



Efficacy and feasibility of a collaborative multidisciplinary program for antibiotic prophylaxis in clean wound surgery

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Received: 22 August 2017 / Accepted: 30 November 2017 / Published online: 12 December 2017
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Abstract

Background Despite national and international guidelines and recommendations, inappropriate prophylactic antibiotic use for clean wound surgery remains a common phenomenon in many Chinese hospitals, causing higher medical costs and bacterial resistance. **Objective** To improve the prescribing behavior for antibiotic prophylaxis and decrease antibiotic abuse and/or misuse in clean wound surgery. **Setting** The teaching hospital of a medical university in Southwest China. **Methods** A collaborative multidisciplinary program involving educational, technical, and administrative strategies was undertaken. It was characterized by a monthly evaluation by clinical pharmacists for randomly selected cases of clean wound surgery, as well as a group discussion attended by correlative personnel, consisting of the administrative staff, experts from the Rational Drug Use Committee, clinical pharmacists and surgeons. **Main outcome measure** The overall incidence of antibiotic prophylaxis, appropriate antibiotics selection, appropriate initial dosage timing, proper drug combination and the duration of antibiotic prophylaxis were measured. Results from 2009 to 2014, the rate of antibiotic prophylaxis for clean wound surgery declined from nearly 100% to 20–30%. Improvements were also observed in drug selection, timing of the first dose, and dosage and duration for antibiotic prophylaxis. Broad-spectrum antibiotics and enzyme inhibitors have seldom been used after 2011. The medical cost for antibiotics also decreased. **Conclusion** A collaborative multidisciplinary program, together with a group discussion, is efficient for improving rational antibiotic prophylaxis for clean wound surgery. This study indicates that clinical pharmacists can play a pivotal role in providing the professional evaluation of medical cases, education, and intervention.

Keywords Multidisciplinary · Antibiotic prophylaxis · Clean wound surgery · Clinical pharmacist · China · Antibiotic resistance

Impacts on practice

- A multidisciplinary collaborative program based on protocols, case review, education and group discussion is efficient for improving the appropriateness of antimicro-

bial prophylaxis in clean wound surgery and decreasing medical costs.

- A multidisciplinary program to improve the appropriateness of antimicrobial prophylaxis offers a great opportunity for clinical pharmacists to participate as key members in medical practice and provides opportunities for improving professionalism.

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Introduction

Patients who develop surgical site infections (SSIs) are up to 60% more likely to spend time in an intensive care unit than patients without SSIs, and they are 5 times more likely to die. In addition, SSIs also incur substantially increased healthcare costs [1]. For clean wound surgery, the key to SSI prevention lies in aseptic technique, although when indicated, antibiotic prophylaxis should be used to further

decrease the risk of SSIs. However, antibiotics could do more harm than good if used inappropriately. Notably, the abuse of antibiotics, e.g., purposely extending the prophylactic period, unnecessarily combining two or even more medications, and using broad-spectrum drugs, not only exposes patients to unnecessary side effects and higher costs but also triggers the development of antibiotic resistance, which in turn jeopardizes the effective prevention and treatment of bacterial infections.

Due to the extremely high workload in the operating room, relatively inadequate aseptic technique, and the lack of primary healthcare professionals who can care for surgical incisions after patient discharge, SSIs have always been a great concern for many hospitals in China. Thus, aggressive or inappropriate antibiotic administration was used to prevent potential infections [2] despite national and international guidelines and recommendations [3–7]. For, based on a survey of 118 hospitals by the Chinese National Health and Family Planning Commission (NHFPC) in 2006, perioperative prophylactic antibiotics were used in 98% of clean wound surgery cases, and the average length of prophylactic antibiotic treatment was 7.4 days. An investigation in 2011 from another Chinese hospital also revealed similar results, as prophylactic antibiotics were administered in 100% of cases but were required in only 51.46% of the cases [8]. Inappropriateness was also seen in the first dose timing and drug combination, and a considerable number of cases lacked a clear indication for an antibiotic prescription [9, 10].

A national campaign against antibiotic abuse and/or misuse was launched by the NHFPC in 2009, in which proper prophylactic antibiotic use for clean wound surgery was a focal issue. As a tertiary medical center, the First Affiliated Hospital of Chongqing Medical University was among the first participating hospitals and implemented a program in 2009 to promote proper antibiotic prophylaxis. It was a collaborative multidisciplinary program consisting of surgeons,

clinical pharmacists, infectious disease specialists and the hospital administration and involving technical, administrative, and educational strategies.

Aims of study

The aim of the study was to improve the prescribing behavior of prophylactic antibiotics and to decrease antibiotic abuse and/or misuse in clean wound surgery. The study also aimed to decrease the medical costs associated with antibiotic usage in prophylaxis.

Ethics approval

Ethical approval for this study was obtained from the research ethics committee of the First Affiliated Hospital of Chongqing Medical University. Informed consent was obtained in writing from each study participant prior to data collection.

Methods

Program design

Program development

The program was launched in 2009, and the first step in program development was the establishment of a multidisciplinary team (Table 1). Team members included the vice president of the hospital, chief medical officer, chief of the department of pharmacy, clinical pharmacists, surgeons, physicians, and clinical microbiologists from the Rational Drug Use Committee (RDUC). An infection preventionist was also included.

Table 1 Team members, roles, and responsibilities

Member (number of participants)	Role	Responsibilities
Vice president (1)	Supervision	Launch and surveillance of program
Chief medical officer (1)	Project leader	Organization of program development, oversight of program implementation, chairing department meeting, providing necessary support
Chief of pharmacy (1)	Program manager	Oversight of program implementation, data monitoring and tracking, writing annual report
Clinical pharmacists (6)	Case evaluator and course lecturer	Evaluation of selected cases, reporting existed problems, lecturing course
Rational Drug Use Committee members (8)	Expert consultant	Assessing reports provided by pharmacists, participating hearing, Judging improper antibiotic prophylaxis
Administrative secretary (1)	Participant	Data collection, meeting organization, liaison
Staff of information department (2)	Participant	Selecting case from electronic patient record system

Perioperative antibiotic prophylaxis protocols for each type of clean wound surgery were first drafted by surgeons from each ward before they were delivered to RDUC members and clinical pharmacists, who then checked compliance with the international guidelines [6], the 2009 NHFPC Guiding Principles for Clinical Application of Antibiotics [11]. If deviations were identified, a group discussion was held with the surgeons, and advice was given such that the protocols could be revised before they were endorsed by the surgeons and medical executive committee. After consensus was achieved, the protocols were adopted as the hospital's formal policies to guide antibiotic prophylaxis in clean wound surgery and were expected to be complied with.

Educational strategies

Educational programs were developed for all prescribing clinicians that teach about the science behind and the principles of rational prescriptions for prophylactic antibiotic use. A rigorous educational effort directed at all surgeons was undertaken, and quizzes were used as a tool to detect knowledge deficits of healthcare providers. A department meeting chaired by the chief medical officer was held regularly in every surgery ward, providing updates on antibiotic prescribing and antibiotic resistance of the hospital and each ward. Didactic presentations by microbiologists, infection preventionists and clinical pharmacists were provided. A variety of web-based educational resources, particularly those developed in an office automation system, were available to help develop educational content. Current topics and areas for the rational use of antibiotics were communicated through posters, flyers, newsletters or electronic communication to staff groups.

Population and sample

Based on the average number of clean surgeries performed each month and the working hours of our program participants, it was decided that 5% of patients undergoing clean wound surgery each month should be enrolled in the study. Patients were randomly selected from the electronic patient record (EPR) system. Patients meeting one of the following conditions were excluded: (1) pre-operative infection and therapeutic antibiotics use, (2) other invasive operations at the same time or within 1 week before or after the operation, and (3) surgeons recording that incision infection could not be ruled out after surgery and using therapeutic antibiotics.

The modification of sampling methods was performed starting in 2014, and 5% of clean wound surgeries performed were extracted, but only 14 categories of procedures were included in study because they were under intensive surveillance by the NHFPC (inguinal hernia repair, thyroid surgery, breast surgery, carotid endarterectomy, craniectomy, cataract

surgery, THA, TKA, adrenalectomy, nephrectomy, CABG, cardiac valve surgery, excision of intracranial tumor, and intracranial hematoma evacuation). Cases were extracted and evaluated each quarter.

Program implementation

Cases were reviewed by clinical pharmacists who specialize in antibiotic therapy. Based on the 2009 NHFPC Guiding Principles for Clinical Application of Antibiotics, our own protocols, as well as the policies endorsed by the surgeons and medical executive committee (Table 2), the appropriateness of antibiotic use in each selected case was tracked and evaluated. Problems were identified and recorded, reports were generated, and recommendations for proper antibiotic prescription were made. The reports were submitted to the RDUC for further evaluation.

A group discussion was held quarterly, and RDUC members, the vice president, chief medical officer, and prescribers of suspicious irrational antibiotic prophylaxis were invited to attend. Feedback regarding the evaluation results was given to the prescribers, who were offered the opportunity to explain to the group their prescriptive considerations. Issues relating to dose, duration, indication, etc. were further discussed in a case-specific manner. Because disputes may exist among group members and because the judgment of clinical pharmacists may also be incorrect, a vote was held among the RDUC members to identify the misuse of antibiotics. Those prescription evaluations were documented and factored into the prescriber's annual performance review.

Data collection and outcome assessment

Data on antibiotics use from 2009 to 2015 were collected. Patients' demographics (gender, age), clinical information (diagnosis, SSIs incidence), surgical information (surgery and operative time), antibiotic usage (generic names, doses, dosing schedules, timing, duration, combinations) and cost (total cost of hospitalization, total drug cost and antibacterial drug cost) were extracted. All costs were recorded in Chinese yuan and were then converted to US dollars (exchange rate, 6.75 yuan = US \$1). The final values are reported in US dollars.

Assessment parameters included the following: (1) the overall rate of antibiotic prophylaxis, (2) the rate of appropriate antibiotics selection, (3) the rate of appropriate timing of first dose, (4) the duration of antibiotic prophylaxis, and (5) the rate of proper drug combination.

Table 2 Criteria for rational antibiotic prophylaxis in clean wound surgeries

Parameters	Justification for rational use
Indications for prophylactic antibiotics	Old age (> 70 years) Operation time > 3 h High risk factors of infection including multiple surgical sites, uncontrolled hyperglycemia, impaired immunity, major surgeries (head cardiac surgery)
Antibiotic selection	1st generation cephalosporin 2nd generation cephalosporin Vancomycin ^a Clindamycin ^b
Accuracy of dose	As is indicated in the package insert
Timing of first dose administration	0.5–2 h before incision ^c
Duration of prophylaxis	Discontinued within 24 h post-operatively
Antibiotics combination	No indication for prophylactic antibiotics

^aVancomycin could be administrated for brain and cardiac surgery, THA and TKA if the rate of MRSA colonization is > 30%

^bIndicated when patients are allergic to cephalosporin

^cCephalosporin and clindamycin should be administrated 0.5 to 1 h prior to surgical incision, vancomycin should be administrated 2 h prior to surgical incision

Statistical analysis

Data were analyzed using SPSS software (version 18.0; SPSS, Inc., Chicago, IL, USA). Descriptive statistics (means and standard deviations) were obtained for quantitative variables. One-way analysis of variance (one-way ANOVA), two-tailed unpaired samples Student's *t* test, and Chi squared test were used for data analysis. Chi square test was used for the comparison of qualitative variables. The significance level was set at $P < 0.05$.

Results

General information about surgeries and surgical patients

In total, 6910 cases were extracted for evaluation from 2009 to 2015, but only 6319 cases were enrolled in the study based on our sampling methods. General information about the surgeries and surgical patients are shown in Table 3. A continual increase was seen for the annual surgeries performed and cases extracted for evaluation ($P < 0.01$). There was no significant difference among patients for each year regarding demographic characteristics, such as age, gender, high infection risk case ratio, average length of hospital stay, and average total drug cost ($P > 0.05$). Although small fluctuations were seen, the SSI incidence after clean surgery remained generally stable

over time ($P < 0.01$). Noticeably, a gradual decline in the average antibiotic cost ($P < 0.01$) and cost ratio ($P < 0.01$) was observed from 2009 to 2015.

Overall situation of antibiotic prophylaxis

In 2009, before the program was initiated, all 620 (100.00%) clean wound surgery patients received prophylactic antibiotics (Table 4). A slight decrease was observed in 2010 (96.29%) but there was no significant difference compared to the data for 2009 ($P > 0.05$). However, after mid-2010, a gradual decrease was seen in the prophylactic rate (Fig. 1), reaching an average of 70.99, 45.99, and 34.16% in 2011, 2012 and 2013, respectively. Significant differences were observed for data compared with those of the previous year ($P < 0.001$).

The overall rates of rational antibiotic prophylaxis were also summarized in Table 4. Criteria for evaluation included antibiotics selection, first dose timing, the duration of antibiotics use, and drug combination. From 2009 to 2013, all parameters demonstrated steady improvements, revealing the effect of this program (Table 4). As a consequence, rapid improvement was seen for the rate of appropriate antibiotic prophylaxis, increasing from 0.32% in 2009 to 90.91% in 2013. The most prominent improvement was observed from 2011 to 2012, as the rate increased from 30.94 to 78.4% (Table 4). Notably, during the initiation of the program, among those cases involving inappropriate application of antibiotic prophylaxis, 29.35% did not meet the indications for prophylaxis, indicating that the overuse of prophylactic

Table 3 General information of surgery and surgical patients

	2009	2010	2011	2012	2013	2014 ^c	2015 ^d	<i>p</i> -value ^e	<i>p</i> -value ^f
Annual surgery number	31975	37238	42673	59817	67712	74721	85950	< 0.01	< 0.01
Annual clean surgery number	13759	18223	18034	15163	19701	23304	30088	< 0.05	< 0.01
Extracted cases	687	915	901	758	980	1165	1504	< 0.01	< 0.05
Evaluated cases ^a	620	808	824	735	903	1032	1397	< 0.01	NS
High infection risk cases, N (%) ^b	167 (26.94)	202 (25.0)	224 (27.18)	195 (26.53)	224 (24.80)	260 (25.19)	367 (26.27)	NS	NS
Male cases, N (%)	317 (51.13)	401 (49.63)	431 (52.31)	392 (53.33)	458 (50.72)	539 (52.23)	750 (54.39)	NS	NS
Age (years)	61.65	61.22	61.37	62.54	61.79	62.15	60.48	NS	NS
Average total drug cost, USD	882.09	877.04	872.63	862.59	857.84	831.46	729.30	< 0.01	< 0.01
Average antibiotics cost, USD	308.67	304.96	174.53	110.93	98.12	67.2	69.75	< 0.01	NS
Average antibiotics cost ratio, %	34.99	34.77	20.00	12.86	11.44	8.08	9.56	< 0.01	< 0.05
Average length of hospital stay (days)	11.79	11.15	11.65	11.34	10.97	10.73	10.62	NS	NS
SSIs for Clean surgery, %	0.71	0.61	0.72	0.66	0.83	0.74	0.59	< 0.01	< 0.01

^aIn some cases, antibiotics were used preoperatively for non-surgical site infection, those patients were excluded from the study

^bRisks include: multiple surgical sites, operating time > 3 h, major surgeries including head and cardiac surgery, surgery with implants, patients aged over 70 or with uncontrolled hyperglycemia, impaired immunity

^{c,d}Cases were extracted from the following procedures: inguinal hernia repair, thyroid surgery, breast surgery, carotid endarterectomy, craniectomy, cataract surgery, THA, TKA, adrenalectomy, nephrectomy, CABG, cardiac valve surgery, excision of intracranial tumor, intracranial hematoma evacuation

^eOne-way ANOVA for data from the year 2009 to 2013

^fTwo-tailed unpaired samples student *t* test for data between the year 2014 and 2015

Table 4 Details of antibiotics used for prophylactic purpose in clean surgery

	2009	2010	2011	2012	2013	<i>P</i> value*			
						A	B	C	D
Using antibiotics, <i>N</i> (%)	620 (100.00)	778 (96.29)	585 (70.99)	338 (45.99)	308 (34.16)	NS	< 0.001	< 0.001	< 0.001
Appropriate drug selection, <i>N</i> (%)	66 (10.72)	87 (10.72)	250 (42.82)	307 (90.73)	287 (93.07)	NS	< 0.001	< 0.001	NS
Proper first dose administration, <i>N</i> (%)	108 (17.41)	130 (16.71)	188 (32.14)	286 (84.62)	291 (94.48)	NS	< 0.01	< 0.001	< 0.01
Duration of prophylaxis(days) ^a Mean ± SD	5.75 (2.78)	4.84 (2.13)	1.92 (0.99)	0.78 (0.35)	0.55 (0.43)	NS	< 0.001	< 0.001	NS
Antibiotic combination, <i>N</i> (%)	269 (43.38)	184 (23.65)	72 (12.37)	0 (0)	8 (2.60)	< 0.001	< 0.001	< 0.001	NS
Appropriate antibiotic prophylaxis, <i>N</i> (%)	2 (0.32)	29 (3.73)	181 (30.94)	265 (78.40)	280 (90.91)	< 0.01	< 0.001	< 0.001	< 0.01
Inappropriate antibiotic prophylaxis, <i>N</i> (%)	618 (99.68)	749 (96.27)	404 (69.06)	73 (21.60)	28 (9.09)	NS	< 0.001	< 0.001	< 0.01
Meeting indications ^b	436 (70.32)	477 (61.31)	222 (37.94)	48 (14.2)	20 (6.49)				

^aTotal duration(days)divided by the number of cases evaluated

^bCases meeting indications for prophylaxis but were considered to be using antibiotics inappropriately as dosage, duration, timing of first dose is concerned

*Unpaired samples student *t* test, A: 2010 versus 2009, B: 2011 versus 2010, C: 2012 versus 2011, D: 2013 versus 2012

antibiotics was highly prevalent among clean surgeries. Great improvements were also seen after years of program implementation, and only 2.60% of reviewed cases (8 cases) involved unnecessary antibiotics prophylaxis.

Antibiotics selection

Antibiotics selection was evaluated for compliance with the protocols of the program based on the criteria listed in Table 2. As demonstrated in Table 4, in 2009, only 66

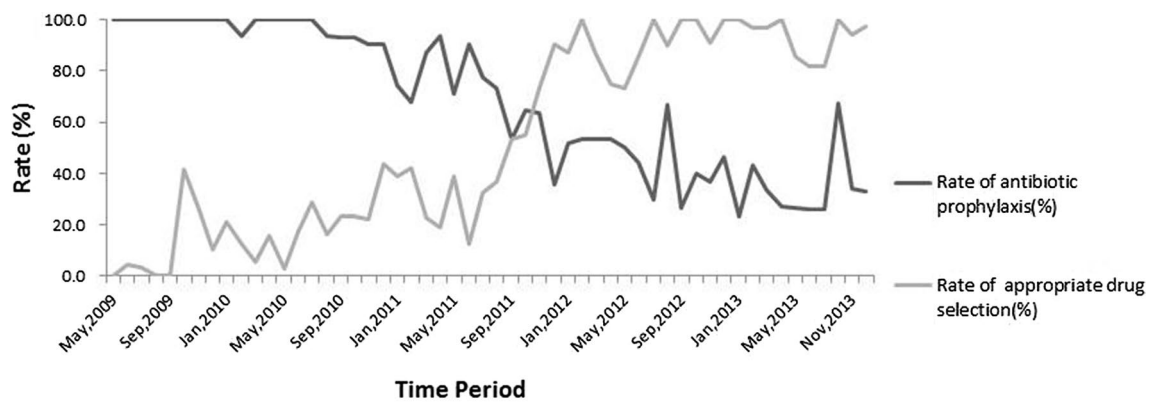


Fig. 1 Rates of the cases using antibiotics for prophylactic purpose and appropriate drug selection

(10.72%) patients were prescribed the proper antibiotics for prophylaxis, and there was no significant change in 2010, with only 87 patients (11.19%) receiving proper antibiotics. However, 2011 to 2012 witnessed a rapid and significant improvement (Fig. 1) ($P < 0.001$), as the rate of proper drug selection increased from 42.82 to 90.73% and remained steady at 93.07% in 2013 ($P > 0.05$) (Table 4).

Although cefazolin is the most widely studied antibiotic agent with proven efficacy for antibiotic prophylaxis [12, 13], it was seldom used at the initiation of the program (8.82%). As shown in Table 5, a high rate of prescription of third-generation cephalosporin (23.11%) was observed

in 2009, followed by prescription of beta-lactams/enzyme inhibitors (19.11%), fluoroquinolones (12.72%), and second-generation cephalosporins (13.92%). With the decreasing application of antibiotic prophylaxis in 2012 and 2013, a decrease was also observed in all categories of antibiotics, except for second-generation cephalosporins, which were prescribed in 23.71 and 20.97% of the cases evaluated in 2012 and 2013, respectively, followed by a reduction in 2014 and 2015. Except for the first-, second-, and third-generation cephalosporins, cephamicins and vancomycin, other antibiotics were no longer prescribed for the purpose of prophylaxis beginning in 2013.

Table 5 Categories of prophylactic antibiotics used for clean surgery, N (%)

	2009	2010	2011	2012	2013	2014	2015
Cephalosporins							
1st generation	55 (8.82)	107 (13.21)	57 (6.94)	76 (10.35)	58 (6.45)	33 (3.22)	38 (2.73)
2nd generation	86 (13.92)	161 (19.95)	57 (6.94)	174 (23.71)	189 (20.97)	120 (11.62)	179 (12.78)
3rd generation	143 (23.11)	310 (38.34)	78 (9.44)	44 (5.99)	29 (3.22)	12 (1.21)	20 (1.45)
4th generation	15 (2.39)	25 (3.11)	0 (0)	0 (0)	0	0	0
Cephamicins ^a	38 (6.13)	69 (8.54)	128 (15.56)	14 (1.92)	15 (1.61)	0	0
Beta-lactams/enzyme inhibitors ^b	118 (19.11)	190 (23.57)	108 (13.06)	8 (1.09)	0	0	0
Penicillins ^c	7 (1.19)	13 (1.55)	21 (2.5)	6 (0.817)	0	0	0
Other beta-lactams ^d	17 (2.71)	15 (1.82)	16 (1.94)	0 (0)	0	0	0
Fluoroquinolones ^e	79 (12.72)	134 (16.58)	69 (8.33)	6 (0.82)	0	0	0
Aminoglycosides ^f	44 (7.13)	59 (7.25)	108 (13.06)	2 (0.27)	0	0	0
Nitromidazoles ^g	43 (6.98)	230 (28.5)	2 (0.28)	2 (0.27)	0	0	0
Clindamycin and lincomycin	12 (2.01)	21 (2.59)	11 (1.39)	4 (0.545)	0	0	0
Vancomycin	1 (0.19)	4 (0.52)	2 (0.28)	0 (0)	8 (0.84)	7 (0.65)	12 (0.89)

^aCefoxitin, cefminox, cefmetazole

^bPiperacillin/tazobactam, amoxicillin/sulbactam, amoxicillin/clavulanate potassium, mezlocillin/sulbactam, ticarcillin/clavulanate potassium

^cPenicillin G, azlocillin, amoxicillin

^dAztreonam

^eLevofloxacin, lomefloxacin, gatifloxacin

^fGentamycin, isepamicin, etimicin

First dose timing

To reach sufficient serum levels of antibiotics at the time of incision, prophylactic antibiotics should be administered 0.5 to 2 h prior to surgical incision. In 2009, only 108 patients (17.37%) reviewed were seen following the protocol (Table 4). Often, antibiotics were administered too early (in the morning of the operation day before the patients were transferred to the operating room) or too late (when they were back into the ward postoperatively) and sometimes even initiated 1 or 2 days before surgery, although no evidence of infection was presented. In 2011, more cases (32.14%) evaluated involved proper timing for the first prophylactic dose. In 2013, 94.48% of clean wound surgery patients received prophylactic antibiotics within 0.5–2 h before surgery. The overall trend for the proper first time dosing was also shown in Fig. 2.

Duration of prophylaxis

For the duration of prophylaxis, it is generally recognized that repeated dosages following wound closure are unnecessary and may induce drug resistance [13]. Except for cases in which extended treatment is warranted [14], the prophylaxis duration should generally be less than 24 h [12]. As shown in Table 4, in 2009, the average duration of prophylaxis was 5.75 days in the cases reviewed, and it gradually decreased beginning in 2010 (Fig. 3). In 2012 and 2013, the average duration for antibiotic prophylaxis was less than 24 h, averaging 0.78 and 0.55 days respectively.

Drug combination

Eradicating the combination of two or more antibiotics for prophylactic purposes in clean wound surgery was another goal of the program. Although justified for

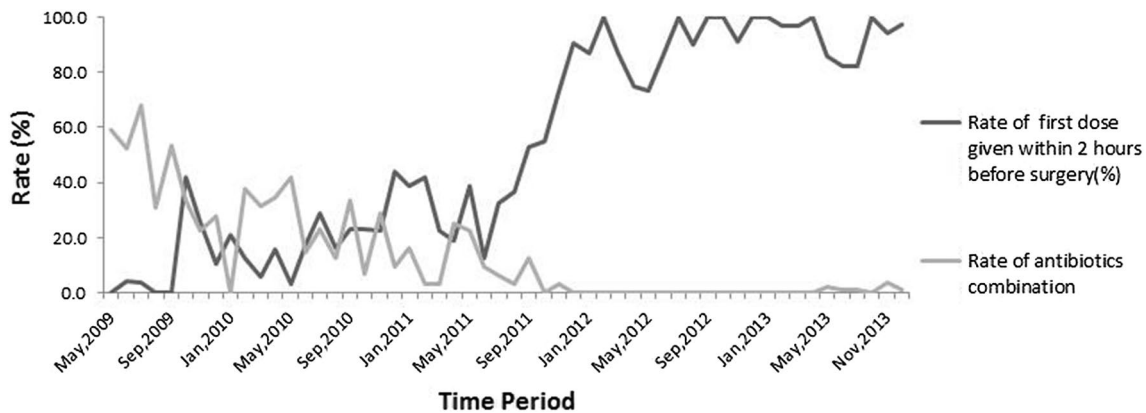


Fig. 2 Rates of the cases with first dose of antibiotics given within 2 h before the surgery and with antibiotics combination

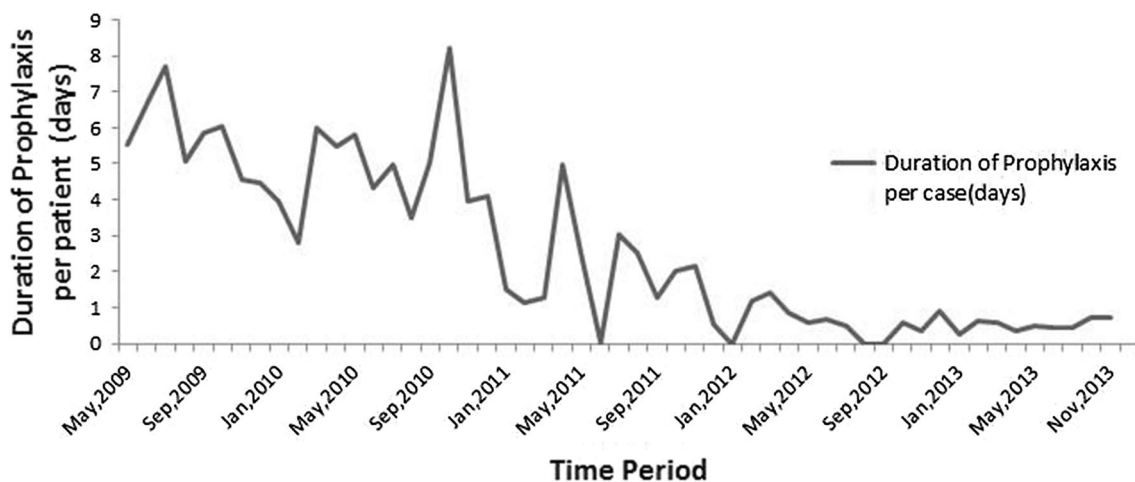


Fig. 3 Mean duration of antibiotic prophylaxis of cases reviewed

clean-contaminated and contaminated surgery, unnecessary combination prophylaxis can increase the cost and drug resistance for clean wound surgery [15]. Thus, any combination prophylaxis for clean wound surgery was considered inappropriate based on the hospital protocol. When the program was launched, drug combinations were applied in over 60% of clean wound surgeries for SSI prophylaxis (Fig. 2), reaching an average rate of 43.38% in 2009 (Table 4). For example, gentamycin combined with β -lactam antimicrobials was frequently used in cataract surgery, and quinolones combined with nitroimidazoles were often administered in herniorrhaphy. In some cases, a combination of three antibiotics was observed. As shown in Table 4, the rate of combinative prophylaxis significantly dropped to 23.65% in 2010 and 12.37% in 2011 ($P < 0.001$). Combinative prophylaxis was no longer applied in cases reviewed in 2012, although 8 cases involving a combination of two antimicrobials were observed in 2013, representing 2.60% of cases reviewed.

Continuing implementation of this program

From 2014, the sampling strategy was modified to enroll cases in 14 categories of clean wound procedures (Table 3). The top five most frequently performed clean wound surgeries were cataract surgery, breast surgery, thyroid surgery, inguinal hernia repair, arthroplasty (total knee arthroplasty (TKA) and total hip arthroplasty (THA)).

The main focus of evaluation was the rate and duration of antibiotic prophylaxis. It was encouraging to note that the rates of prophylactic antibiotics use were 15.2, 15.7, 16.3, and 17.2% for each quarter in 2014, reaching an average of 16.1%. The duration for prophylaxis was 0.56, 0.63, 0.73, and 0.67 days for each quarter (average duration 0.65 days). The same pattern was also observed in 2015, and in each quarter, 16.4, 17.6, 19.4, and 18.2% cases of prophylactic antibiotic use were observed, with an average of 17.9%. The duration of prophylaxis was 0.74, 0.62, 0.81, and 0.61 days for each quarter (mean duration 0.72 days).

Discussion

The abuse and/or misuse of antibiotics are longstanding and prevailing problems in Chinese hospitals. For that reason, the NHFPC launched a national campaign against antibiotics abuse and/or misuse in 2009. However, significant challenges exist when trying to make a change in this hospital. First, the program was not supported at first by all surgeons, as some of them were uncomfortable with interference in their practice, and the program would also call into question the increase in SSI incidence, leading to more medical disputes. It was observed that driven by these concerns, the prescription of prophylactic antibiotics was more focused on

the antimicrobial spectrum: the wider the spectrum was, the better. Other factors, such as safety, pharmacokinetic profile, cost, and the possibility of inducing drug resistance, were often neglected. Therefore, education and communication would be extraordinarily important to achieve the success of this program. Second, there was a shortage of technical and administrative personnel for surveillance, and the review process by clinical pharmacists was highly time-consuming. Moreover, the information system was not efficient in supporting antimicrobial selection and preventing dosing errors or contraindicated drug combinations. All these factors could jeopardize the outcome of this program.

Surprisingly, after 7 years of continuing implementation of the program, dramatic improvements were seen in all metrics examined. Inappropriate use of antibiotics, particularly broad-spectrum drugs, was greatly eliminated. As a result, the average antibiotics cost per case greatly decreased from 308.67 USD in 2009 to 69.75 USD in 2015. By contrast, although fluctuations were present, the incidence of SSIs was not elevated with the implementation of this program, further increasing the confidence of and support from the surgeons. Together, these outcomes suggest the efficacy and feasibility of this collaborative multidisciplinary program.

The key to the success of this program is multidisciplinary collaboration. Through this program and the group discussion of RDUC, surgeons, internal medicine physicians, and clinical pharmacists are able to discuss and share their views about the prophylactic antibiotic protocols, each contributing their expertise to the optimization of practice. As mentioned above, distrust of the program's efficacy from some surgeons and their reluctance to comply with the protocols were major obstacles to the success of the program. During the first year (from 2009 to 2010) when the program was initially implemented, there was no significant improvement in all assessed aspects. However, through effective communication and continuing education, the surgeons' attitudes transformed, and more active participation was seen. In the following years, the surgeons began to voluntarily consult clinical pharmacists and infectious disease specialists about their antibiotic strategies. Correspondingly, the years after 2011 witnessed more rapid and significant improvements in all parameters. By contrast, clinical pharmacists were also offered opportunities to become involved in assessing patients' conditions and decision making, which helped them to perform the patient evaluation more accurately and provide more readily accepted recommendations. For example, in 2014 and 2015, prolonged prophylactic antimicrobial prophylaxis continued to be used in almost all TKA and THA cases reviewed because infection was reported as a leading reason for the failure of knee and hip replacement and was observed in more than half of the cases [16, 17]. After the clinical pharmacists understood the surgeons' concerns, they focused more on clinical manifestations and

laboratory tests, such as body temperature, white blood cell count, erythrocyte sedimentation rate, C-reactive protein level, procalcitonin level, and bacterial culture results. The evaluation of these patients could be confounded by the reactions provoked by possible postoperative stress. Close communication among surgeons, clinical pharmacists, and other specialists is required in such circumstances. Once suggestions were made, they were far more reliable and highly accepted by surgeons.

Notably, substantial success was observed from 2011 to 2012. Except for the more voluntary cooperation from the surgeons mentioned above, another important reason for this success is that the Chinese government signed documents in 2011 that set more strict policies on the application of antibiotics in hospitals [18]. Improvements were also made in 2012 by other researchers leading similar investigations [8, 10]. However, our research showed continuous improvement and maintenance of success during the 7 years of the study.

The major limitation of the program was that the prolonged working time devoted to the complicated evaluation process and cost-effectiveness of pharmacist intervention have not been evaluated. If favorable economic outcomes were observed by this program, it could be more helpful in providing valuable data for making health policies. Additionally, this study was a retrospective study based on a yearly evaluation and comparison. Therefore, it is less convincing than a prospective study with a simultaneous control group.

Conclusion

Implementation of a multidisciplinary collaborative program can lead to a significant reduction in antibiotics abuse and/or misuse, and the medical costs associated with antibiotics also decreased as a result. Moreover, the incidence of SSIs was not elevated with the implementation of this program. Educational, technical, and administrative strategies are all required components, and multidisciplinary collaboration is the key to the success of this program. Clinical pharmacists' work is crucial in providing professional evaluation of medical cases, education, and intervention. This program may serve as a successful model in China's national campaign for the rational use of antibiotics.

Acknowledgements We would like to thank all pharmacists, experts from the Rational Drug Use Committee and administrative staff who participated in this program. We thank all doctors and nurses in our hospital for their support and assistance.

Funding No funding was obtained for this study.

Conflicts of interest The authors declare that they have no conflicts of interest.

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