ± 2.8	33	6.2 ± 2.7	35	7.3 ± 3.0
<b>BAC culture (-)</b>	78	6.2 ± 2.1 *	42	5.8 ± 2.1 #	36	6.7 ± 2.2 ^
<b>BAC culture (+)</b>	39	8.2 ± 4.3 *	19	7.9 ± 4.8 #	20	8.4 ± 3.8 ^
<b>BAC (+)</b>	2	4.5 ± 0.7	0	-	2	4.5 ± 0.7
<b>BAC (-)</b>	37	8.4 ± 4.3	19	7.9 ± 4.8	18	8.8 ± 3.7
* # ^ significant statistical difference (P<0.05)						

## Discussion

Sixty years after its introduction into clinical practice, vancomycin continues to be recommended intravenously as a treatment for severe and complicated infections and is the most common antibiotic agent used against perioperative infections when no other antibiotic was available[7]. The implant-associated and SSI are among the most dreaded complications encountered by orthopedic surgeons, which are associated with increased length of hospital stay, decreased patient satisfaction, and increased morbidity and mortality[8]. All these reasons further popularized the usage of vancomycin in orthopedics.

The infection related with orthopedic surgery cause high medical, economic, and social costs. In one study of 36 patients with SSI after lumbar fusion surgery, treatment of SSI required an average of 2.1 operations per patient, and a total of 1121 days of extra hospitalization [9]. The Gram-positive bacteria, especially Staphylococcus were the most frequent causes of these orthopedic-related infections. In many parts around the world, around 80% of *S. epidermidis* isolated from hospitalized patients are resistant to methicillin [10]. In addition, the low cost of vancomycin and easy accessibility than other antibiotics also makes it a very attractive option, especially in developing countries [11].

The current study revealed that the main reasons for the orthopedic patients receiving intravenous vancomycin treatment were postoperative SSI for treatment. For the prophylaxis purpose, the most common reasons focus in postoperative suspicious infection with clinical signs, such as incision problem, pyrexia, extreme increase of CRP and ESR. The eradication of infections in orthopedics often requires long-term therapy for a duration of intravenous vancomycin usage [8, 12]. The mean duration of vancomycin medication was longer in Treatment than Prophylaxis group in our study.

Most of the spine and joint surgery are involved with biomedical implants, including spinal pedicle screw and joint prosthesis, which eases the development and progression of SSI. The SSI after spine surgery was the most common cause (51.5%) for vancomycin treatment medication in our study. According to a study involve a large group of more than 108,000 patients, superficial and deep SSI after spine surgery were found in 0.8% and 1.3% of patients, respectively [13]. A meta-analysis [14] revealed that the rates of *S. aureus*, *S. epidermidis* and methicillin-resistant Staphylococci for SSI after spine surgery were 37.9%, 22.7% and 23.1%, respectively. For genus level, the rates of Staphylococcus, Enterococcus, Streptococcus were 50.2%, 8.2% and 6.9%, respectively. Some authors also reported that the microbiology of SSI in spine surgery is predominantly *S. aureus* and *S. epidermidis* [15, 16]. In the current study, for the cases in the Spine group, the infection was mostly due to *S. epidermidis* (37.0%), *S. aureus* (21.7%), and MRSA (8.7%).

Many reports have revealed that Gram-positive cocci, especially *S. aureus* and coagulase-negative staphylococci (CNS) were the most common infective organisms for PJI [17–19]. Empirical antibiotic treatment of early PJIs include coverage of vancomycin was recommended until definitive culture results become available [20]. In a prospective cohort study of microbiologic epidemiology of PJI, the results revealed 28.9% of *S. aureus*, 28.6% of CNS, 14.1% of Enterobacteriaceae and 13.1% of streptococci [21]. In our research, the cases in Joint subgroup receiving vancomycin were mostly PJI after TKA and THA, followed by SSI after other joint surgery. These infections were mostly due to *S. aureus* (39.3%), *S. epidermidis* (32.8%) and MRSA (6.6%).

In the current study, *S. epidermidis* was the main cause for spine cases receiving vancomycin treatment, which was different from *S. aureus* responsible for joint cases. The microbiological results were consistent with previous reports related with PJI and SSI after spine surgery. In addition, the duration of vancomycin treatment was longer for MRSA than *S. epidermidis* ( $P = 0.03$ ) and *S. aureus* ( $P = 0.14$ ).

Empirical vancomycin treatment should be stopped when available culture results fail to reveal  $\beta$ -lactam-resistant Gram-positive bacterial infections. So, it is regarded as inappropriate that the empirical

vancomycin use is continued for a proportion of patients [22]. Misan et al reported that 97% of the patients receiving vancomycin for prophylaxis purposes were classified as inappropriate use [23].

No matter treatment or prophylactic medication, vancomycin, as an antibiotic, was used to achieve the ultimate goal of eradicating infection. For the certain infection, vancomycin was used for the purpose of treatment. However, for some clinical suspicious infection, it was also important and urgent to use vancomycin to prevent the infections and avoid serious consequences. Based on the HICPAC criteria, vancomycin use was documented to be treatment and prophylactic in 89.4% and 10.6% patients, respectively [11].

In the current study, 54.6% of the cases were for treatment and 45.4% were for prophylaxis. Prophylaxis medication should target the most common organisms for SSI in orthopedics, including *S. aureus* and *S. epidermidis*[24]. However, the bacterial culture may be negative in some infection cases. In 23.2% of patients with PJI, no bacteria were detected despite clinical suspicion of an infection [25]. Given the disastrous consequences of SSI following joint and spine surgery, vancomycin was still continued until the clinical sign of infection was alleviated.

There were also some limitations for the study. First, this was the retrospective study in single center with limited cases number. As for the investigation of drug usage, a large number of cases from multicenter could be more important and convincing. Second, as regard to the prophylaxis mediation of intravenous vancomycin in our study, some controversy maybe exist and need further analysis. A perfect monitor system could be set and maybe a good method to monitor and guide the standardized vancomycin use.

## Conclusion

In order to prevent or treat the device-related and SSI, intravenous vancomycin is often used for the purpose of treatment or prophylaxis. Taken together, our research firstly revealed the treatment and prophylaxis usage profile of intravenous vancomycin medication in orthopedics. It provides the different purposes, main causes, bacteriological data and medication duration for treatment and prophylaxis vancomycin usage in orthopedics. The studies of larger scale from multicenter are needed to better analysis and guide the rational vancomycin use.

## Abbreviations

MRSA

methicillin-resistant *Staphylococcus aureus*; SSI:surgical site infection; BAC:bacteria; PJI:periprosthetic joint infection; TKA:total knee arthroplasty; THA:total hip arthroplasty

## Declarations

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### **Authors' contributions**

LW, ML and LQ planned and designed the study. LW and YJ extracted and analyzed the data. ML and LQ interpreted the results. LW and LQ drafted the manuscript. All authors critically reviewed and approved the final version of the manuscript.

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### **Competing interests**

The authors declare no conflicts of interest related to this work.

### **Availability of data and materials**

The data used and analyzed during the current study are available from the corresponding author upon request.

### **Consent for publication**

Not applicable.

### **Ethics approval and consent to participate**

Ethical approval for the study was approved by the Ethics Committee of our institute (Qilu Hospital of Shandong University) and the data were retrospectively collected and no identifiable patient data was presented in the study.

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## Figures

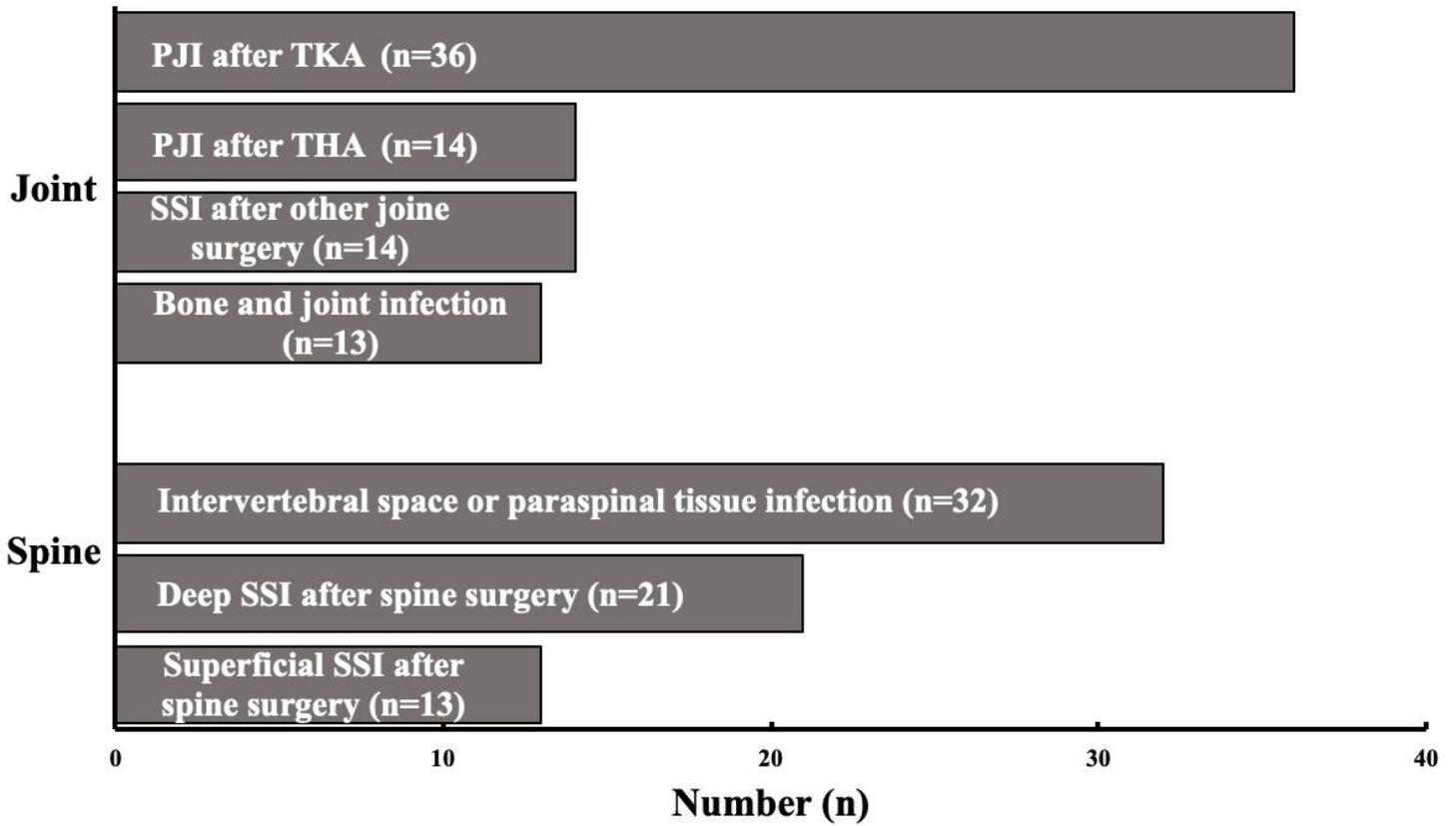
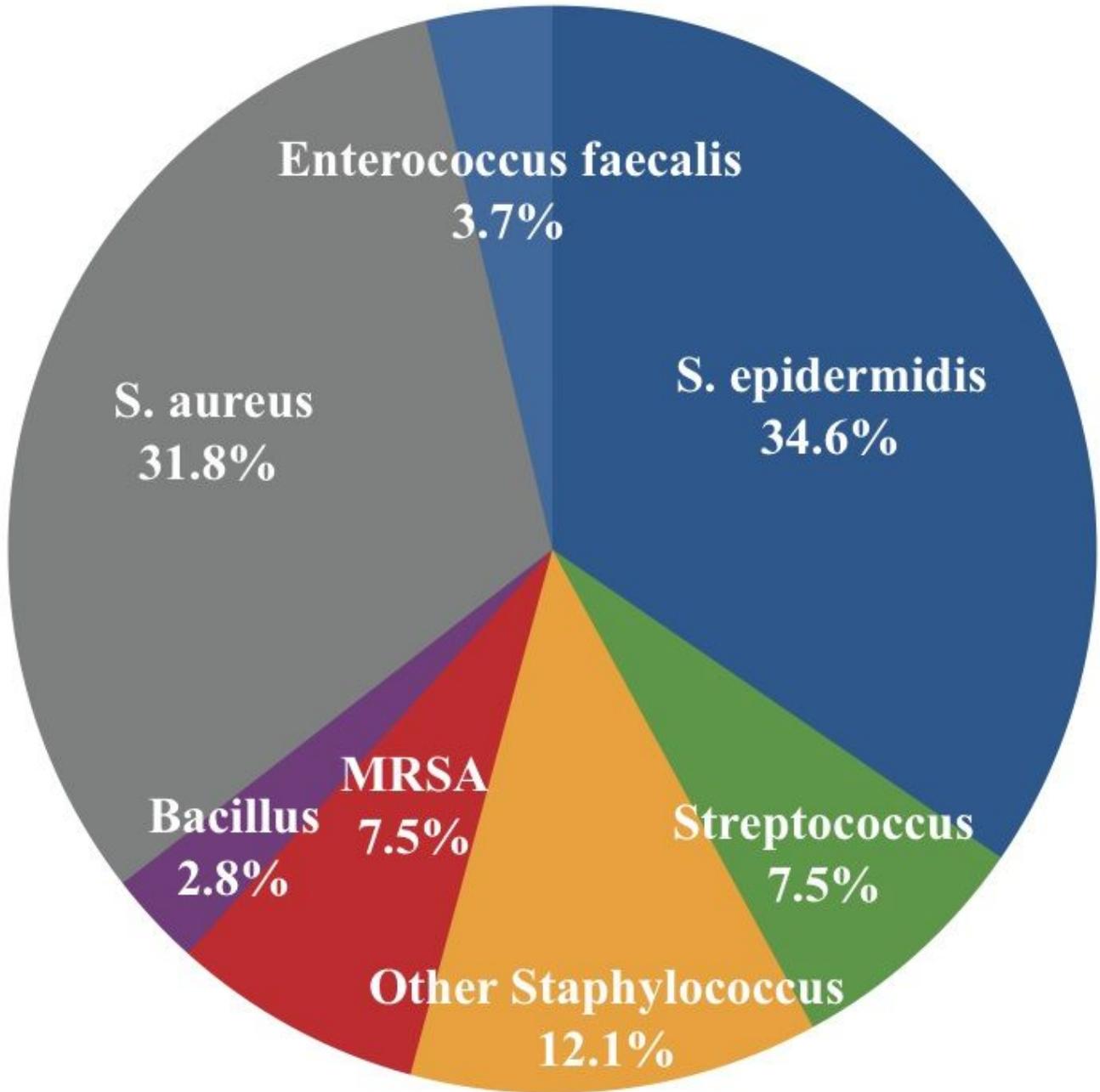


Figure 1

The main reasons for the cases receiving intravenous vancomycin medication in Treatment group.



**Figure 2**

The detailed bacteriological results for the cases with BAC(+) in Treatment group.