Original Article

Yonsei Med J 2023 Mar;64(3):213-220
https://doi.org/10.3349/ymj.2022.0546

Yonsei Medical Journal
YMJ
pISSN: 0513-5796 · eISSN: 1976-2437

How Does Medical Policy on the Use of Prophylactic Antibiotics Affect Medical Costs, Length of Hospital Stay, and Antibiotic Use in Orthopedics?

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Purpose: The purpose of this study was to compare patients who had undergone spine surgery (SS) and hip arthroplasty surgery (HAS) and to analyze how medical policies drawn from "The Evaluation of the Appropriate Use of Prophylactic Antibiotics" have affected length of hospital stay (LOS), direct medical costs (DMC), and the duration of antibiotics use in Korea.
Materials and Methods: This retrospective nationwide study identified subjects from the Korean National Health Insurance Review and Assessment Service database from January, 2011 to December, 2018. Evaluation of HAS (control group) was implemented in 2007, and that for SS (case group) was conducted for the first time in 2014 (intervention time). In our comparative interrupted time series analysis, we compared DMC, LOS, and use of antibiotics between both groups.
Results: 177468 patients who underwent SS and 89372 patients who underwent HAS were included in the study. In 2016, DMC increased for HAS, compared to SS, by 1.03 times (p=0.041). However, cost changes during other observational periods for SS were not higher than those for HAS (p>0.05). SS incurred a reduced LOS of 3% in the first 2 years (p<0.05). Thereafter, LOS changes in SS were not smaller than those in HAS. A decrease in the usage of total antibiotics and broad spectrum antibiotics was observed for 5 years.
Conclusion: This medical policy was effective in terms of reducing usage and duration of antibiotics use, especially in the first 2 years after the implementation of the policy.

Key Words: Antibiotic prophylaxis, orthopedic surgery, medical policy

INTRODUCTION

Surgical site infection (SSI) is a major postoperative complication.[1] Patient-related risk factors for SSI include older age, obesity, smoking, diabetes, immunosuppressive disease, shock, hypothermia, and irradiation, and surgery-related risk factors are contaminated wounds, long operation time, or inadequate skin preparation.[2] Although hematogenous infection from internal organ rarely causes SSI, the most common source of infective organisms is a patient's skin.[3] In the orthopedic field, the most isolated organism is aerobic gram-positive cocci, especially *Staphylococcus aureus*, which often is resistant to methicillin.[3]

For prevention of SSIs, adequate management of patient-related risk factors in the perioperative period and appropriate surgical procedures, along with proper preoperative prophylactic antibiotics use, are essential.[4] In a systematic review of the effectiveness of antibiotic prophylaxis in patients undergoing hip and knee arthroplasty surgery, antibiotic prophylaxis reduced the risk of SSI by 81%, compared to the no prophylaxis.[5]

Received: December 19, 2022 **Revised:** January 9, 2023
Accepted: January 11, 2023 **Published online:** February 13, 2022
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•The authors have no potential conflicts of interest to disclose.

A meta-analysis also reported that the use of prophylactic antibiotics during spine surgery (SS) effectively reduced SSI rates.[6] Research indicates that preoperative prophylaxis should be administered within 30–60 minutes of skin incisions, because the concentration of antibiotics reaching the surgical site must be adequate during surgery to prevent SSI.[7,8] Therefore, in the field of orthopedics, antibiotic prophylaxis has become an important element of all surgical procedures.

In relation to medical policy, most research on the use of prophylactic antibiotics is reported in studies designed to secure evidence for the production of guidelines.[9] Although national antibiotic prophylaxis guidelines for surgery have been suggested and although the effects of such policy on the use of prophylactic antibiotics and the incidence of SSI have been analyzed, studies of effect on medical systems are rare, and a nationwide analysis has not been conducted.[10-13] In Korea, "The Evaluation of the Appropriate Use of Prophylactic Antibiotics" began in 2007 to raise interest in promoting SSI prevention and to motivate medical institutions to improve quality of care. Since then, target surgeries for adequacy evaluation have been added and are in progress. It is estimated that the government's medical political supervision on whether or not the use of antibiotics is properly used will elicit a change in the overall behavior of medical personnel regarding the use of antibiotics, as well as in infection prevention. Also, as in previous studies, we believe that it can affect health care quality indicators, such as medical costs and length of hospital stay (LOS).[14,15]

Therefore, the purpose of this study was to compare patients who had undergone SS and hip arthroplasty surgery (HAS) and to analyze how "The Evaluation of the Appropriate Use of Prophylactic Antibiotics" in the field of orthopedic surgery has affected hospitalization period, medical costs, and the amount and duration of antibiotics use.

MATERIALS AND METHODS

Data and patient sample

This retrospective nationwide study identified subjects from the Korean National Health Insurance Review and Assessment Service (HIRA) database from January 2011 to December 2018. The HIRA collects data from claims submitted by healthcare providers for reimbursement under Korea's universal healthcare insurance system, with a fee-for-service model that covers the entire South Korean population.[16] Information in the dataset includes all inpatient and outpatient medical claims data, including treatment procedure codes and diagnostic codes. Therefore, medical claims data for all spine and HASs that occurred during the study period were identified. The protocol of this study was approved by our Institutional Review Board (IRB No. 2021-12-011).

Intervention - evaluation of prophylactic antibiotics for SS

The HIRA in Korea has been conducting "Evaluation of the Appropriate Use of Prophylactic Antibiotics in Surgery" since 2007, and a total of eight evaluations were made up to 2018. This intervention is being conducted to prevent SSIs and to prevent misuse of antibiotics by selecting and administering prophylactic antibiotics that meet standards for clean and contaminated surgery. In addition, the policy seeks to improve the quality of medical services by giving incentives to hospitals with excellent results.

In the field of orthopedic surgery, HAS has been evaluated under the policy since it was first implemented in 2007. Evaluation of SS, however, was conducted for the first time from 2014. Thus, in order to evaluate "The Evaluation of the Appropriate Use of Prophylactic Antibiotics" for SS, patients who underwent SS were set as the case group in our study. Furthermore, the intervention time (time zero) was defined as 2014.

Identification of patients who underwent HAS (control group) or SS (case group)

Eligibility criteria for patients with hip fracture who underwent hip arthroplasty were as follows: 1) admission to an acute care hospital with diagnostic codes of femoral neck fractures [International Classification of Diseases, 10th Revision (ICD-10) S720] or intertrochanteric fracture (ICD-10 S721); 2) undergoing hemiarthroplasty or total arthroplasty. Eligibility criteria for patients who underwent SS were as follows: 1) admission to an acute care hospital; 2) undergoing thoracic or lumbar SS with procedure codes of posterior instrumentation, discectomy, or posterior decompression.

We excluded patients younger than 50 years of age at the time of surgery and those under the Medical Aid program to eliminate the possibility of incomplete information. Finally, to eliminate the impact of death on antibiotics use and medical costs, patients who died within 30 days of hospitalization for surgery were excluded.

Direct medical costs (DMC) and LOS per surgical episode

DMC and LOS per surgical episode were arranged in time series for 3 years before time zero and 5 years after time zero. DMC represents the sum of the amount paid by the National Health Insurance Service (NHIS) and the patient's co-payments for insured medical services, excluding uncovered payments. DMC includes all costs for inpatient care and drugs, as well as all components covered by the NHIS.[17] DMC was inflated to 2021 Korean won using the 2021 conversion index.[18] Finally, Korean won was converted to US dollars by applying an exchange rate of 1462 won per dollar. LOS per surgical episode was selected as a medical utilization outcome variable.

https://doi.org/10.3349/ymj.2022.0546

Use of antibiotics

Outcome variables to evaluate the effect of "The Evaluation of the Appropriate Use of Prophylactic Antibiotics" were total antibiotics usage within 30 days from admission and the duration of antibiotics use per surgical episode. Investigated antibiotics included 1st, 2nd, 3rd, and 4th generation cephalosporins, quinolones, and vancomycin. Among them, 3rd and 4th generation cephalosporins, quinolones, and vancomycin were defined as broad spectrum antibiotics. These variables were also arranged in time series for 3 years before time zero and 5 years after time zero.

Statistical analysis

In this comparative interrupted time series analysis, we compared DMC, LOS, and use of antibiotics between case and control groups.[19] Time series were constructed using the time unit of 1 month and were divided into six segments (before time zero and every year after time zero). Changes in baseline trends and intercepts were considered during the baseline period, but only intercept changes were considered in segments after the baseline period. We used a generalized linear model with a gamma distribution and logarithmic link function for segmented regression analysis adjusting for all baseline characteristics. We used a generalized estimating equation using a robust standard error to avoid overestimation of standard errors of the parameter estimates. All calculated *p*-values were two-sided, and *p*-values<0.05 were considered significant. All analyses were performed using SAS Enterprise Guide version 7.1 software (SAS Institute, Cary, NC, USA).

Baseline characteristics, including sex, age group, seasonality, type of hospital where surgery was performed (tertiary general hospital, general hospital, hospital), calendar year of surgery, Charlson Comorbidity Index (CCI), and past medical history, were investigated as covariates. Past medical history included the number of hospitalizations and outpatient visits within 3 years before spinal or hip surgery. CCI was calculated by weighting and scoring comorbid conditions using Quan's method, with additional points given to comorbidities that affect the health outcomes of patients.[20]

RESULTS

Study flow and baseline characteristics of the case and control groups

A total of 216432 patients who underwent SS and 109196 patients who underwent HAS from January 1, 2011 to December 31, 2018 met the inclusion criteria. Among them. 22326 patients under 50 years of age at the time of surgery were excluded (spine: 21178, hip: 1148). Of the remaining patients, 31716 patients under the Medical Aid program (spine: 15743, hip: 15973) were also excluded. Finally, 4746 people who died within 30 days of the episode start date (spine: 2043, hip: 2703) were excluded. Finally, 177468 patients who underwent SS and 89372 patients who underwent hip surgery were included in the study (Table 1). The mean age of the case group was 66.2 (±8.3) years, and the control group average age was 78.7 (±8.6) years. The proportion of males was higher in the case group (n=66977, 37.7%). Based on CCI, comorbidities were more common in the control group (*p*<0.001).

Differences in DMC and LOS

Considering the differential changes in DMC before time zero, DMC were slightly higher in the case group than those in the control group, but these differences were not significant until 2 years after the intervention (*p*>0.05) (Table 2). In 2016, DMC increased relatively significantly in the case group, compared to the control group, by 1.03 times {difference-in-difference (DID) estimate ratio of 1.03 [95% confidence interval (CI) 1.00 to 1.06]; *p*=0.041}. However, cost changes in the case group were not higher than those in the control group thereafter (*p*>0.05).

Considering the differential changes in LOS before time zero, we noted that the case group incurred a reduced LOS of 3% [DID estimate ratio of 0.97 (95% CI 0.95 to 0.99); *p*=0.011] after intervention. This relative decrease in LOS was maintained until 2015 [DID estimate ratio of 0.97 (95% CI 0.95 to 1.00); *p*=0.034]. Nevertheless, LOS changes in the case group were not smaller than those in the control group thereafter (*p*>0.05) (Table 2).

Trends in the use of antibiotics

The rates of 1st and 2nd generation cephalosporins use per year in both groups are shown in Fig. 1A. In the control group, the rates of 1st and 2nd generation cephalosporins use per year followed a slight upward trend in 2012 and then decreased. Thereafter, the rates of 1st and 2nd generation cephalosporins use per year remained horizontal. However, in the case group, the rates of 1st and 2nd generation cephalosporins use showed a sharp rise up to the intervention period, then slightly bent and then increased again.

In the control group, the rate of broad spectrum antibiotics use steadily decreased after the intervention (Fig. 1B). On the other hand, in the case group, the rate of broad spectrum antibiotics use sharply decreased from 2014 to 2015. However, an increase in the rate of broad spectrum antibiotics use was observed thereafter.

Fig. 2 shows the mean usage of broad spectrum antibiotics within 30 days of hospitalization for surgery and the duration of broad spectrum antibiotics use. In both groups, a decreasing trend was observed in the mean usage and duration of broad spectrum antibiotics use during the entire observation period. In particular, the mean usage and duration of broad spectrum antibiotics use in the case group at 2014 and 2015 decreased sharply, compared to the control group.

Differences in the use of antibiotics

Within 30 days after admission for surgery, total usage of antibiotics decreased significantly by 0.88 times [DID estimate ratio of 0.88 (95% CI 0.86 to 0.91); p<0.001] in the case group, compared to the control group, in 2014 considering the differential changes in usage of antibiotics before time zero (Table 3). This trend was observed for the whole observational period after intervention (p<0.05). The duration of use of antibiotics

Table 1. General Characteristics of the Study Population (n=266840)

Variables	SS (case group) (n=177468, 66.5%)	HAS (control group) (n=89372, 33.5%)	*p* value
Sex			<0.001
Male	66977 (37.7)	23306 (26.1)	
Female	110491 (62.3)	66066 (73.9)	
Age (yr)	66.2±8.3	78.7±8.6	<0.001
Age group			<0.001
50–59 year	42703 (24.1)	2947 (3.3)	
60–69 year	67650 (38.1)	9111 (10.2)	
70–79 year	59156 (33.3)	32164 (36.0)	
80–89 year	7840 (4.4)	37580 (42.0)	
>90 year	119 (0.1)	7570 (8.5)	
Month at the time of surgery			<0.001
January to March	45251 (25.5)	24170 (27.0)	
April to June	44304 (25.0)	21085 (23.6)	
July to September	42871 (24.2)	20426 (22.9)	
October to December	45042 (25.4)	23691 (26.5)	
Type of hospital where surgery was performed			<0.001
Tertiary general hospital	50235 (28.3)	18070 (20.2)	
General hospital	48078 (27.1)	47327 (53.0)	
Hospital	79155 (44.6)	23975 (26.8)	
Calendar year			<0.001
2011	20838 (11.7)	10538 (11.8)	
2012	22488 (12.7)	10955 (12.3)	
2013	21956 (12.4)	10935 (12.2)	
2014	21537 (12.1)	10949 (12.3)	
2015	22109 (12.5)	11251 (12.6)	
2016	23488 (13.2)	11222 (12.6)	
2017	22471 (12.7)	11578 (13.0)	
2018	22581 (12.7)	11944 (13.4)	
Charlson Comorbidity Index			<0.001
0	56481 (31.8)	25996 (29.1)	
1	49455 (27.9)	23136 (25.9)	
2	30883 (17.4)	15032 (16.8)	
>3	40649 (22.9)	25208 (28.2)	
Past medical history			
Number of admissions within 3 years before surgery			<0.001
None	73753 (41.6)	34406 (38.5)	
1 to 3	79530 (44.8)	33667 (37.7)	
4 or more	24185 (13.6)	21299 (23.8)	
Number of outpatient visits within 3 years before surgery			<0.001
0 to 50	52972 (29.8)	41299 (46.2)	
51 to 99	49448 (27.9)	23023 (25.8)	
100 or more	75048 (42.3)	25050 (28.0)	

SS, spine surgery; HAS, hip arthroplasty surgery.
Values are presented as numbers (%) or means±SD. *p*-values were obtained by chi-square test or t-test.

https://doi.org/10.3349/ymj.2022.0546

Table 2. Differential Changes in DMC and LOS after Implementation of "The Evaluation of Appropriate Use of Prophylactic Antibiotics" in Patients Undergoing SS

SS (case group) vs. HAS (control group)	Ratio (95% CI)	*p* value
Total DMC of the episode within 30 days*		
Ratio of baseline difference in DMC	0.81 (0.80–0.82)	<0.001
Ratio of DMC increase per month	0.998 (0.996–1.00)	0.040
Ratio of difference in the slope of the medical cost†	1.00 (1.00–1.00)	0.959
DID estimate‡		
2014 (initiation of evaluation)	1.01 (1.00–1.03)	0.158
2015	1.02 (1.00–1.04)	0.068
2016	1.03 (1.00–1.06)	0.041
2017	1.02 (0.98–1.05)	0.370
2018	1.03 (0.99–1.07)	0.167
Hospital LOS of the episode*		
Ratio of baseline LOS difference	0.81 (0.80–0.82)	<0.001
Ratio of LOS increase per month	0.99 (0.99–0.99)	<0.001
Ratio of difference in the slope of the LOS†	1.00 (1.00–1.00)	0.069
DID estimate‡		
2014 (initiation of evaluation)	0.97 (0.95–0.99)	0.011
2015	0.97 (0.95–1.00)	0.034
2016	1.00 (0.96–1.03)	0.782
2017	0.99 (0.96–1.03)	0.767
2018	1.02 (0.97–1.07)	0.396

DMC, direct medical costs; LOS, length of hospital stay; SS, spine surgery; HAS, hip arthroplasty surgery; DID, difference-in-difference.
*Indicators of the predicted graph for DMC (or LOS), considering the increase in DMC (or LOS) of both groups before 2014; †Slope difference: difference in the slope of the increase in DMC (or LOS) in the patients with SS and hip surgery; ‡DID estimate: the ratios of DMC (or LOS) at each time point, considering the difference in DMC (or LOS) before and after time zero in the case group and the difference in DMC (or LOS) before and after time zero in the control group.

also continued to decrease significantly during 5 years in the case group, compared to the control group ($p<0.05$).

Furthermore, total usage of broad spectrum antibiotics also decreased relatively by 8% in the 1st year after the intervention [DID estimate ratio of 0.92 (95% CI 0.87 to 0.97); $p=0.003$], and this trend remained significant until 2018 ($p<0.05$) (Table 4). The duration of use of broad spectrum antibiotics also continued to decrease significantly over 5 years in the case group, compared to the control group ($p<0.05$).

DISCUSSION

The main findings of our study are as follows. The first is that "The Evaluation of the Appropriate Use of Prophylactic Antibiotics" in orthopedic field reduced LOS and increased DMC in the short term after policy implementation, but had insignificant effects on LOS and DMC thereafter. The second is that the evaluation reduced not only the total usage and duration of antibiotics but also the total usage and duration of broad spectrum antibiotics and lasted for 5 years.

SSIs are preventable hospital-acquired infections that can increase LOS and DMC, as well as increase morbidity and mortality in patients.[21] A study that analyzed the effectiveness of antibiotic prophylaxis in elective caesarean section patients claimed that it was effective in reducing costs and the incidence of SSI.[22] They explain that this is because the cost of prophylactic antibiotics is lower than the cost of treating infected patients. Ng-Kamstra, et al.[23] reported that by using a protocol to control the duration of antibiotics use in patients with intra-abdominal infection, it was possible to reduce the use of daptomycin and lower medical costs, particularly for the use of antibiotics and the cost of laboratory testing for infection. The incidence of SSIs has been reported at 2.6% in a study of 1922 consecutive hip arthroplasty patients from 11 hospitals.[24] Also the incidence of

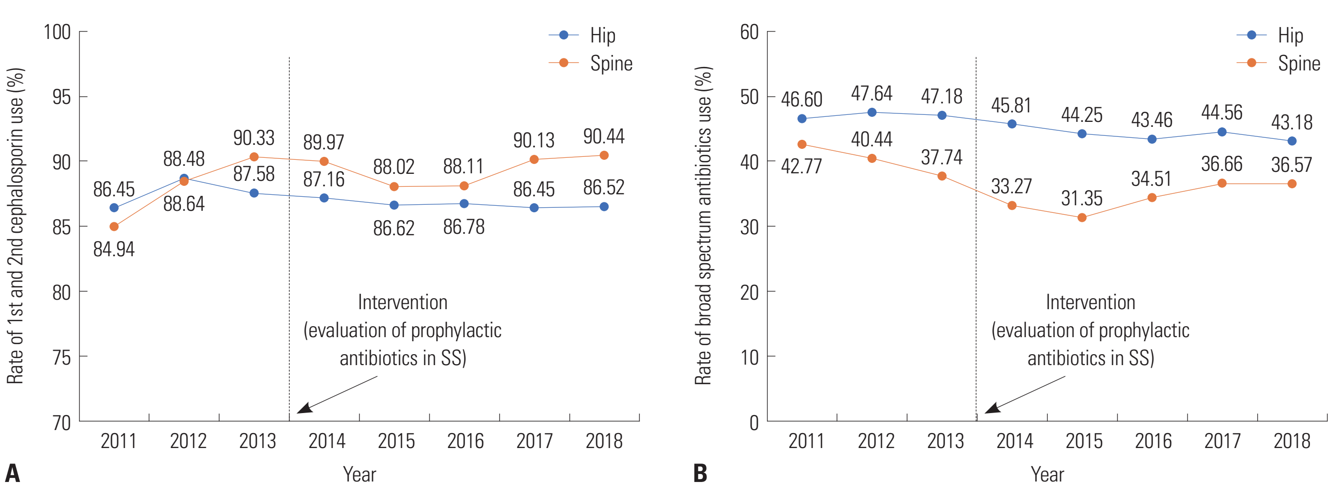

Fig. 1. Trends in the rates of 1st and 2nd cephalosporins (A) and broad spectrum antibiotics (B) use in spine surgery (SS) and hip arthroplasty before and after implementation of "The Evaluation of Adequate Use of Prophylactic Antibiotics."

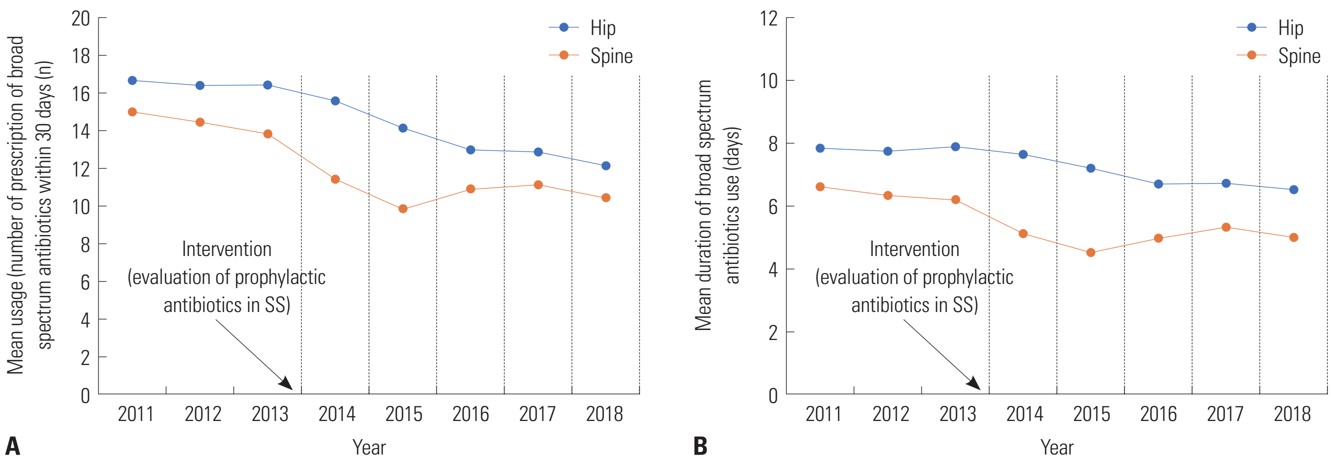

Fig. 2. Trends in the usage (A) and duration (B) of broad spectrum antibiotics use in spine surgery (SS) and hip arthroplasty before and after implementation of "The Evaluation of Adequate Use of Prophylactic Antibiotics."

postoperative SSIs after SS has been reported to range from 0.7% to 12%.[15] However, Stefánsdóttir, et al.[8] reported that less than 50% of patients in their institution received antibiotics within 15–45 minutes prior to initiation of surgery and that the adequacy of prophylactic antibiotics was observed in only about 57% of the Swedish knee arthroplasty register. Appropriate medical political controls for the use of prophylactic antibiotics in the orthopedic field appear to be necessary. Therefore, we estimated that SSIs would be prevented and that LOS and DMC would also be reduced if appropriate prophylactic antibiotics were used. However, after intervention, a significant increase was observed in DMC for SS at 2016, but no statistically significant difference was observed in the other observational period, compared to the control group. In addition, a decrease in LOS was observed only in a short period of about 2 years after intervention. Ikeda Kurakawa, et al.[14] reported that prophylactic antibiotic use in patients with acute pancreatitis increased LOS and increased medical costs in a nationwide inpatient administrative database. They argued that the side effects of the antibiotics were responsible for these results: antibiotics sometimes cause unintended consequences, such as allergy, the development of antibiotic resistance among organisms, acute kidney injury, and *Clostridium difficile* infection.[25] Therefore, discontinuation of prophylactic antibiotics within 24 hours of the completion of surgery is recommended.[26] Although the effect of evaluation in our study lasted up to 2 years, it was minimal at 3%. Thus, it is thought that long duration of antibiotics still induces complications of prophylactic antibiotics and offsets the effect of reducing LOS and DMC due to infection prevention.

Prophylactic antibiotics are now mandatory for patients to prevent SSI after surgery. First and second generation cephalosporins are the most commonly recommended antibiotics because they work well against commonly isolated pathogens, such as *Staphylococcus aureus* and *Staphylococcus epidermidis*. Also, they have the advantage of having a safety profile and low cost. Thus, several guidelines recommend them as primary prophylactic antibiotics, and vancomycin should only be used in patients with a beta-lactam allergy or infections with a high frequency of methicillin-resistant *Staphylococcus* species, such as *S. aureus* and *Staphylococcus epidermidis*.[21] A study in India reported that antibiotic use is on the rise despite a global trend of declining infectious diseases, reflecting antibiotic misuse, as well as health and economy burdens.[27] Skender, et al.[28] noted that private facilities often fail to implement proposed guidelines, although national prescription guidelines are applicable to both public and private healthcare facilities in India. Therefore, we believe that it is essential not only to suggest national prescription guidelines for prophylactic antibiotics use, but also to manage and supervise their implementation so that the effectiveness of the medical policy is sustained. In our study, "The Evaluation of the Appropriate Use of Prophylactic Antibiotics" in SS increased the usage rate of 1st and 2nd generation antibiotics in patients who underwent SS and decreased the usage rate of broad-spectrum antibiotics. In SS, the usage and duration of total antibiotics, as well as the usage and duration of broad spectrum antibiotics, were reduced, and these effects continued for 5 years. Such evaluation is required to identify the types of antibiotics used and the timing of injections, as well as the side effects of antibiotics and infections that occurred during hospitalization. This seems to have had a clear effect of forcing the use of appropriate antibiotics, as well as alerting medical staff to appropriately use antibiotics. Also, we believe that the cause of the observed long-term effect is the periodic implementation of "The Evaluation of the Appropriate Use of Prophylactic Antibiotics." This evaluation was repeated at intervals of about 2 years to evaluate medical institutions, and it is considered a very desirable method in terms of policy continuity and maintainability.

The limitations of this study are as follows. The first is that preoperative antibiotics and postoperative antibiotics could not be analyzed separately. However, we hypothesized that these medical policies would affect the overall antibiotics used

https://doi.org/10.3349/ymj.2022.0546

Table 3. Differential Changes in Usage and Duration of Antibiotics after Implementation of "The Evaluation of Appropriate Use of Prophylactic Antibiotics" in Patients Undergoing SS

SS (case group) vs. HAS (control group)	Ratio (95% CI)	*p* value
Total usage of antibiotics of the episodes within 30-days*		
Ratio of baseline difference in usage of antibiotics	0.99 (0.97–1.01)	0.265
Ratio of usage of antibiotics increase per month	0.99 (0.97–1.01)	0.002
Ratio of difference in the slope of usage of antibiotics†	1.00 (0.99–1.00)	0.001
DID estimate‡		
2014 (initiation of evaluation)	0.88 (0.86–0.91)	<0.001
2015	0.87 (0.84–0.91)	<0.001
2016	0.91 (0.87–0.95)	<0.001
2017	0.92 (0.87–0.98)	0.005
2018	0.91 (0.85–0.97)	0.004
Duration of use of antibiotics of the episodes*		
Ratio of baseline duration of use of antibiotics difference	0.95 (0.93–0.97)	<0.001
Ratio of duration of use of antibiotics increase per month	0.99 (0.99–1.00)	0.001
Ratio of difference in the slope of duration of use of antibiotics†	1.00 (1.00–1.00)	0.001
DID estimate‡		
2014 (initiation of evaluation)	0.88 (0.86–0.91)	<0.001
2015	0.85 (0.82–0.88)	<0.001
2016	0.89 (0.85–0.93)	<0.001
2017	0.91 (0.86–0.96)	0.001
2018	0.89 (0.84–0.95)	0.001

SS, spine surgery; HAS, hip arthroplasty surgery; DID, difference-in-difference; DMC, direct medical costs.
*Indicators of the predicted graph for DMC (or LOS), considering the increase in DMC (or LOS) of both groups before 2014; †Slope difference: difference in the slope of the increase in DMC (or LOS) in the patients with SS and HAS; ‡DID estimate: the ratios of DMC (or LOS) at each time point, considering the difference in DMC (or LOS) before and after time zero in the case group and the difference in DMC (or LOS) before and after time zero in the control group.

Table 4. Differential Changes in the Use of Broad Spectrum Antibiotics and Duration after Implementation of "The Evaluation of Appropriate Use of Prophylactic Antibiotics" in Patients Undergoing SS

SS (case group) vs. HAS (control group)	Ratio (95% CI)	*p* value
Total usage of broad spectrum antibiotics of episodes within 30-days*		
Ratio of baseline difference in usage of broad spectrum antibiotics	0.99 (0.95–1.03)	0.525
Ratio of usage of broad spectrum antibiotics increase per month	0.99 (0.99–1.00)	0.028
Ratio of difference in the slope of usage of broad spectrum antibiotics†	1.002 (1.00–1.00)	0.005
DID estimate‡		
2014	0.92 (0.87–0.97)	0.003
2015	0.88 (0.82–0.94)	0.001
2016	0.91 (0.83–0.99)	0.028
2017	0.88 (0.80–0.98)	0.024
2018	0.82 (0.73–0.93)	0.002
Duration of use of broad spectrum antibiotics of episodes*		
Ratio of baseline difference in duration of use of broad spectrum antibiotics	0.95 (0.92–0.99)	0.005
Ratio of duration of use of broad spectrum antibiotics increase per month	0.99 (0.99–1.00)	0.011
Ratio of difference in the slope of the duration of use of broad spectrum antibiotics†	1.003 (1.00–1.00)	0.001
DID estimate‡		
2014	0.90 (0.85–0.94)	<0.001
2015	0.84 (0.79–0.90)	<0.001
2016	0.86 (0.79–0.93)	0.001
2017	0.86 (0.78–0.95)	0.003
2018	0.78 (0.70–0.88)	<0.001

SS, spine surgery; HAS, hip arthroplasty surgery; DID, difference-in-difference.
*Indicators of the predicted graph for total usage of broad spectrum antibiotics (or duration), considering the increase in usage of antibiotics (or duration) of both groups before 2014; †Slope difference: difference in the slope of the increase in total usage of broad spectrum antibiotics (or duration) in the patients with SS and hip surgery; ‡DID estimate: the ratios of total usage of broad spectrum antibiotics (or duration) at each time point, considering the difference in usage of antibiotics (or duration) before and after time zero in the case group and the difference in usage of antibiotics (or duration) before and after time zero in the control group.

in patients undergoing orthopedic surgery. In fact, "The Evaluation of the Appropriate Use of Prophylactic Antibiotics" evaluates both preoperative and postoperative antibiotics use. Second, it was not possible to analyze whether assessment reduced postoperative infection rates and what effect it had on patients who developed infection. Due to the inherent limitations of claim data, it is very difficult to identify patients with SSIs. Therefore, we could not present the incidence rate of SSI. However, many studies have already reported that prophylactic antibiotics prevent SSI. Also, to the best of our knowledge, our study is the first to investigate the effects of medical policy for prophylactic use of antibiotics in the orthopedic field in Korea. Third, although the protocol for prophylactic antibiotics use may differ from hospital to hospital and compliance rates for adequacy of prophylactic antibiotics use may vary, this was not reflected in the study design. Further studies are needed to determine how these factors affect infections in the future.

In conclusion, "The Evaluation of the Appropriate Use of Prophylactic Antibiotics" policy appears to have had insignificant effects on LOS and DMC in the orthopedic field. However, it has been effective at reducing the usage and duration of antibiotics use, especially in the first 2 years after implementation of the policy. In order to maintain the initial effectiveness of the policy, continuous management and supervision are important.

ACKNOWLEDGEMENTS

This study was conducted as a Joint Project on Quality Assessment Research of the Health Insurance Review & Assessment

Service. This study was based on data from the HIRA (research data number: M20220219833).

AUTHOR CONTRIBUTIONS

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REFERENCES

1. Southwell-Keely JP, Russo RR, March L, Cumming R, Cameron I, Brnabic AJ. Antibiotic prophylaxis in hip fracture surgery: a meta-analysis. Clin Orthop Relat Res 2004;419:179-84.
2. Cheadle WG. Risk factors for surgical site infection. Surg Infect (Larchmt) 2006;7 Suppl 1:S7-11.
3. Prokuski L. Prophylactic antibiotics in orthopaedic surgery. J Am Acad Orthop Surg 2008;16:283-93.
4. Abola MV, Lin CC, Lin LJ, Schreiber-Stainthorp W, Frempong-Boadu A, Buckland AJ, et al. Postoperative prophylactic antibiotics in spine surgery: a propensity-matched analysis. J Bone Joint Surg Am 2021;103:219-26.
5. AlBuhairan B, Hind D, Hutchinson A. Antibiotic prophylaxis for wound infections in total joint arthroplasty: a systematic review. J Bone Joint Surg Br 2008;90:915-9.
6. Barker FG 2nd. Efficacy of prophylactic antibiotic therapy in spinal surgery: a meta-analysis. Neurosurgery 2002;51:391-400; discussion 400-1.
7. Prokuski L, Clyburn TA, Evans RP, Moucha CS. Prophylactic antibiotics in orthopaedic surgery. Instr Course Lect 2011;60:545-55.
8. Stefánsdóttir A, Robertsson O, W-Dahl A, Kiernan S, Gustafson P, Lidgren L. Inadequate timing of prophylactic antibiotics in orthopedic surgery. We can do better. Acta Orthop 2009;80:633-8.
9. Inglis GD, Jardine LA, Davies MW. Prophylactic antibiotics to reduce morbidity and mortality in ventilated newborn infants. Cochrane Database Syst Rev 2007;2007:CD004338.
10. Chung WTG, Shafi H, Seah J, Purnima P, Patun T, Kam KQ, et al. National surgical antibiotic prophylaxis guideline in Singapore. Ann Acad Med Singap 2022;51:695-711.
11. Kaimal AJ, Zlatnik MG, Cheng YW, Thiet MP, Connatty E, Creedy P, et al. Effect of a change in policy regarding the timing of prophylactic antibiotics on the rate of postcesarean delivery surgical-site infections. Am J Obstet Gynecol 2008;199:310.e1-5.
12. Ben Shoham A, Bar-Meir M, Ioscovich A, Samueloff A, Wiener-Well Y. Timing of antibiotic prophylaxis in cesarean section: retrospective, difference-in-differences estimation of the effect on surgical-site-infection. J Matern Fetal Neonatal Med 2019;32:804-8.
13. DiLuigi AJ, Peipert JF, Weitzen S, Jamshidi RM. Prophylactic antibiotic administration prior to hysterectomy: a quality improvement initiative. J Reprod Med 2004;49:949-54.
14. Ikeda Kurakawa K, Okada A, Jo T, Ono S, Bessho K, Michihata N, et al. Effects of prophylactic antibiotics on length of stay and total costs for pediatric acute pancreatitis: a nationwide database study in Japan. Pancreas 2020;49:1321-6.
15. Grabel ZJ, Boden A, Segal DN, Boden S, Milby AH, Heller JG. The impact of prophylactic intraoperative vancomycin powder on microbial profile, antibiotic regimen, length of stay, and reoperation rate in elective spine surgery. Spine J 2019;19:261-6.
16. Healthcare Bigdata Hub. [accessed on 2022 November 1]. Available at: https://opendata.hira.or.kr/home.do.
17. Jang SY, Lee JW, Kim KJ, Kim HY, Choy WS, Cha Y. Comparative interrupted time series analysis of long-term direct medical costs in patients with hip fractures and a matched cohort: a large-database study. Clin Orthop Relat Res 2022;480:891-902.
18. Health insurance review and assessment service. Medical charge for 2021_Unit price per score [accessed on 2022 November 1]. Available at: https://www.hira.or.kr/rc/drug/insuadtcrtr/bbsView.do?isPopupYn=Y&pgmid=HIRAA030069000400&brdScnBltNo=4&brdBltNo=51708&isPopupYn=Y.
19. Hallberg K, Williams R, Swanlund A, Eno J. Short comparative interrupted time series using aggregate school-level data in education research. Educ Res 2018;47:295-306.
20. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol 2011;173:676-82.
21. Garey KW, Lai D, Dao-Tran TK, Gentry LO, Hwang LY, Davis BR. Interrupted time series analysis of vancomycin compared to cefuroxime for surgical prophylaxis in patients undergoing cardiac surgery. Antimicrob Agents Chemother 2008;52:446-51.
22. Jansson MH, Cao Y, Nilsson K, Larsson PG, Hagberg L. Cost-effectiveness of antibiotic prophylaxis in elective cesarean section. Cost Eff Resour Alloc 2018;16:66.
23. Ng-Kamstra JS, Soo A, McBeth P, Rotstein O, Zuege DJ, Gregson D, et al. STOP signs: a population-based interrupted time series analysis of antibiotic duration for complicated intra-abdominal infection before and after the publication of a landmark RCT. Ann Surg 2021 Oct 5 [Epub]. Available at: https://doi.org/10.1097/SLA.0000000000005231.
24. van Kasteren ME, Manniën J, Ott A, Kullberg BJ, de Boer AS, Gyssens IC. Antibiotic prophylaxis and the risk of surgical site infections following total hip arthroplasty: timely administration is the most important factor. Clin Infect Dis 2007;44:921-7.
25. Walker H, Patton A, Bayne G, Marwick C, Sneddon J, Davey P, et al. Reduction in post-operative acute kidney injury following a change in antibiotic prophylaxis policy for orthopaedic surgery: an observational study. J Antimicrob Chemother 2016;71:2598-605.
26. Brajcich BC, Ko CY, Liu JB, Ellis RJ, D Angelica MI. A NSQIP-based randomized clinical trial evaluating choice of prophylactic antibiotics for pancreaticoduodenectomy. J Surg Oncol 2021;123:1387-94.
27. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci U S A 2018;115:E3463-70.
28. Skender K, Singh V, Stalsby-Lundborg C, Sharma M. Trends and patterns of antibiotic prescribing at orthopedic inpatient departments of two private-sector hospitals in Central India: a 10-year observational study. PLoS One 2021;16:e0245902.