Review Article
Food Science and Technology

ISSN 0101-2061 (Print)
ISSN 1678-457X (Online)

DOI: https://doi.org/10.1590/fst.34921

Impact of antibiotic therapy management by clinical pharmacists on rational drug use in the perioperative period of retinal detachment surgery in china: a retrospective study from the perspective of prescription structure

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Abstract

Background: This paper aims to assess the impact of antibiotic therapy management by clinical pharmacists on rational drug use (RDU) in the perioperative period of patients receiving retinal detachment surgery in China from the perspective of prescription structure. Methods: In this study, a retrospective study was used to compare the differences in the RDU between 233 patients (the experimental group) receiving medical treatment and 210 patients (the control group) without clinical pharmacist intervention. The data were collected with a set of indicators adjusted from the core medication use indicator proposed by the World Health Organization and the International Network of Rational Use of Drugs according to the background of China. Results: There were significant differences in average number of drugs per prescription (19.7 and 20.8, P = 0.001), percentage of drugs on the reimbursable list (98.32% and 72.4%, P = 0.003), and average treatment expenditure per prescription (555.3 yuan and 707 yuan) between the experimental group and the controlled group, while average number of antibiotics per prescription (4.2 and 4.3, P = 0.114), average number of injections per prescription (12.02 to 11.96, P = 0.804) were not changed significantly. Conclusions: More efforts are needed to improve the effectiveness of the antibiotic therapy management by clinical pharmacist on rational drug use, meanwhile the objective of cost-saving should be included in the service pattern of clinical pharmacy services.

Keywords: antibiotic therapy; clinical pharmacist; rational drug use; perioperative period; retinal detachment surgery.

Practical Application: The role of the antibiotic pharmacist on retinal detachment surgery.

1 Introduction

In recent decades, pharmaceutical industries and medical health systems have developed rapidly worldwide, resulting in a rapid increase in the use of pharmaceuticals and consequently leading to various drug-related problems. The pharmaceutical care is one of the most important approaches to promoting rational drug use (RDU) (Hepler & Strand, 1990). As the core content of the pharmaceutical care, clinical pharmacy services (CPSs) is drawing increasing attention (ASHP Statement on Pharmaceutical Care, 2004), especially in the developing countries (Upadhyay & Ooi, 2018; Sharma et al., 2019), among which China is actively exploring an appropriate and efficient CPS mode (Tian & Yu, 2005). The Chinese government has introduced a series of policies to facilitate the performance of CPSs and the staffing of clinical pharmacy (CP) in health care institutions. However, similar to other developing countries, Chin's CPSs foundation still have a large gap with developed countries, facing imperfect systems and regulations , inefficient service delivery systems and a shortage of medical information support (Liang & Zhang, 2010).

CPs are core providers of CPSs, and RDU is a reflection of the construction of the CPS system and its value (Dahdal & Maddux, 2005). Therefore, evaluating the achievement of CP in promoting RDU is sensitive in assessing the quality of CPSs (Farris & Kirking, 1993). The literature indicates the effectiveness of CPSs by CPs in promoting rational drug use in many countries (Mehuys et al., 2008; Cabello-Muriel et al., 2014; De Oliveira et al., 2017). However, the evaluation of CPSs in China mainly focuses on the implementation quantity of outpatient prescription checking and patient medication guidance, and attention to the outcomes of promoting RDU is lacking (Yao et al., 2017; Cui et al., 2018), but the quality of inpatient CPSs could be equally or even more important, since the inpatients usually have more complexed medical conditions with increased chance of inappropriate medication. The uncertainty of the quality of inpatient CPSs may hinderer the effective clinical decision-making of patient and policy formulation of CPS development.

Among all categories of the drug-related problems, those occurring in the perioperative period may result in more severe and complicated consequences, and they are increasingly related to surgical treatment (Nanji et al., 2016). CPSs to mitigate these drug-related problems may considerably reduce postoperative complications, preserve patients' quality of life and reduce

Received 20 May, 2021
Accepted 31 May, 2021
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medical costs. Regarding the high occurrence rate of bacterial infection among patients receiving surgical treatment, antibiotic therapy is a vital part of pharmacotherapy in the perioperative period, making antibiotic therapy management by CPSs crucial in the perioperative period. Also, promoting rational use of antibiotics is one of the current concerns of the reform of health care system in China.

Hospitals in China are classified into primary, secondary and tertiary by their service capabilities. Because the health professionals and health resources for establishing a clinical pharmacy system are accessible to only some tertiary hospitals and very few secondary hospitals, CPSs are performed mainly in tertiary hospitals, and some of them tentatively provide antibiotic therapy management by CPs to patients receiving surgical treatment (Yao et al., 2017; Cui et al., 2018).

Performing CPSs in the perioperative period has generated controversy due to their clinical value and the cost of the medical resources they consume, which are both comprehensively limited in China (Xi et al., 2017; Xi et al., 2018). Due to the lack of evidence on the outcome of CPS, in the current context of China, it is difficult for government policy makers, medical institution managers, and medical professionals to understand the status and quality of perioperative CPS, thus hindering these aspects in the entire health system Reasonable decision to allocate health resources for CPS.

Retinal detachment is an eye disease with an extremely high blindness rate. It causes permanent visual damage due to the separation of retinal neuroepithelial cells and the pigment epithelium, resulting in retinal photoreceptor cell death. In this regard, the most common type is rhegmatogenous retinal detachment (RRD).

The primary therapeutic method for RRD is surgical treatment, which promotes the reattachment of the detached retina by surgery and replenishes damaged retinal photoreceptor cells to reduce the mortality of such cells. Antibiotic therapy is frequently performed during the RRD surgery process, and it leads to a relatively high probability of drug-related problems such as excessive drug use, insufficient drug dosage, and medication errors in retinal surgery, which not only decrease the therapeutic effectiveness of retinal surgery but also increase the occurrence rate of side effects and increase the economic burden of patients (Bali et al., 2010). In China, the excessive use of drugs has caused particular concern among the government, hospital management and the public.

Accordingly, this paper aims to assess the impact of antibiotic therapy management by CPs on RDU in the perioperative period of patients receiving RRD surgery in China to provide evidence for the benefit of CPSs in the perioperative period in rational use of antibiotics in the context of tertiary hospital in China.

2 Investigations and results

2.1 Characteristics of sample

The clinical data and cost information were sourced from Shanghai General Hospital. Upon CPs' introduction in 2016, they intervened to provide perioperative medication for retinal detachment patients. The 210 cases from 2015 to 2016 were used as the control group before the intervention of CPs, and the 233 cases treated after CP intervention from 2016 to 2017 were used as the experimental group.

2.2 Study design and participants

A retrospective study was adopted for this research. The data, including the prescribed perioperative medications and their costs of a total of 442 patients with retinal detachment, were collected from the hospital information system (HIS) in Shanghai General Hospital, a tertiary hospital with a pharmaceutical staff developed on the basis of Provisions on the Administration of Pharmaceutical Affairs in Medical Institutions issued by National Health Commission of the People's Republic of China.

The inclusion criteria were as follows: the patients aged 18 to 60 years; a new diagnosis of retinal detachment; no history of antibiotic allergy; no drug dependency history; and no pregnant or lactating women.

2.3 Instrument

Mainly referring to the core medication use indicator proposed by the World Health Organization and the International Network of Rational Use of Drugs (WHO/INRUD) (Ghei & Kafle, 1993), this study established a set of indicators to investigate drug use in the perioperative period of patients receiving RRD surgery in China. In this regard, the use of antibiotics, the use of injectable drugs and the costs were not only the original core indicator of RDU investigations, but it also met the importance of optimal use of antibiotics in patients with monocular retinal detachment during the perioperative period (Yan et al., 2017).

With all above, this study made minor adjustments to the indicators used based on the following factors and evidence presented in the Table 1.

1: the primary unit of each medication use in China is a prescription, and the cost per prescription is frequently used in China rather than the number of drugs; thus, the average number of drugs per encounter (ANDPE) was replaced by two separate indicators, the average number of drugs per prescription (ANDPP) and average treatment expenditure per prescription (AEPP).

2: the percentage of drugs prescribed by generic name (PDPGN) and percentage of drugs prescribed from essential drugs list (PDPEDL) were replaced by the percentage of drugs on the reimbursable list (PDRL) to reflect the relationship between medical expenses and the economic burden of patients for three reasons: (1) replacing drugs that are not on reimbursable list of social health insurance of China with those that are on the list is a more common method of reducing medical costs in China; (2) most drugs prescribed in China are generic drugs, which makes PDPGN less effective in this study; and (3) the essential drug list of China is mostly covered by the reimbursable list, and using indicators related to both lists may lead to redundancy.

Table 1. WHO/INRUD prescription indicator and adjusted prescription evaluation indicator.

WHO/INRUD prescription indicator	Adjusted prescription evaluation indicator
Average number of drugs per encounter(ANDPE) $\frac{\text{Total number of drugs}}{\text{Number of patients}}$	Average number of drugs per prescription(ANDPP) $\frac{\text{Total number of drugs in the prescription}}{\text{Total number of prescriptions}}$
Percentage of drugs prescribed from essential drugs list or formulary(PDPEDL) $\frac{\text{Total number of essential drugs in the prescription}}{\text{Total number of drugs in the prescription}} \times 100\%$	Percentage of drugs in the reimbursable list(PDRL) $\frac{\text{Number of medical insurance drugs in prescription}}{\text{Total number of drugs in the prescription}} \times 100\%$
Percentage of drugs prescribed by generic name (PDPGN) $\frac{\text{The number of generic drugs in the prescription}}{\text{Total number of drugs in the prescription}} \times 100\%$	Average treatment expenditure per prescription(AEPP) $\frac{\text{Total prescription expenditure}}{\text{Total number of prescriptions}}$
Percentage of encounters with an injection prescribed(PEIP) $\frac{\text{prescriptions encounters with an injection prescribed}}{\text{Total number of prescriptions}} \times 100\%$	Average number of antibiotics per prescription(ANAPP) $\frac{\text{Number of antibiotics in prescriptions}}{\text{Total number of prescriptions}} \times 100\%$
Perwcentage of encounters with an antibiotic prescribed(PEAP) $\frac{\text{prescriptions encounters with an antibiotic prescribed}}{\text{Total number of prescriptions}} \times 100\%$	Average number of injections per prescription(ANIPP) $\frac{\text{The number of injectables in the prescription}}{\text{Total number of prescriptions}} \times 100\%$

3: the percentage of encounters with an injection prescribed (PEIP) and percentage of encounters with an antibiotic prescribed (PEAP) were replaced by the average number of antibiotics per prescription (ANAPP) and average number of injections per prescription (ANIPP), respectively, mainly because the phenomenon in which a single prescription contained multiple injections and/or antibiotics was still common in China, which made PEIP and PEAP to investigate the use of injections and antibiotics in China less efficiently.

The first three indicators (ANDPE, PDPEDL and PDPGN) reflected the method, quantity, and cost of prescriptions. The last two indicators (PEIP and PEAP) were quality indicators. They were chosen based on the consensus that antibiotics and injections were extremely common in China and represent an excessive and irrational use of drugs. In addition to these five indicators, this study specifically analyzed the distribution of the number of drugs per prescription and treatment expenses.

2.4 Data collection

Based on the registered patient's hospitalization ID, CP collected all relevant indicators from the HIS during the patient's hospitalization, including the number of medications, antibiotics and injections, and the cost of treatment. After obtaining the patient's consent, the patient's research data was collected in accordance with the data collection form, and intervention or routine care was provided. Follow-up lasted 6 months. All information was stored at the pharmacy. A research assistant collected the information in hardcopy or by fax for data entry. A blinded data analyst conducted the final analysis. Ethics approval was obtained from the ethics committee of Shanghai General Hospital (approval number: 2019KY051).

2.5 Statistics

The data were extracted from each prescription as a variable, and Microsoft Office Excel and SPSS 23.0 were used to perform descriptive statistical analysis based on mean ± SD and percentages. The t-test was used to analyze the means of the five indicators of the two groups, and Fisher's exact test was used to compare the percentage of the average of the drug treatment expenditures of the two groups. The statistically significant level was $p<0.05$.

2.6 Average Number of Drugs Per Prescription (ANDPP)

Table 2 showed the changes in ANDPP before and after CP's intervention. After intervention, the ANDPP was increased from 19.7 to 20.8, and there was a significant difference (P=0.001). However, regardless of whether or not the CP's intervention was performed, its 19.7 and 20.8 were much higher than the WHO's ANDPP standard of 1.6-1.8 drugs (Kopp et al., 2008).

In general, the number of the drugs in a single prescription medication for monocular retinal detachment patients during the perioperative period was mainly concentrated in the range of 15-25. As Table 2 showed, in the experimental group, compared with the control group, the percentage of 15-20 drugs per prescription decreased, while the percentage of 20-25 drugs per prescription increased. Therefore, the total number of drugs used showed an increasing trend.

2.7 Percentage of drugs on the reimbursable list (PDRL)

In this study, the "Class A drugs" and "Class B drugs" of the reimbursable list in prescriptions were combined into "medical insurance drugs". Table 2 showed the percentage of drugs on the reimbursable list (PDRL) per prescription. From 2015 to 2016, the PDRL accounts for 98.32%, after CP's intervention, it was decreased to 97.46%, and there was a significant difference

Table 2. Optimal medication use in the perioperative period of patients receiving retinal detachment surgery.

	Control group (N=210)	Experimental group (N=233)	P
Average number of drugs per prescription[a]	19.7(3.46)	20.8(3.51)	0.001
Number of drugs per prescription[b]			
0-5	1(0.5%)	1(0.4%)	
5-10	0(0.0%)	2(0.9%)	
10-15	11(5.2%)	5(2.1%)	
15-20	77(36.7%)	54(23.2%)	
20-25	115(54.7%)	149(64.0%)	
25-30	4(1.9%)	21(9.0%)	
30-35	1(0.5%)	1(0.4%)	
35-40	1(0.5%)	0(0.0%)	
Percentage of drugs on the reimbursable list[a]	98.32%(2.89%)	97.46%(3.06%)	0.003
Average number of antibiotics per prescription[a]	4.2(1.1)	4.3(1.2)	0.114
Number of antibiotics per prescription[b]			
0.0	1(0.5%)	1(0.4%)	
1.0	3(1.4%)	2(0.9%)	
2.0	7(3.3%)	5(2.1%)	
3.0	42(20.0%)	52(22.3%)	
4.0	72(34.3%)	73(31.3%)	
5.0	70(33.3%)	55(23.6%)	
6.0	15(7.1%)	44(18.9%)	
7.0	0(0.0%)	1(0.4%)	
Average number of injections per prescription[a]	12.02(2.5)	11.96(2.4)	0.804
Number of prescription injections per prescription[b]			
0-5	4(1.9%)	3(1.3%)	
5-10	16(7.6%)	22(9.5%)	
10-15	175(83.3%)	193(82.8%)	
15-20	13(6.2%)	14(6%)	
20-25	1(0.5%)	1(0.4%)	
25-30	1(0.5%)	0(0.0%)	
Average treatment expenditure per prescription[a]			
Self-pay	72.7(64.5)	97.5(70.8)	
Reimburse	482.6(231.9)	609.5(340.3)	
Total	555.3(268.1)	707(382.5)	

[a] mean(SD); [b] n(%).

(P<0.05) before and after CP's intervention. In the control group, 72.4% of the prescription drugs were completely on the reimbursable list, and drugs with PDRL greater than 95% accounted for 84.8% of the control group. In the experimental group, the prescriptions of all drugs belonging to the medical insurance list reached 52.4%, and the PDRL exceeded 95%, accounting for 86.6% of the total prescriptions.

2.8 Average Number of Antibiotics Per Prescription (ANAPP)

The treatment of retinal detachment mainly includes surgical treatment, while the perioperative drugs are mainly aimed at anti-infection. Therefore, 100% of the subjects' prescriptions (total 443 patients) contained antibiotics.

ANAPP was 4.2 in the control group and 4.3 in the experimental group, with no significant difference (P = 0.114, Table 2). Table 2 showed the number of antibiotics used in each prescription. In the control group, the number of antibiotics used in each prescription is mostly 3-5, and the sum of the percentages is 87.6%. In the experimental group, the number of antibiotics used in each prescription was mainly concentrated between 3-6 types, accounting for 96.1% of the total. We found that the types of antibiotics used were often four, which accounted for 34.3% and 31.3% of the control and experimental groups, respectively.

2.9 Average Number of Injections Per Prescription (ANIPP)

All patients' prescriptions included injections. ANIPP was 12.02 before CP's intervention and 11.96 after CP's intervention. The difference was not statistically significant (P>0.05). In the control group, the ANIPP was mainly between 11-13, accounting for 66.6% of the total. In the experimental group, most prescriptions contained 12 to 14 ANIPP, accounting for 60.5% of the total.

2.10 Average treatment expenditure per prescription (AEPP)

The drug expenditures were shown in Table 2. After the CP's intervention, the AEPP was increased from 555.3 yuan to 707 yuan. The expenditure of each patient fluctuated drastically.

In the control group, the total cost per prescription ranged from 102.5 to 1890.1. In the experimental group, the total cost per prescription ranged from 67.02 to 2223.413 yuan. Medication expenditures consist of a self-pay part and a reimbursable part. In experimental group, the medical treatment, the reimbursable part of the cost was increased by 126.9 yuan, and the proportion of the reimbursable part was decreased by 0.7% compared with the control group.

3 Discussion

This study assessed the impact of antibiotic therapy management by CPs on RDU in the perioperative period of patients receiving retinal detachment surgery in China. The results showed that compared with the non-CP's intervention, the adapted indicators of WHO/INRUD were mostly not improved as expected.

Compared with no CP's intervention, the average number of prescriptions for patients with monocular retinal detachment has increased. In a study of RDU in 17 developing countries, the average number of prescription drugs per outpatient was 2.2, with the highest average number of drugs per prescription being 3.8 (Reynolds & McKee, 2009). Therefore, the abuse of drugs by patients is a serious trend in China. In higher-level hospitals, CP has been able to intervene in clinical prescriptions; however, their interventions tend to focus on optimization and do not consider streamlined treatment options, and to some extent, they lead to more drug delivery problems. To solve the problem of similar excessive drug administration, a tertiary hospital in China has adopted regular sampling and correction of outpatient and discharge prescriptions, and this has been linked to the performance evaluation of the relevant personnel, to some extent reducing excessive drug administration.

Whether or not there is the intervention of CPs, the proportion of medical insurance drugs in prescriptions is high, and the financial burden of patients is relatively low. However, after the PC's intervention, the PDRL was decreased, and the financial burden on society and individuals was increased, which also reflected that in tertiary hospitals, CPs have been able to intervene in actual prescriptions. Doctors are no longer the only personnel with absolute prescription rights. However, the CP's intervention is less considerable in regard to economic problems and is more focused on treatment optimization. Prescription drugs that involve antibiotics and injections are usually more expensive than those that do not. The amount of antibiotics is always high, which is perhaps one of the reasons why the drug cost cannot be reduced. To achieve RDU to improve people's quality of life and save social medical resources, the use and management of antibiotics should become the focus of CPs and physicians.

Compared with the case without CP's intervention, each prescription was prescribed with antibiotics and injections, and the dosage was higher. On the one hand, this result proved the grim situation of the misuse of antibiotics and injections in China. On the other hand, in China, the use of antibiotics and injections was relatively strict, and the penalties for abuse increased year by year. However, their utilization rate was still high. This indicated that China's CPS system must be refined and improved. The same standards cannot be applied to all diseases and all departments. Antibiotic and injection abuse may be related to the medication habits of doctors and economic factors. Ophthalmology is mainly based on perioperative antibiotics. Some doctors are reluctant to change because of years of use; some doctors are affected by different types of reasons related to the economics of drugs. The French National Health Insurance Center launched a public education campaign aimed at reducing the use of antibiotics and popularized the use of antibiotics in various ways and successfully controlled the use of nonessential antibiotics, which is referential to Chinese government.

In Conclusion, The results also showed that CPs pay more attention to the comprehensiveness of treatment, less attention to the streamlining and economics of prescriptions, and did not significantly reduce the use of antibiotics and injections during the prescription intervention process. Therefore, the government, while strengthening publicity and education regarding RDU, need further to improve the evaluation and supervision mechanism at all levels and to improve the list of basic drugs and medical insurance drugs. Medical institutions need to improve their own training and assessment mechanism, strengthen the supervision of physician prescription behavior, and establish reasonable and sound drug regulations in accordance with the department.

Abbreviations

RDU: rational drug use. CPSs: clinical pharmacy services. CP: clinical pharmacy. RRD: rhegmatogenous retinal detachment. HIS: hospital information system. WHO/INRUD: World Health Organization and the International Network of Rational Use of Drugs. ANDPE: average number of drugs per encounter. ANDPP: average number of drugs per prescription. AEPP: average treatment expenditure per prescription. PDPGN: percentage of drugs prescribed by generic name. PDPEDL: percentage of drugs prescribed from essential drugs list. PDRL: percentage of drugs on the reimbursable list. PEIP: percentage of encounters with an injection prescribed. PEAP: percentage of encounters with an antibiotic prescribed. ANAPP: average number of antibiotics per prescription. ANIPP: average number of injections per prescription.

Competing interests

The authors declare that they have no competing interests.

Funding

N/A.

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