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Nursing care of patients with anaphylactic shock complicated with ventricular fibrillation induced by flurbiprofen during perioperative period

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Abstract: *Based on the case of anaphylactic shock after application of flurbiprofen exfoliate in a 60-year-old patient undergoing lumbar internal fixation, the literature was analyzed and summarized to discuss the pharmacological characteristics of flurbiprofen exfoliate, the clinical manifestations of anaphylactic shock and the emergency treatment measures. It's critical to be alert to the occurrence of allergic reactions during the perioperative period after use of flurbiprofen. For patients under general anesthesia with most of their skin covered under sterile drapes, close attention should be paid to changes in circulatory function and respiratory parameters.*

Keywords: *Flurbiprofen; Anaphylactic shock; Adverse drug reactions; Case analysis; Nursing care*

1. Case data

A 60-year-old male patient with a height of 155 cm and a weight of 50 kg was admitted to hospital with the chief complaint of "more than one year after the operation of lumbar fracture". On admission, plain radiographs of the lumbar spine showed: (1) The changes after internal fixation of the lumbar spine were blurred compared with the fracture line of the anterior lumbar 3 vertebrae. (2) Lumbar degenerative changes, diagnosed as: lumbar fracture after internal fixation. No significant abnormalities were found in the rest of the medical history and examination, and no history of food and drug allergy was reported. "Removal of spinal internal fixation" was performed at a selected time.

2. Anesthesia procedure

There is no difference between pre-anesthesia assessment and pre-anesthesia preparation. Intended anesthesia method: tracheal intubation, static inhalation combined with general anesthesia. NIBP, ECG, SpO2 and BIS were routinely monitored after admission, and peripheral veins were opened. Pre-anesthetic medication: intravenous injection of penehyclidine hydrochloride 0.6 mg, dexamethasone sodium phosphate 10 mg. Anesthesia induction medication: intravenous injection of midazolam 1 mg, etomidate 12 mg, Sufentanil 30 ug and cis-atracurium 12 mg. After the muscle relaxant took effect, 3ml 2% lidocaine was given for airway surface anesthesia, and a 7.0# tracheal catheter was successfully inserted under a visual laryngoscope at a depth of 22 cm. After the intubation was completed, the tracheal catheter was connected to the anesthesia machine to control ventilation, and the respiratory parameters were adjusted to control PetCO2 within 35~45 mmHg. Reverse the patient's position and change to prone position. Intraoperative combined anesthesia was performed: intravenous injection of remifentanil 0.3μg/(kg.min), propofol 4 mg/(kg.h), supplemented by appropriate concentration of sevoflurane, BIS value maintained at 40-60, intermittent addition of cis-atracurium.

70 minutes after the operation, when all the internal fixation had been removed, the surgeon began to suture the muscle and subcutaneous tissue, stopped sevoflurane inhalation, continued to inject propofol and remifentanil intravenously to maintain anesthesia, and administered flurbiprofen 50 mg intravenously. Ten minutes later, the patient's ECG showed ventricular premature beat and ventricular premature dichotomy, NIBP 56/33 mmHg, and arterial blood pressure was immediately monitored by left radial artery puncture catheter. At this time, the invasive blood pressure dropped to 62/37 mmHg,

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and the airway pressure did not change significantly. The surgeon was advised to stop the procedure, all anesthetic drugs were discontinued, and intravenous administration of lidocaine hydrochloride 80 mg to correct ventricular hyperthermia and ephedrine 6 mg to boost pressure was given.

The blood pressure did not rise, but continued to decrease. After 2 minutes, the ECG chart showed: Ventricular tachycardia, ventricular fibrillation, Heart rate 233 / min, blood pressure 30/26 mmHg, the patient's limbs were cold, and the oxygen saturation of the finger pulse could not be detected. Immediately ask the surgeon to simply cover the incision with sterile gauze and then roll the patient onto the flat car. At this time, large petechiae and red rash can be seen on the patient's neck and anterior chest wall, and the anesthesiologist determines that the patient has anaphylactic shock. Electrical defibrillation (two-way electrode 200 J) was immediately administered once, at the same time, 1:10,000 epinephrine 200ug intravenous infusion was administered intermittenously for 3 times, and arterial blood gas analysis was performed simultaneously (marked "T1" at this time, Table 1). After 2 minutes, the electrocardiogram of the patient gradually recurred to sinus tachycardia, HR 135 times/min, AIBP 189/102 mmHg, intravenous administration of nicardipine 0.2 mg, methylprednolone 40mg. Nasopharyngeal temperature was monitored (body temperature was normal), and CVP was monitored by right internal jugular vein puncture and rapid infusion of 500 ml crystal solution and 500 mL hydroxyethyl starch. Blood gas analysis at T1 showed increased blood potassium and lactic acid. The nurse was instructed to catheterize urine and immediately inject 1g 10% calcium gluconate injection, 5mg Furosemide injection, 5% sodium bicarbonate injection 100 ml intravenously, and 1g sodium creatine phosphate intravenously. Arterial blood gas analysis was performed again about 15 minutes after defibrillation (at this time marked "T2", see Table 1), and blood potassium dropped to the normal range. After 10min, the patient's vital signs were as follows: HR 92 times/min, AIBP 126/71 mmHg, SpO299%, ECG rhythm regular, lying on the right side of the flat car, the surgeon disinfected again, and performed skin suturing to complete the operation.

After all the above treatment, the patient's postoperative vital signs were stable, HR 96 times/min, blood pressure 139/76 mmHg, arterial blood gas analysis was performed again (at this time marked as "T3", see Table 1), blood potassium was normal, and lactic acid was significantly lower than before. After operation, the patient was sent to ICU with controlled breathing and tracheal catheter.

Table 1: Results of arterial blood gas analysis at different time points

Index	T1	T2	T3
PH	7.35	7.41	7.42
Hct	45%	43%	43%
K+	6.2 mmol/L	3.8 mmol/L	3.8 mmol/L
Lac	2.8 mmol/L	2.5 mmol/L	2.3 mmol/L
Na+	135 mmol/L	142 mmol/L	140 mmol/L
HGB	140 g/L	133 g/L	133 g/L
pCO2	38 mmHg	37 mmHg	37 mmHg
pO2	412 mmHg	300 mmHg	273 mmHg
BE(B)	0.3 mmol/L	5.8 mmol/L	4.0 mmol/L
Glu	8.3 mmol/L	9.4 mmol/L	8.7 mmol/L

Note: T1: when defibrillation; T2:15 minutes after defibrillation; T3: Out of the operating room.

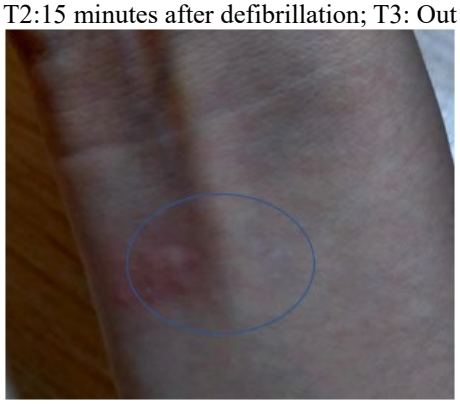

Figure 1: Skin condition

One day after ICU admission, the patient regained consciousness, circulation was stable, tracheal catheter was removed, and blood gas results were normal. Three days later, the patient was transferred

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to a general ward. After communication with the patient and family members, intradermal tests of suspected allergic drugs were performed. Among all intraoperative drugs, the diameter of flurbiprofen was 3 mm larger than before, accompanied by erythema and itching, indicating a strong positive reaction (FIG. 1). The patient was discharged 7 days after surgery.

3. Discussion

The anesthesia induction and operation process of the patient in this case were smooth, and the vital signs were stable before the administration of flurbiprofen exfoliate. However, 10min after the administration of flurbiprofen exfoliate, a rapid drop in blood pressure, undetectable oxygen saturation of the finger pulse, ventricular tachyventricular fibrillation, petechiae on the neck and anterior chest wall, red rash and other suspicious allergic reactions occurred immediately. Considering that the patient had severe allergic reactions combined with ventricular fibrillation caused by flurbiprofen exfoliate. The prognosis was good after anti-anaphylactic shock treatment. The etiology of severe anaphylaxis was diagnosed during perioperative period after operation, and the intradermal reaction of flurbiprofen ester was strongly positive, which confirmed that anaphylactic shock caused by flurbiprofen ester occurred during the operation.

Flurbiprofen ester is a non-selective cyclooxygenase inhibitor, and its injection is the first targeted preparation of non-steroidal anti-inflammatory drugs (NSAIDs). It is mainly composed of lipid microspheres and flurbiprofen ester wrapped in them [1], and its excipients also contain soy protein. Flurbiprofen coated by lipid microspheres can be targeted to inflammation, trauma and tumor sites, and the hydrolyzed flurbiprofen can inhibit the synthesis of prostaglandins and thus effectively inhibit acute pain [2]. In this case, the reason for the patient's allergy to flurbiprofen ester may be related to the molecular configuration of NSAIDs as a propionic acid derivative, as well as the soy protein and microlipid globules contained in the injection. A seven-year single-center study abroad showed that patients with NSAIDs allergy accounted for the largest proportion of all the studied patients, reaching 43%[3], indicating that the incidence of allergic reactions caused by NSAIDs drugs was higher than that of other drugs. Flurbiprofen ester was a chiral non-steroidal anti-inflammatory drug of 2-arylpropionic acid, and severe anaphylactic shock was frequently reported. It also has cross-allergic reactions with ibuprofen, aspirin and diclofenac [4]. The rapid hypersensitivity reaction (i.e. anaphylactic shock) of the patient in this case may also be due to the strong immune response caused by the body thinking that the lipid microspheres and/or soy protein in the injection are foreign bodies entering the body, resulting in the IgE mediated type I allergic reaction of the patient [5].

Allergic reaction is caused by the fact that after the sensitized body is exposed to the same antigen again, the tissue mast cells and peripheral basophils are stimulated to release a variety of vasoactive mediators, resulting in increased vascular permeability and causing systemic or local skin reactions [6], which can be divided into four types. The patient's anaphylactic shock is a type I rapid systemic allergic reaction mediated by IgE. After IgE is combined with the antigen, effector cells are induced to release a large amount of vasoactive mediators, triggering cascaded systemic inflammatory cascade in a short time, resulting in extensive capillary leakage, which is one of the main factors leading to circulatory failure and other severe allergic symptoms in the patient [7]. In cases of severe allergy, diagnosis is mainly based on clinical history. In clinical practice, it is necessary to quickly identify suspicious allergic symptoms and conduct timely and effective intervention for patients. During general anesthesia, due to the unconscious inability of patients to complain, severe allergic reactions are often manifested as three groups of symptoms in respiration, circulation and skin [8]: rapid increase in airway pressure; the decrease of blood pressure and the increase of heart rate without obvious inducement can also be combined with obvious arrhythmia; skin edema or various rashes. A clinical diagnosis can be made when two or more groups of these manifestations are present. Severe allergic reactions occur quickly, and about 80% of patients can develop the above suspicious symptoms within 30 minutes after drug administration [9]. The patient saw large petechiae and red rash on the neck and anterior chest wall about 10min after intravenous injection of flurbiprofen exate, his HR rose to 233times/min, and his blood pressure dropped to 30/26 mmHg. According to the severity of immediate hypersensitivity [10], this patient could be classified as grade III (life-threatening symptoms: Collapse, tachycardia or bradycardia, arrhythmia, bronchospasm), fits neatly into the diagnosis of severe anaphylaxis and the temporal logic of drug allergy.

The diagnosis of anaphylactic shock in this patient is clear, but it is also necessary to make differential diagnosis of anaphylactic shock during general anesthesia to exclude arrhythmias and blood pressure drop caused by other reasons: (1) Hereditary angioedema. This is a chromosomal genetic

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disease with the deficiency of complement C1 esterase inhibitor. The patient develops under the stimulation of non-specific factors such as infection and trauma, manifested as angioedema of the skin and respiratory mucosa, airway obstruction and increased airway pressure, which is very similar to anaphylactic shock [11]. However, the disease has an obvious family genetic history and should be paid attention to during preoperative visits. In addition, blood biochemical indicators related to IgE mediated hypersensitivity such as serum IgE, nitric oxide, TNF-α, PGD2, interleukin-4 (IL-4) and tryptase can be identified [12]. (2) Severe, near-death bronchial asthma occurred during the operation. When asthma occurs, bronchospasm and wheezing occur simultaneously, airway pressure increases, and airway pressure can decrease after airway spraying with β2-R agonist. (3) Acute left heart failure. Acute left heart failure and anaphylactic shock both have sudden onset, similar clinical manifestations of blood pressure drop, cold limbs, and abnormal auscultation sound of the lungs. The identification of the two is mainly based on comprehensive analysis of medical history. Patients with acute left heart failure are generally complicated with basic cardiovascular diseases before surgery, such as hypertension and coronary heart disease, and there are causes of acute left heart failure during the operation, such as excessive and rapid fluid replenishment [13]. (4) Heat source reaction during infusion [14]. The infusion agent used or its clinical compound is contaminated by bacteria, fungi, insoluble particles, etc., and the body has pyrogen reaction: chills and fever, most of them have normal blood pressure, and chills, fever, and shock when bacterial pollution.

Ventricular fibrillation is a serious arrhythmia characterized by rapid, irregular, uncoordinated, and lack of effective myocardial contraction and ventricular pumping rhythm. In this case, the earliest arrhythmia in the case of ventricular fibrillation is ventricular premature, and the ventricular premature triggering of ventricular fibrillation is mostly related to early and subsequent depolarization of Purkinje fibers and right ventricular outflow tract[15]. Electrolyte disturbance (high potassium, low magnesium) can also induce ventricular premature. As for the mechanism of ventricular fibrillation caused by severe allergic reactions, it has been reported [16] that the antigen-antibody complex formed by allergic reactions can cause inflammation in the conduction tissues and autonomic cells of myocardium, resulting in hyperemia, edema and exudation of surrounding tissues, thus leading to arrhythmia. In addition, histamine, interleukin and other vasoactive substances can accelerate the automatic depolarization rate of atrial muscle and ventricular muscle during diastole, enhance the automaticity, form microreentry, and induce tachyarrhythmia and ventricular fibrillation.

A multicenter retrospective study [17] showed that the incidence of perioperative severe anaphylaxis was 1.25/10000, but the fatality rate could reach 1.4%. Therefore, early diagnosis and treatment are required for patients with perioperative severe anaphylaxis. The guidelines for reducing the risk of perioperative anaphylaxis approved by the European Agency for the Evaluation of Drug Allergy in 2011 suggest [10] that perioperative anaphylaxis management should be judged and handled according to the specific situation of the patient. Treatment measures mainly include basic therapy, adrenaline, volumetric therapy, glucocorticoids, antihistamines and other symptomatic treatments [18]. In this case, when a significant fluctuation in the patient's circulation was recognized, all drug use was stopped immediately and the surgeon was asked to stop the operation, which was the basic treatment for immediate disconnection from the suspected allergen. Epinephrine is an alpha and beta agonist that relives bronchial smooth muscle spasm and reduces airway pressure. Constricting blood vessels and reducing blood vessel leakage; At the same time, it can stimulate the myocardium, increase cardiac output and thus increase blood pressure, and is the only first-line recommended drug for anaphylactic shock [19], which should be injected intravenously as soon as possible. Meanwhile, invasive blood pressure monitoring should be carried out [20]. When the patient's blood pressure dropped to 62/37 MMHG for the first time, the blood pressure did not improve after 6mg of ephedrine was administered, and then the blood pressure increased after 0.6 mg of epinephrine was administered intermittenously. In the event of severe allergic reaction, capillary dilation and increased vascular permeability cause fluid leakage into the tissue space, and more than half of the intravascular fluid is redistributed in a short time, resulting in shock [21]. Therefore, volumetric therapy should be performed in the early stages of severe anaphylaxis, with appropriate colloid supplementation along with the infusion of crystals under hemodynamic monitoring. In this case, right internal jugular vein puncture was performed immediately after anaphylactic shock, CVP was monitored, and 500ml crystal solution and 500ml hydroxyethyl starch were given quickly. Glucocorticoids and antihistamines have a slow effect and are mainly used for common anaphylaxis and to prevent the further development of anaphylaxis, and are not used as first-line drugs for rescue [22]. Therefore, in this case, 40mg methylprednone injected intravenously in time was used as second-line drugs. In addition, the corresponding symptomatic management measures should be taken for ventricular fibrillation, hyperkalemia and hyperlactacemia occurring during the operation.

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Perioperative patients with severe allergic reactions may lack specific skin manifestations, and patients under general anesthesia are covered with sterile sheets, and skin reactions may not be detected in time, so the main manifestations are respiratory and circulation fluctuations. When other causes of blood pressure drop are excluded and conventional pressor drugs are ineffective, anaphylactic shock should be highly suspected and experimental anti-allergy and anti-shock therapy should be conducted in time. With the increase of perioperative anaphylaxis year by year, anesthesiologists and nurses should be vigilant, improve preoperative visit and strengthen intraoperative monitoring to reduce the incidence of severe anaphylaxis.

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