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Original Article

Clinical effectiveness analysis of dextran 40 plus dexamethasone on the prevention of fat embolism syndrome

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Abstract: This study aims to investigate the clinical efficacy of Dextran 40 plus dexamethasone on the prevention of fat embolism syndrome (FES) in high-risk patients with long bone shaft fractures. According to the different preventive medication, a total of 1837 cases of long bone shaft fracture patients with injury severity score (ISS) > 16 were divided into four groups: dextran plus dexamethasone group, dextran group, dexamethasone group and control group. The morbidity and mortality of FES in each group were analyzed with pairwise comparison analysis. There were totally 17 cases of FES and 1 case died. The morbidity of FES was 0.33% in dextran plus dexamethasone group and significantly lowers than that of other groups ($P < 0.05$). There was no significant difference among other groups ($P > 0.05$). Conclusion from our data is dextran 40 plus dexamethasone can effectively prevent long bone shaft fractures occurring in high-risk patients with FES.

Keywords: Fat embolism syndrome, dextran 40, dexamethasone, prevention, fractures

Introduction

Fat embolism syndrome (FES) is an infrequent clinical consequence, arising from the systemic manifestations of fat emboli within the microcirculation. Fat embolization is characterized by release of fat droplets into systemic circulation after a traumatic event, which cause direct tissue damage as well as induce a systemic inflammatory response resulting in pulmonary, cutaneous, neurological, and retinal symptoms [1, 2]. The first case of fat embolism syndrome (FES) in a patient suffering from crush injury was described by Zenker [3]. Classically, FES presents with the triad of pulmonary distress, mental status changes, and petechial rash 24 to 48 hours after pelvic or long-bone fracture [2], rare cases of FES have been reported to occur following bone marrow transplantation, osteomyelitis, pancreatitis, alcoholic fatty liver, and even liposuction [4]. The pathophysiology of FES is poorly understood. Some theories involving mechanical and biochemical mechanisms explained how fat emboli manifest as FES. Whether there is a causal relation between intramedullary nailing and FES onset remains controversial [5-7]. Clinical diagnosis of FES is difficult because FES is a heterogeneous disease with no pathognomonic features, and the laboratory and radiographic findings are nonspecific [8, 9]. If FES is diagnosed early, supportive pulmonary therapy and other resuscitative measures may halt the pathophysiologic cascade and prevent clinical deterioration.

FES incidence increases with the number of fractures sustained by an individual. Curative treatments developed specifically for FES have been largely unsuccessful [10-12]. Many scholars studied the fat embolism syndrome, including experimental and clinical studies [13, 14]. We investigated the clinical efficacy of Dextran 40 plus dexamethasone on the prevention of fat embolism syndrome (FES) in high-risk patients with long bone shaft fractures.

Table 1. The basic information of patients in four groups before treatment

	Gender (case)		Age (y)	Weight (kg)	Injury to admission time (h)	Major fracture sites (case)				Fracture type (case)		ISS rating (score)
	Male	Female				Radius	Tibiofibula	Humerus	Radius and ulna	Close	Open	
A	701	508	38.5±11.3	58.4±5.3	5.2±3.7	302	365	260	282	946	263	19.01±2.32
B	235	171	37.9±12.1	57.9±3.5	5.3±2.9	99	109	103	95	320	86	19.01±2.31
C	75	50	38.9±11.1	59.2±3.2	5.4±3.5	40	22	23	40	91	34	18.85±2.23
D	60	37	39.1±11.7	58.6±4.5	5.4±3.6	26	32	19	20	76	21	18.73±2.26
P	0.866		0.760	0.172	0.832			0.194		0.536		0.665

Table 2. Diagnostic criteria score method

Clinical features	Score
Skin ecchymosis	5
Typical chest X-ray	4
Non cerebral trauma cerebral symptoms	3
Hypoxemia (PaO_2 < 60 mmHg)	3
Anemia (Hb < 100 g/L)	1
Respiration (> 30/min)	1
Fever (> 38.5°C)	1
Rapid pulse (> 120/min)	1
Thrombocytopenia (< 100 × 10^5)	1

Methods

Patients

A total of 1837 patients were recruited from inpatients in our hospital from January 2004 to December 2012, who were fracture patients with injury severity score (ISS) > 16 and without a history of chronic heart, lung, liver and renal insufficiency. 1071 cases are male, 766 cases are female; age between 11 to 68 years old; Injury causes: 1066 cases of traffic accident, 573 cases of injury by falling, 193 cases of pressure drop and crush injury, 5 cases of gunshot wounds; major fracture sites: 467 cases of femur, 528 cases of tibia and fibula, 405 cases of humerus, 437 cases of radius and ulna; 573 cases of combined traumatic with hemorrhagic shock, 259 cases of vascular injury, 563 cases of skin avulsion, 229 cases of spinal cord and nerve damage, 438 cases of bone fascia compartment syndrome, 462 cases of chest, abdomen, head and facial trauma. They were divided into four groups according to different medication methods: dextran plus dexamethasone group (combination group), dextran group, dexamethasone group and the control group (**Table 1**). On the basis of correcting shock rapidly, stabilizing fractures and offering symptomatic treatment, drugs-related preventive measures were taken immediately. All patients signed an informed consent form. This study was approved by the Ethics Committee of our hospital.

FES diagnosis and treatment

The patients were diagnosed using the scoring method (**Table 2**), those patients whose score ≥ 6 points combined with the history and fracture performance can be diagnosed as FES. Conventional treatments applied to them [2]. Patients' gender, age, weight, injury to admission time, the main fracture site, fracture type, ISS score, FES morbidity and number of mortality were recorded.

Data analysis

The analysis was performed with statistical software (SPSS 19.0). Used X^2 test to compare the patients' gender, major fracture site, fracture type and incidence of FES, and used single-factor analysis of variance to compare the patients' age, weight, injury to admission time, ISS score and medication time, $P < 0.05$ was considered statistically significance.

Results

FES occurred in combination group, dextran group, dexamethasone group and control group, there were 4, 7, 3 and 3 cases respectively (**Table 3**), the dead all died of FES. Statistical comparison showed that in each group, sex, age, weight, injury to admission time, the main fracture site, fracture type, ISS score and medication time all had no significant difference ($P > 0.05$); the incidence of FES in combination group had significant difference with other groups ($P < 0.05$), while there was no significant difference in other three groups ($P > 0.05$).

Table 3. Medication time and incidence

Group	Medication time (d)	Incidence (cases)	Incidence (%)	The number of deaths (case)
Combination group	4.5 ± 1.6	4	0.33%	1
Dextran group	5.3 ± 1.2	7	1.72%Δ	0
Dexamethasone group	4.2 ± 2.1	3	2.40%*,Δ	0
Blank group	-	3	3.09%*,Δ	0
Test statistic	-0.532	-	13.583	-
P	0.595	-	0.04	-

*Comparison between former group and next group P > 0.05; ΔCombination group and this group P < 0.05.

Discussion

The treatment of FES was difficult for the lack of specific diagnostic indicators. Symptomatic treatments such as protecting critical tissues and organs (such as the lungs and brain), correcting hypoxemia, respiratory support, and prevention of complications were performed as major therapeutic measures, death and disability remain major threats to these patients [15, 16]. Given the current research progress, prevention is essential. How to take effective and precautionary drug measures based on conventional treatment will undoubtedly bring important significance on improving the success rate of treatment and reducing the rate of disability.

There were some reports about the adrenal steroid hormones on the prevention of high-risk patients with FES [15-17], but the effect was not obvious when with low-dose [18]. Prospective clinical study showed that short-range and high-dose may be effective in preventing long bone fracture incidence in patients with FES, maintaining PaO2 levels, lowing plasma free fatty acid concentrations [15, 16]. However, due to its large doses (total dose of 90 mg), coupled with expensive drugs as well as concerning about heavy use of hormones may bring about appropriate complications and other reasons [19], it has not been widely promoted this method in China. We currently selected Dexamethasone as the preferred method according to national conditions.

Dextran plus dexamethasone is a more effective drug treatment for FES and we also have similar clinical experience, but as for its ability to prevent FES, there is no literature repored. The group applied detran FES plus dexamethasone for high-risk patients for FES, and used scoring method for early FES diagnosis, and compared it with dexamethasone group, dextran group and the control group, the results showed that: 1. the differences of gender, age, weight, injury to admission time, the main fracture site, fracture type, ISS score and preventive medication of patients in each group were not statistically significant indicating they were comparable; 2. statistical comparison showed that, combination group can effectively prevent FES occurrence, suggesting that dextran plus dexamethasone was feasible and effective on the prevention of FES; 3. the dose of dexamethasone in combination group was small, and did not appear complications related to hormones such as stress ulcer, aseptic necrosis of the femoral head, and no bleeding tendency, induced heart failure and pulmonary edema happened, indicating that combination method was safe; 4. Combination method is inexpensive, and suitable for the current situation, which is also practical. Although the FES incidence was lower in dextran group and dexamethasone group compared with control group, the difference was not statistically significant, the reasons may contain: single use of low molecular weight dextran or dexamethasone indeed have no preventive effect on FES; it has a preventive effect, but observed cases were quite small, or because the smaller doses of dexamethasone, we can not draw the right conclusions.

Although the use of drugs in this group has obvious preventive effect, it should be emphasized that drug prevention must be based on an early reliable fixation of the fracture [20], the early corrective hypovolemic shock and other conventional measures. For heart failure, pulmonary edema, bleeding tendencies or (and) those patients can not use corticosteroids [16], it should not adopt this way to prevent FES. Although taking different drug prevention measures, there is still a certain incidence of FES, indicating that war trauma is a major factor for FES, and complete prevent of FES is difficult. 1 death in this group showed that although the prevention and treatment are significantly improved, FES is still an important factor threatening trauma patients.

Dextran plus dexamethasone on the prevention of FES may be related to one of the following factors: 1. reduce the viscosity of the intravascular component, so that the blood fat droplets are difficult to form a sufficient amount or large enough to play a similar lipid soluble and suppository effect; 2. increase blood volume and reduce the possibility of formation of intravascular fat plug in tissues and organs; 3. maintain cell membrane stability, improve microcirculation, reduce capillary permeability, thereby reducing the amount of fat plug into the bloodstream; 4. reduce the reaction intensity of the tissue organs on free fatty acids and fat plug in the blood.

In summary, the same as their usage in the treatment of FES, the prevention mechanism of dextran plus dexamethasone may be quite complex. This clinical studies have shown that low molecular weight dextran alone or dexamethasone for prevention of FES were not significantly effective, but combined both of them had an obvious effect, showing that synergy is a major factor in their access to treatment. It's believed that with further FES research, the elucidation of its mechanism of action will become increasingly clear.

Disclosure of conflict of interest

None.

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