

# Efficacy of Corticosteroids in Prevention of Fat Embolism Syndrome in Patients with Long Bone Fracture

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## Abstract

Fat embolism syndrome refers to a constellation of symptoms secondary to the presence of fat globules in the lung parenchyma and/or peripheral blood circulation. The syndrome is most often seen in association with long bone or pelvic fractures and can cause significant morbidity and mortality. The present randomized double blind placebo-controlled trial was conducted to evaluate the efficacy of prophylactic corticosteroids in the prevention of fat embolism syndrome and arterial hypoxia in patients with long bone fractures. Ninety-one patients with long bone fractures were randomized to case and control groups; 38 and 53 individuals, respectively. The patients in the case group received a single dose of 10 mg/kg intravenous methylprednisolone succinate upon presentation to the emergency room. The control group received placebo (normal saline). The primary endpoints evaluated were the presence of fat embolism syndrome, based on the Gurd criteria. Total two patients with fat embolism syndrome were observed in the corticosteroid-treated group (5/2%) compared with five patients in the control (9.4%;  $P=0.4$ ). Arterial hypoxemia was observed in one patient in the corticosteroid-treated group (2/6%) versus eight patients in the control group (17/0%;  $P=0.07$ ). Mean arterial oxygen was not significantly different between the two groups ( $P=0.07$ ). It seems that single dose methylprednisolone succinate (10 mg/kg intravenously) is not effective as prophylaxis for fat embolism syndrome and arterial hypoxemia.

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**Keywords** • Fat embolism • corticosteroid • fracture

## Introduction

**F**at embolism syndrome refers to the triad of respiratory distress, central nervous system (CNS) disturbances, and a petechial rash associated with the release of fat emboli into the systemic circulation after trauma. The syndrome is most commonly associated with long bone fractures and is one of the important causes of morbidity and mortality in this setting. Several pharmacologic and supportive measures have been evaluated as both prophylaxis and treatment of fat embolism syndrome; the strongest evidence has been about the efficacy of corticosteroids.<sup>1</sup> In fact these drugs have been used for many years and in various doses to prevent and treat the fat embolism syndrome, although different studies

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have reached upon different results on the safety and effectiveness of these drugs.<sup>2-10</sup> Accordingly, the present study evaluated the efficacy of these agents in the prevention of fat embolism syndrome in patients with long bone fracture(s), with or without concurrent pelvic fractures.

**Patients and Methods**

A randomized double blind placebo-controlled trial was performed from July 2003 to April 2004 on 91 patients with long bone fractures in Shahid Mohammadi Hospital (the main hospital of Hormozgan province) Bandar Abbas, south of Iran.

Included patients had age between 15 and 55 years, were able to provide informed consent, presented to the emergency room within the first 24 hours of the fracture. They had no systemic or chronic disease, pathologic fracture, pregnancy, previous steroid treatment, fractures with compartment syndrome, or accompanied head, chest, or abdominal trauma. They had open fractures graded not higher than type II in Gustillo-Anderson classification.<sup>11</sup>

The patients were randomized to case and control groups, of which the case group received a single intravenous dose of 10 mg/kg methylprednisolone succinate in the emergency room, while the patients in the control group received placebo, consisted of 50 ml intravenous normal saline. Randomization was performed as follows: 10 closed envelopes containing a letter on which the word placebo or drug was written (5 drugs and 5 placebos) were held by the corresponding author. On arrival of a patient meeting the inclusion criteria, one of the envelopes was opened blindly and the drug or placebo was delivered to the nursing staff.

The patients were followed for 5 consecutive days from their arrival in the hospital. Serial physical examinations and laboratory tests including five arterial blood gas analyses were performed daily.

All of the fractures were immobilized after the arrival of the patient by splinting for tibial fractures. For femoral fractures skin traction was used, which was changed to skeletal within 24 hours. All of the patients underwent

surgical operation for their fractures at least 2 days after arrival at the hospital, which was the usual interval for non-emergent operations. The operation consisted of open reduction and plating the fractures. More sophisticated devices were not available at the time of study. Fat embolism syndrome was diagnosed based on the Gurd criteria.<sup>12</sup>

Hypoxemia was defined as PO<sub>2</sub> less than 80 mm/Hg and severe arterial hypoxemia was defined as PO<sub>2</sub> less than 60 mm/Hg, evaluated by arterial blood gas analysis.

**Results**

Ninety-one patients were enrolled and completed the trial (81 men and 10 women). The age range of the patients was from 16 to 55 years (mean age: 27.38 ± 11.04 years). At the end of the study period, 38 patients were in the corticosteroid group and 53 patients to the control group. There were no statistically significant differences between the two groups regarding the age, sex, and fracture.

In the case group, two patients developed fat embolism syndrome (5.3%), whereas in the control group, 5 patients developed the syndrome (9.4%). All of the seven patients, who developed fat embolism syndrome, presented with the known respiratory, cutaneous and CNS manifestations of the syndrome. No complications related to corticosteroid treatment were observed, although the follow up period was short for most of the patients. Isolated arterial hypoxemia (PO<sub>2</sub> less than 80 mmHg) occurred in nine patients: eight from the control group (17%) and one from the case group (2.8%). Isolated severe arterial hypoxemia (PO<sub>2</sub> less than 60 mmHg) and PCO<sub>2</sub> more than 40 mmHg were not observed in either group. The mean PO<sub>2</sub> in the case group was 88.46 ± 4.88 mmHg (range: 77.22-95.55 mmHg) and 86.81±7.52 mmHg (range: 70.28-98.78 mmHg) in the control group. Statistical analysis revealed no significant difference between the two groups with regard to the number of fat embolism cases, number of patients with arterial hypoxemia or mean arterial oxygen pressure. The P values for these cases were 0.461 (Chi-square test), 0.07 (Fisher's exact test), and 0.386 (Mann-Whitney U test) respectively (table 1).

**Table 1:** Incidence of fat embolism, arterial hypoxia, and the mean arterial pressure in the two groups with the corresponding P value.

	Fat embolism No (%)	Arterial hypoxia No (%)	Mean arterial oxygen pressure (mm Hg)
Control	5 (9.4)	8 (17.0)	86.81 ±7.25
Steroid	2 (5.2)	1 (2.6)	88.46±4.88
P value	0.461	0.07	0.386

## Discussion

Since the first description of fat embolism syndrome controversy has been permeated about the subject. Gossling et al. found fat embolism syndrome in about 10% of patients with multiple long bone fractures. We observed the same in our control group.<sup>4</sup> Levy reported fat embolism in 90% and fat embolism syndrome in 3-4% of traumatic injuries of the limbs.<sup>5</sup> Robert reported an incidence of 0.26% with a mortality of 20% in 20 patients with long bone and pelvis fractures for the syndrome.<sup>6</sup> Fat embolism as a subclinical entity occurs in almost all long bone fractures, with an incidence of at least 90%.<sup>7</sup> The most severe form that appears in a few hours, progresses relentlessly and is fatal in most cases was not seen in our patients.<sup>1</sup>

In 1966, Ashbaugh recommended prophylactic corticosteroid therapy and the treatment has been administered widely to patients with long bone fractures since then, although there is no laboratory evidence demonstrating its beneficial effect in experimental models of this syndrome.<sup>7</sup> Rokkanen et al. were the first to use prophylactic corticosteroids for this purpose.<sup>8</sup> They noticed a six times reduction in the rate of fat embolism syndrome in the group receiving corticosteroid. Lindeque et al. studied the prophylactic effect of methylprednisolone succinate on fat embolism syndrome and its effect on PO<sub>2</sub>, which proved to be successful.<sup>9</sup> They used 30 mg/kg and repeated it after 12 hours, which was much higher than ours. Kallenbach et al. tried to prevent fat embolism syndrome by using a minimum dose of 9 mg/kg methylprednisolone succinate in 82 patients with long bone fractures.<sup>10</sup> Ten patients in the control and one in the case group developed fat embolism syndrome. Severe arterial hypoxemia was seen in seven patients in the control and one in the case group. The authors questioned the safety of such treatment because one of their patients died, and corticosteroids had been cited to produce fat embolism syndrome.<sup>13,14</sup>

A study by Stoltenberg failed to demonstrate a statistically significant difference between the two groups that had and had not received prophylactic steroids regarding the incidence of fat embolism syndrome.<sup>3</sup> However, the authors believed that this treatment could be valuable in selected patients because it decreased the incidence anyway. In the latest study on the topic methylprednisolone succinate was examined in a dose of 5 mg/kg and was not effective in prevention of fat embolism syndrome, although it decreased its incidence.<sup>2</sup>

In that study methylprednisolone could effectively increase the PO<sub>2</sub> on the second and third days of admission, but considering that subclinical hypoxemia is common after long bone fractures,<sup>15</sup> this finding may be insignificant clinically. With these findings, the authors reached the conclusion that although the result was not statistically significant; the decrease in the fat embolism syndrome warranted this treatment for patients with long bone fractures.

As stated earlier, corticosteroids have been used in various doses for this purpose. We decided to use 10 mg/kg as it was not a very high dose and because of the ease of calculations. In our study methylprednisolone succinate did not effectively prevent fat embolism or arterial hypoxemia, although it decreased its incidence. The difference between the two groups was not statistically significant.

A new systematic review about the role of corticosteroids in prevention of fat embolism after long bone fractures has been published recently. This article concludes that the use of corticosteroids reduces the incidence of fat embolism syndrome and hypoxemia in adult patients who have suffered isolated diaphyseal fracture of a lower limb. In this study, the pooled risk for fat embolism after a long bone fracture was 0.16 after corticosteroid prophylaxis.<sup>16</sup>

In summary, based upon our results, methylprednisolone succinate in a single dose of 10 mg/kg is not effective in prevention of fat embolism syndrome, although it decreased its incidence. Corticosteroid therapy can be administered in selected cases such as patients with multiple or bilateral long bone fractures.

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**Conflict of Interest:** None declared

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