Rational use of antibacterials and drug sensitivity analysis in the repair of large lip defect with skin flap

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Abstract: In this study the wound status of skin flap repair patients were closely observed, there were sign of infection. The secretion were taken for bacterial culture and sensitivity analysis and given sensitive antibiotics to active treatment. Patients received intravenous antibiotics 30 minutes before surgery to prevent infection. If postoperative infection occurred, according to susceptibility test results, patients were given sensitive antibiotics. Drug sensitivity analysis showed that 85.71% of gram-negative bacteria were sensitive to cefoperazone/shubatan and imipenem and 72.72% of gram-negative bacteria were sensitive to cefoperazone/tazobactam, so these 3 antibiotics were the first choice for treatment. And gram-positive bacteria were sensitive to teicoplanin and vancomycin. Therefore, scientific and rational use of antibiotics has great significance to effectively prevent postoperative infection and reduce the production of drug-resistant bacteria. At the same time, L-extension deltopectoral flap was used to reconstruct a full-thickness labiomental defect concurrent infection. All the surgeries were successful without any necrosis. There are many kinds of pathogens for skin flap infection, and their sensitivity to antibiotics is not the same. Therefore, it is suggested that combination therapy should be carried out at the early stage, so as to ensure a good antibacterial effect.

Keywords: Antiseptic drugs, pathogenic bacteria, drug sensitivity, deltopectoral flap, labiomental defect, cephalosporin.

INTRODUCTION

In the field of surgery, infection is the most common complication after surgery, and is often an important factor affecting the success or failure of surgical treatment (Kertmen *et al.,* 2015). The application of antibiotics plays an important role in preventing and treating surgical infection, improving the success rate and safety of operation (Liu *et al.,* 2016). However, with the wide application of antibiotics in the field of surgery, the phenomenon of irrational application is becoming increasingly prominent, and the harm brought by it is also gradually highlighted (Mellotte *et al.,* 2015). In recent years, China has paid more attention to the rational use of antimicrobial drugs, and has formulated a number of notifications and norms for the application of antibacterial drugs in China, and has taken a series of measures to control the application of antimicrobial drugs (Mukai *et al.,* 2012). In addition, with the growing maturity of surgical minimally invasive surgery, the antibacterial drugs are more obvious in the surgical application. However, despite the fact that the irrational use of antibiotics is still widespread, the problem of bacterial resistance is still noteworthy. Therefore, the rational use of antibiotics is still one of the urgent problems in clinical surgery.

The principle of surgical prevention should be based on factors such as the category of the surgical incision, the degree of surgical trauma, the possible species of contaminated bacteria, the duration of the operation, the opportunity and severity of the infection, the evidence of evidence-based medicine for the effect of antimicrobial agents, the influence of the antimicrobial resistance and the economic evaluation (Okada *et al.,* 2011). Prevent the use of antibiotics. For clean surgery, there is no pollution in the surgical site. It is usually not necessary to prevent the use of antibiotics, but in the following cases, the preventive medication can be considered: (1) The operation range is large, the operation time is long, and the chance of pollution is increased. (2) Surgery involves important organs, which can cause serious consequences if the infection occurs, such as craniocerebral operation and cardiac surgery. (3) Implantation of foreign body, such as artificial heart valve implantation, permanent pacemaker implantation, artificial joint replacement, etc. (4) There are high risk factors for infection, such as advanced age, diabetes, and low immune function (especially malnutrition).

The selection of antimicrobial agents should be considered according to the categories of surgical incision, the possible species of contaminated bacteria and their sensitivity to antibiotics and the effective concentration of drugs in the surgical site (Ozgur *et al.,* 2015). It is necessary to select effective evidence-based medical evidence, safety and use for the possible existing contaminated bacteria. An appropriate price categories, and single antibiotics should be selected as far as possible. Such as cardiovascular, head and neck, chest abdominal

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wall, soft tissue of extremities, and Department of orthopedics, usually choose antibacterial drugs against *Staphylococcus aureus*; colon, rectal and pelvic surgery should be used for antibiotics such as intestinal Gram-negative bacteria and bacilli (Pistevou *et al.,* 2015). At present, there is a common problem in the application of antibacterial drugs in China. Preventive medicine has a high starting point and a large variety of applications (Andrew *et al.,* 2009). In the selection of antimicrobial agents, the guidelines for clinical application of antibacterial drugs, such as guidelines for clinical application of antibacterial drugs, were selected in the central plains, and more antibiotics were used. The highest frequency of antibiotics used in surgical I incision patients was the three generation cephalosporin plus enzyme inhibitors, such as cefotaxime (Chun *et al.,* 2012). The irrational use of antibiotics, on the one hand, will cause great waste of health resources, on the other hand, the excessive use of antibiotics can aggravate the production of bacterial resistance. In order to promote the standardized use of antibiotics in perioperative period, we investigated and analyzed the perioperative use of antibiotics in our hospital.

Skin flap repair patients should closely observe the wound status, there are signs of infection, secretions would take at the first time for bacterial culture and drug sensitivity analysis, and give sensitive antibiotics to active treatment (Mahaffey, 1985; Chun *et al.,* 2012). Both the bacteria culture and the drug sensitivity test need a certain time (António *et al.,* 2009; Anyanwu, 2011). After the result is fully reported, the treatment is often delayed. Therefore, a retrospective analysis of the common pathogens and drug resistance of patients with skin infection after skin flap repair can provide guidance for clinical early empirical medication (Charles *et al.,* 1995; Andrew *et al.,* 2009).

The labiomental defects after tumor resection are always reconstructed by local flaps (Gerald, 1976; Eric *et al.,* 2009). But for some larger defects, there is not enough local tissue for us to use. We tried deltopectoral flaps to deal with this problem and got satisfactory results. Large labiomental defects after tumor resection usually cannot be reconstructed by local flaps (Chul, 1973; Frank *et al.,* 2006). Distant skin flaps or musculocutaneous flaps are needed. Cases reconstructed by musculocutaneous flaps such as pectoralis major myocutaneous (PMMC) flaps are sometimes too much bloated (Kiyonori, 1974; Kalanovic *et al.,* 2016). Skin of the deltopectoral flap is similar with the labiomental skin in color. The L-extension deltopectoral flaps even without expanding can provide enough skin for large labiomental defects (Leonard, 1980; Lee *et al.,* 2015). Both deltopectoral flap and L-extension deltopectoral flap can be folded to reconstruct full-thickness labiomental defects (Mahaffey, 1985; Parikh *et al.,* 2016).

MATERIALS AND METHODS

Clinical data

We selected 352 patients who have surgery in our hospital; there were 185 male patients and 167 female patients. The ages were from 45 to 57 years old. The basic information and drug use of the patients, including the type of surgical incision, the name, specification, usage, dosage and duration of drug use, were used to make a questionnaire on the use of antibiotics. Meanwhile, in all of the patients, 54 patients with large lip defects and skin flap operations were selected for the key analysis. These patients suffered oral cancer and whose lip and chin were invaded. All the patients were selected from head and neck department of our department between 2015 February to April. The defects needed to be reconstructed were 4cm x 5cm minimum and 7cm x 10cm maximum. One L-extension deltopectoral flap was used to reconstruct a full-thickness labiomental defect concurrent infection. In the other cases, deltopectoral flaps were used combining with pectoralis major myocutaneous flaps. All patients were approved by Ethics Committee of our hospital and signed on the informed consent.

Research method

Clinical symptoms red swelling fever and pain to flap repair site, and purulent infection should be considered in the presence of possible; the wound secretions from bacterial culture, and the cultured strains were isolated and identified and drug sensitive test, the bacteria were identified by bio Merieux company ATB semi automatic bacteria analyzer, drug sensitivity test using KB disk diffusion method

STATISTICAL ANALYSIS

The data were analyzed by SPSS17.0 software package, and the data were measured by means of mean ($x\pm s$). Measurement data were analyzed by one-way ANOVA, counting data usage and percentage, and $\chi 2$ test was used to test the level of $\alpha = 0.05$.

RESULTS

Use of antibiotics

In the 352 cases, 328 patients were treated with antibacterials, and the rate of use was 93.18%. A total of 10 kinds of antibiotics were involved in 24 species, of which 2 or more antibiotics were used in 197 patients. The most frequently used species were cephalosporins, followed by cephalosporins/enzyme inhibitors. The top 3 drugs were cefuroxime, Cefoperazone/Shubatan and cefazamiprid. The results showed in tables 1 and 2.

Distribution of pathogenic bacteria

In the 352 patients, 54 cases were infected by skin flap repair, and the infection rate was 15.34%. 89 strains of pathogenic bacteria were isolated from bacterial culture.

Gram negative bacteria accounted for 69.66%. Among them, *Pseudomonas aeruginosa* and *Escherichia coli* were the most common. Gram positive bacteria accounted for 29.21%, of which *Staphylococcus aureus* was the main form, and result showed in table 3.

Fig. 1: Delay of the L-shaped deltopectoral flap.

The result shows that Gram-negative bacteria were more sensitive to cefoperazone, imipenem and cefoperazone. And has low sensitivity to ampicillin, sulfamethoxazole/ trimethoprim, piperacillin and cefazolin, as showed in table 4. The sensitive rate of Gram positive bacteria to teicoplanin and vancomycin was 100%, while for penicillin, erythromycin, sulfamethoxazole sensitivity is low, as showed in table 5.

Surgical techniques

Delay of the deltopectoral flap if it is a L-shaped one may be the first stage (Stage I). If the defect is a larger one, delay of the L-shaped deltopectoral flap will increase the survival rate of the flap. We take L-shaped deltopectoral flap as an example to describe the progress of this delay stage. The region needs delay is on the surface of deltoideus triangularis muscle and is below the distant end of the traditional deltopectoral flap. The length-width ratio of the delayed flap with a upward pedicle is from 1:1 to 2:1. The undermining layer is below the deep fascia and the undermining region contains the delay region and the distant end of the traditional deltopectoral flap. After the harvest of the delayed flap, the flap should be foldedand sutured to fix it. The donor site can be primary closed (fig. 1). Stage II surgery can be taken after 1 week.

Fig. 2: Harvest the deltopectoral flap

Fig. 3: Folded and transplant the deltopectoral flap while the donor site was covered by skin graft.

Harvest and transplant of the deltopectoral flap is the second stage (Stage II). Taking the 2^{nd} and the 3^{rd} intercostal space as the pedicle of the deltopectoral flap to design a deltopectoral flap from the lateral sternal line to the surface of the deltoideus triangularis muscle. The upper border of the flap is the infraclavicula line and the lower border is the 4^{th} rib. The undermining layer is below the deep fascia (fig. 2) After the harvest of the deltopectoral flap, rotate the flap into the defect and suture layer by layer.the border of the other part of the flap should be sutured together to form a tube. The donor site can be primary closed or covered by skin graft (fig. 3).

Pedicle division is the last stage (Stage III). Pedicle division is always 4 weeks after the flap transplant. If there is another facial defect, the pedicle can be used to reconstruct it as retrograde deltopectoral flap with a 1:1 length-width ratio. If the length-width ratio of the retrograde deltopectoral flap is larger than 1:1, delay

Table 1: Use of antibiotics

Drug types	Antimicrobial agents		Cases of Antibacterials	
	Number	Constituent ratio (%)	Number	Constituent ratio (%)
Cephalosporins	9	37.5	261	74.14
Cephalosporins/enzyme inhibitors	2	8.33	189	53.69
Nitazolate	3	12.5	123	34.94
Quinolones	2	8.33	102	28.97
Other beta lactam	2	8.33	60	17.04
Lincosamides	1	4.16	43	12.21
Penicillins	1	4.16	15	4.261
Aminoglycoside	2	8.33	8	2.27
Macrolide	1	4.16	2	0.56
Penicillin/enzyme inhibitor	1	4.16	1	0.28

Table 2: Frequency and utilization of antimicrobial agents

Sort	Antiseptic drugs	Frequency of use	Usage rate (%)	Sort	Antiseptic drugs	Frequency of use	Usage rate (%)
1	Cefuroxime	140	39.77	13	Metronidazole	22	6.25
2	Cefoperazone / sulbactam	95	26.98	14	Cefodi	21	5.96
3	Ceftazine	87	24.71	15	Cefimazole	18	5.11
4	Levofloxacin	76	21.59	16	Cephalosporin Mino	16	4.54
5	Five water cefazolin	75	21.30	17	tinidazole	12	3.40
6	Ornidazole	74	21.02	18	Clozo	10	2.84
7	Cefepime	62	17.61	19	Cefatriaxone	9	2.55
8	Fu Xi di	59	16.76	20	Cefpamine	8	2.27
9	Clindamycin	42	11.93	21	Penicillin	8	2.27
10	Cefoperazone	37	10.51	22	Azithromycin	5	1.42
11	Cefoxitin	32	9.09	23	ampicillin	4	1.13
12	Pazufloxacin	28	7.95	24	Tobramycin	2	0.56

Table 3: Distribution and constituent ratio of pathogenic bacteria

Pathogenic bacteria	Number	Constituent ratio
Gram-negative bacteria	54	71.1
Pseudomonas aeruginosa	21	27.6
Escherichia coli	13	17.1
Klebsiella pneumoniae	15	19.7
Other	5	6.5
Gram-positive bacteria	21	27.6
Staphylococcus aureus	15	19.7
Staphylococcus epidermidis	3	3.9
Other	3	3.9
Fungus	1	1.3
Total	76	100
Fungus	1	1.3

surgery to cut off the perforating branches of the internal thoracic artery of the flap (Gao *et al.*, 2016).

DISCUSSION

According to the requirements of the guiding principles for the clinical application of antibiotics, class I incision operation: There is no pollution in the operative field, usually without the use of antibiotics (Pistevou *et al.*, 2015). Most patients in type II incision surgery need to prevent the use of antibiotics. Type III incision operation should be prevented by using some antibiotics. Those who undergo clean surgery should be given 0.5 -2 hours before the operation (Liu *et al.*, 2016). If the operation time exceeds 3 hours, or the blood loss is large (>1500m L), second doses can be given during the operation. The duration of prophylactic use of type II incision surgery was 24 hours and extended to 48 hours if necessary. The

Table 4: Sensitivity of Gram-negative bacteria to antibiotics

Antiseptic drugs	*Pseudomonas aeruginosa* (n=21)		*Escherichia coli* (n=13)		*Klebsiella pneumoniae* (n=15)	
	Number	Sensitivity rate	Number	Sensitivity rate	Number	Sensitivity rate
Ampicillin	0	0	0	0	0	0
Cefazolin	4	19.1	2	15.3	3	20
Ceftazidime	7	33.3	5	38.4	4	26.6
Levofloxacin	10	17.6	9	69.2	6	40
Sulfamethoxazole	3	14.2	1	7.6	5	33.3
Cefoperazone	18	85.7	13	100	10	66.7
Piperacillin	16	76.3	11	84.6	11	73.3

Table 5: The sensitivity of Gram-positive bacteria to antibiotics

Antiseptic drugs	*Staphylococcus aureus* (n=15)		*Staphylococcus epidermidis* (n=3)		Other (n=3)	
	Number	Sensitivity rate	Number	Sensitivity rate	Number	Sensitivity rate
Penicillin	0	0	1	33.3	1	33.3
Erythromycin	2	13.3	1	33.3	2	66.6
Teicoplanin	15	100	3	100	3	100
Sulfamethoxazole	3	20	2	66.6	0	0
Vancomycin	15	100	1	33.3	1	33.3

first generation of cephalosporins, such as cefazolin or cefradine, is commonly used in type I incision surgery (Mellotte *et al.,* 2015). At present, gram-positive cocci are the main bacteria causing the infection of type I incision operation. The bacteria that cause the infection of class II incision operation are mainly gram-negative enterobacteriaceae, and gram-positive coccus. Second generation cefuroxime (cefuroxime) and three generation cefoperazone/sulbactam (cefoperazone/sulbactam) were used for the pre operative treatment of type I incisional surgery and the fourth generation cefepimes (cefpimidins) were used in some surgical prophylactic use. Some patients use antibiotics which are not recommended as preventive, such as azithromycin and ipromicin (Mukai *et al.,* 2012). Long term and extensive use of broad-spectrum antibiotics can not reduce the incidence of infection in the surgical site, but may cause bacterial disorder, double infection and increase bacterial resistance (Okada *et al.,* 2011).

There are many unreasonable phenomena in the use of surgical antibacterial drugs, such as improper selection of drugs, irrational choice of drug use time, no indication of combined use of drugs or no synergy, etc (Ozgur *et al.*, 2015). In order to standardize the rational application of antibiotics in the perioperative period of surgical operation in hospital, to ensure the safety of the patients and to reduce the drug resistance, the hospital should establish and improve the management system of antibiotics and define the prescriptions of antibiotics at all levels (Chun *et al.,* 2012). We should establish and improve the monitoring system for the clinical application of antibiotics, strengthen the management of clinical application of antimicrobial agents and train the knowledge of rational use of antibiotics for medical staff. The selection starting point of antibacterials is higher (Anyanwu *et al.*, 2011). Cleaning operations such as abdominal hernia and non infected thyroid surgery usually do not need antibiotics. If necessary, they can be given before surgery. In this survey, all 2 types of operations were used after the operation (Eric *et al.,* 2009). Abdominal hernia, head and neck surgery, breast surgery, and other possible infections of the bacteria, mainly *Staphylococcus aureus, coagulase negative staphylococcus*, if needed, first generation cephalosporins such as cefazolin or cefradine should be used to prevent infection. For example, in appendectomy, the most likely pathogenic bacteria are Gram-negative and anaerobes, and metronidazole combined with cefuroxime or cefotaxime should be selected. This survey showed that some cases were infected by clindamycin, third generation cephalosporins and beta lactamase inhibitors, which resulted in unnecessary waste of drugs and increased the production of drug-resistant bacteria.

For the skin flap repair operation, the patient should closely observe the condition of the wound. If there is a sign of infection, the secretion should be taken at the first time for bacterial culture and drug sensitivity analysis, and the sensitive antibiotics should be given active treatment (Mahaffey, 1985; Chun *et al.,* 2012). Both bacteria culture and drug sensitivity tests take some time. After the complete report, treatment is often delayed. Therefore, the common pathogenic bacteria and drug resistance of the infected patients after the skin flap repair can be reviewed and analyzed, which can provide guidance for the early clinical empiric drug use. Gram negative bacteria accounted for 71.05%, Gram-positive bacteria accounted for 27.63%, fungi only accounted for 1.31%. Drug sensitivity analysis showed that 85.71% of

Gram-negative bacteria were sensitive to cefoperazone/ sulbactam and imipenem, and 72.72% of Gram-negative bacteria were sensitive to cefoperazone/tazobactam. Therefore, the 3 antibiotics were the first choice for treatment, while Gram-positive bacteria were sensitive to teicoplanin and vancomycin (Andrew *et al.,* 2009). Because vancomycin resistant *Staphylococcus aureus* has been reported in recent years, it is not recommended that it be used as a routine drug. Teicoplanin can be combined with gram-negative bacteria sensitive antibiotics when the pathogen is not clear.

Skin flap repair patients should closely observe the wound status, if there are signs of infection we should take secretions at the first time for bacterial culture and drug sensitivity analysis, and give sensitive antibiotics to active treatment (Dobson *et al.,* 2015; Ruben, 2016). Both the bacteria culture and the drug sensitivity test need a certain time. After the result is fully reported, the treatment is often delayed (Lee *et al.,* 2015; Rha *et al.,* 2016). Therefore, the common pathogenic bacteria and drug resistance of the infected patients after the skin flap repair can be reviewed and analyzed, which can provide guidance for the early clinical empiric drug use (Mellotte *et al.,* 2015; Sterling *et al.,* 2015). Drug sensitivity analysis showed that gram negative bacteria to cefoperazone, piperacillin sensitivity, so the 2 kinds of antimicrobial agents can be used as the preferred drug treatment; and gram positive bacteria were sensitive to vancomycin and teicoplanin (Sterling *et al.,* 2015; Tannir *et al.,* 2016). In recent years due to a vancomycin resistant *Staphylococcus aureus* have been reported, therefore, is not recommended as a routine medication (Tom *et al.,* 1986; Ueda *et al.,* 2016). The pathogen is not clear, the teicoplanin and gram negative bacteria generally sensitive to antimicrobial agents in combination.

Large labiomental defects after tumor resection usually can not be reconstructed by local flaps (Price, 1984; Wu, 2016). Distant skin flaps or musculocutaneous flaps are needed. Cases reconstructed by musculocutaneous flaps such as pectoralis major myocutaneous (PMMC) flaps are sometimes too much bloated (Hase *et al.,* 2016). Skin of the deltopectoral flap is similar with the labiomental skin in color. And L-extension deltopectoral flaps even without expanding can provide enough skin for large labiomental defects (August *et al.,* 2016; Horgan *et al.,* 2016; Imada *et al.,* 2016; 2016; Morise *et al.,* 2016).

CONCLUSION

Rational use of antibiotics is of great significance for effective prevention of postoperative infection, reduction of drug-resistant bacteria and reduction of incidence of nosocomial infections. Therefore, hospitals should strengthen the management of clinical application of anti bacteria drugs, standardize the use of drug time in the perioperative period, restrict the use of antibacterial drugs in clean surgery and promote the effective, safe and economic prevention of antibiotics. There are many kinds of pathogenic bacteria in the skin flap to repair infection, and their sensitivity to antibiotics is different. Therefore, it is suggested that combined use of drugs in the early stage can be properly used in order to ensure good antibacterial effect and the bacteria culture and drug sensitivity test should be carried out before the combined use of drugs, so as to adjust the medication in time.

There are some disadvantages of this technique. The first is that the lip reconstructed only by deltopectoral flap is dysfunctional because of the lack of the complete oral sphincter. The second is that this method has 2-3 stages which will bring inconvenience to the patients. Using free deltopectoral flap can shorten the stages of the surgery to be 1 or 2. But there are shortages in equipment and technique about microsurgery in some rural primary hospitals. So deltopectoral flap can be one choice of distant cutaneous flap to reconstruct large labiomental defects.

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