

# The use of corticosteroid for the prophylaxis of fat embolism syndrome in patients with long bone fracture

## *Uso de corticoide na profilaxia para síndrome de embolia gordurosa em pacientes com fratura de osso longo*

DOUGLAS FINI SILVA<sup>1</sup>; CÉSAR VANDERLEI CARMONA<sup>2</sup>; THIAGO RODRIGUES ARAÚJO CALDERAN<sup>3</sup>; GUSTAVO PEREIRA FRAGA<sup>4</sup>; BARTOLOMEU NASCIMENTO<sup>5</sup>; SANDRO RIZOLI<sup>6</sup>

### A B S T R A C T

The "Evidence-based Telemedicine - Trauma & Acute Care Surgery" (EBT-TACS) Journal Club conducted a critical review of the literature and selected three recent studies on the use of corticosteroids for the prophylaxis of fat embolism syndrome (FES). The review focused on the potential role of corticosteroids administration to patients admitted to the intensive care unit (ICU) at risk of developing post-traumatic fat embolism. The first study was prospective and aimed at identifying reliable predictors, which could be detected early and were associated with the onset of fat embolism syndrome in trauma patients. The second manuscript was a literature review on the role of corticosteroids as a prophylactic measure for FES. The last manuscript was a meta-analysis on the potential for corticosteroids to prophylactically reduce the risk of fat embolism syndrome in patients with long bone fractures. The main conclusions and recommendations reached were that traumatized patients should be monitored with non-invasive pulse oximetry and lactate levels since these commonly-available tests may predict the development of FES, and the lack of evidence to recommend the use of steroids for the prophylaxis of this syndrome.

**Key words:** Adrenal cortex hormones. Primary prevention. Embolism, fat. Patients. Fractures, bone.

### INTRODUCTION

Fat embolism syndrome (FES) is common in patients with long bone fractures and can be fatal. Delayed diagnosis of this syndrome increases the risk of devastating consequences<sup>1-4</sup>. For this reason FES should be considered and treated early<sup>5</sup>.

The use of corticosteroids in FES has been proposed in numerous small clinical trials, but its recommendation remains controversial<sup>1</sup>.

The participants of the "Evidence-based Telemedicine - Trauma & Acute Care Surgery" (EBT-TACS) Journal Club, after reviewing the literature on this topic, selected three articles that address important questions about the use of corticosteroids for the prevention of

FES: 1) the existence of markers capable of predicting the development of FES, which could be used in clinical practice and lead prophylactic measures for FES; 2) the recommendation for the use of corticosteroids in the prevention of FES<sup>1-3</sup>.

### STUDY 1

"Early, reliable, utilitarian predictive factors for fat embolism syndrome in polytrauma patients"<sup>1</sup>

#### Background

Fat embolism syndrome (FES) is a very serious condition and delayed diagnosis may have serious

The "Evidence-based Telemedicine - Trauma & Acute Care Surgery" (EBT-TACS) Journal Club's session on September 17<sup>th</sup>, 2013, with the participation of following institutions: Trauma Program of the Department of Surgery of Sunnybrook Health Sciences Center, University of Toronto, Toronto, Canada; Trauma Program of St Michael's Hospital, Toronto, Canada; Division of Trauma Surgery, Department of Surgery, School of Medical Sciences, University of Campinas, Campinas, SP, Brazil.

1. Douglas Fini Silva. Emergency Care Physician at Hospital de Clinicas (HC) at the University of Campinas (Unicamp), Campinas, SP, Brazil; 2. César Vanderlei Carmona. Attending Physician and Coordinator of the Trauma ICU, Division of Trauma Surgery, Department of Surgery, School of Medical Sciences, University of Campinas, Campinas, SP, Brazil; 3. Thiago Rodrigues Araujo Calderan. Attending Physician, Division of Trauma Surgery, Department of Surgery, School of Medical Sciences, University of Campinas, Campinas, SP, Brazil; 4. Gustavo Pereira Fraga, TCBC, FACS. Professor Coordinator of the Division of Trauma Surgery, Department of Surgery, School of Medical Sciences, University of Campinas, Campinas, SP, Brazil; 5. Bartolomeu Nascimento. Assistant Professor, Department of Surgery, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada; 6. Sandro Rizoli, FRCSC, FACS. Full Professor in the Department of Surgery and Critical Care Medicine, University of Toronto, and Director of Trauma at St Michael's Hospital, Toronto, Canada.

consequences. Therefore predictors can be very useful in guiding prevention and treatment.

### Question

Are there reliable and useful predictors that early, reliably and economically predict the development of FES in trauma patients?

### Main findings of this study

There is a correlation between admission serum lactate levels ( $> 22$  mmol/l), FES ( $p = 0.07$ ) and hypoxemia ( $p = 0.003$ ).

Continuous noninvasive pulse oximetry during the first 72 hours in the ICU is associated with the onset of pulmonary complications. There is a correlation (100% sensitivity) between at least one episode of desaturation during the first 24 hours and the development of FES.

In this study, the increase in the serum lactate levels ( $> 22$  mmol/l) and episode(s) of hypoxemia, even when transient, were associated with an increased chance of developing FES ( $p < 0.02$ ).

### Strengths

1. The topic is current and clinically relevant in view of the growing number of patients victims of high-energy trauma;
2. Analyzed routinely measured parameters that require little change in care routine;
3. Low cost of detection suggested by the study.

### Limitations

1. Included a small number of patients ( $n=67$ ).
2. Exclusion criteria for the analysis meant common conditions such abdominal trauma, brain and thoracic injury were disregarded, thus limiting the generalizability of the findings.
3. It is unclear whether patients were uniformly treated, i.e. time interval for fracture fixation, allowing for the interpretation that these parameters may have affected the outcome of patients, increasing the risk of developing FES.

## STUDY 2

"Role of corticosteroids as a prophylactic measure in fat embolism syndrome: review of the literature"<sup>2</sup>

### Background

FES is a serious condition in trauma patients with fractures of the lower limbs, and it is not yet clear whether corticosteroids should be used as a prophylactic measure for this syndrome.

### Question

What is the real role of corticosteroids in the prophylaxis of FES?

### Main findings of this study

This study analyzes seven clinical trials that included 483 patients: 223 patients prophylactically treated with corticosteroids and 260 not (control group). Of the total, 9 patients in the group receiving corticosteroids developed FES versus 60 in the control group, resulting in a statistically significant difference ( $p < 0.05$ ).

### Strengths

1. Clinical trials whose designs prioritized equal distribution between the intervention and control groups, according to severity of the injuries.
2. The study designs included an analysis of possible adverse effects and complications from the use of corticosteroids.
3. Low cost medication, easy access and management.
4. Easily reproducible results

### Limitations

1. Lack of uniformity in the diagnostic criteria for FES among the different studies.
2. The majority of the studies were old, making it difficult to make a comparative analysis with the current critical care of patients.
3. Large differences in the dose and interval of corticosteroids in the various studies.
4. Despite statistically significant use of corticosteroids for the prophylaxis of FES, the studies do not provide evidence about the actual role of the medication.
5. Small number of patients included in the analysis.

## STUDY 3

"Do corticosteroids reduce the risk of fat embolism syndrome in patients with long bone fractures? A meta-analysis"<sup>3</sup>

### Background

The incidence of fat embolism in patients with long bone and pelvis fractures is high, exceeding 80%. The cases of FES represent up to 33% of cases of patients with bilateral femur fractures, with mortality rates ranging from 5 to 20%. This justifies finding a treatment that prevents the appearance of FES.

### Question

Based on available studies, is there evidence that the use of corticosteroids in trauma patients with long bone fractures reduces the risk of FES?

### Main findings of this study

The manuscript is a meta-analysis of several English language and non-English language studies that

were published from 1966 to 2006 using the MEDLINE, EMBASE, HealthSTAR, CINAHL and Cochrane research databases, related to the subject of active research, and of papers in orthopedic magazines, as well as orthopedic conference proceedings and orthopedic textbooks.

104 studies related to the topic were found, of which seven met the criteria of being randomized or semi-randomized studies on the use of corticosteroids for the prevention of FES in patients with fractures of at least one long bone. The patients were divided into receiving the treatment and control group (no prophylaxis).

Combined analysis of studies included 389 patients, and found that corticosteroids reduced the risk of FES in 78% (relative risk [RR] 0.22).

There was a 61% reduction of the risk of hypoxia, with no influence on the appearance of petechial rash or on overall mortality.

Using a sensitivity analysis, it was concluded that low-dose corticosteroids (methylprednisolone 6 mg/kg for 48 h in 6 divided doses) would be more effective than higher doses.

The use of corticosteroids was not associated with an increased incidence of infection.

### Strengths

1- A meta-analysis with extensive review of English and non-English language literature was conducted.

2- Randomized studies were selected and two were considered quasi-randomized by alternate sequence selection.

3- The studies were selected by experts blinded to the origin of the study and patient outcome. The reviewers were also blinded to origin and outcome.

4- The quality of the articles was determined using a score of 21 points, which were converted into grades ranging from 0 to 100, the higher the score, the better the quality.

### Limitations

1 - With the exception of a 2004 article, the other six studies were more than 20 years old<sup>6-8</sup>.

2 - The number of patients included in this meta-analysis was small (389), which was split into two groups and originating from few prospective and randomized studies.

3 - The grades used to measure the quality of evaluated articles ranged from 24 to 74, according to the authors themselves.

4 - Although this meta-analysis came up with a result largely supporting the use of corticosteroids, the authors suggest that other non-measured variables, which could influence the outcome, were not included. Non-measured variables include the more recent changes in the standards of care, such as earlier fixation of fractures, protective ventilation with lower tidal volumes and the similarity in the clinical diagnosis of SIRS and FES may have over the course of time that these studies span, confounded the results, leading to false conclusions.

## CONCLUSIONS

FES is a serious complication that occurs in trauma patients, and the standardization of care in order to achieve early detection of this condition may represent a fundamental aspect of the proper therapeutic approach to these patients. The non-invasive monitoring using continuous pulse oximetry, as well as an elevated serum lactate had a good correlation with increased risk of developing FES.

The use of corticosteroids as a prophylactic measure has been recommended by the available clinical trials. However, this recommendation is not without controversy, mainly due to significant differences among the designs of the clinical trials, as well as the lack of uniformity in diagnostic parameters and the interval / dosage of corticosteroid used.

## RECOMMENDATIONS

Recommendations for the treatment of trauma patients at risk for development of FES are:

1. Continuous monitoring, using noninvasive pulse oximetry.

2. Admission serum lactate levels.

3. Conducting further clinical trials with standardization of diagnostic and therapeutic parameters for an adequate analysis of the evidence.

4. There is still not enough evidence to recommend the use of prophylactic corticosteroids in patients with long bone fractures.

**R E S U M O**

A reunião de revista "Telemedicina Baseada em Evidência - Cirurgia do Trauma e Emergência" (TBE-CiTE) realizou uma revisão crítica da literatura e selecionou três artigos recentes sobre o uso de corticoide para a profilaxia da síndrome de embolia gordurosa. O foco desta revisão foi a indicação ou não do uso de corticoide nos pacientes admitidos na unidade de terapia intensiva (UTI) com risco de desenvolverem embolia gordurosa pós traumática. O primeiro artigo foi um estudo prospectivo com o objetivo de estabelecer fatores preditivos confiáveis, precoces e úteis associados ao aparecimento da síndrome da embolia gordurosa (SEG) em pacientes traumatizados. O segundo artigo foi uma revisão de literatura sobre o papel do corticoide como medida profilática à síndrome de embolia gordurosa. O último artigo foi uma meta-análise sobre a capacidade do corticoide em reduzir o risco de síndrome da embolia gordurosa nos pacientes com fraturas de ossos longos. As principais conclusões e recomendações foram que pacientes traumatizados devem ser monitorizados na UTI com oximetria de pulso e medida do lactato já que estes fatores podem prever o aparecimento de SEG e que não existe evidência suficiente para recomendar o uso de corticoide para a profilaxia desta síndrome.

**Descritores:** Corticosteroides. Prevenção primária. Embolia gordurosa. Pacientes. Fraturas ósseas.

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**Statement**

The opinions and assertions contained herein represent the private views of the participants of the Evidence-based Telemedicine - Trauma and Acute Care Surgery (EBT-TACS) Journal Club, and are not to be construed as reflecting the views of the institutions that they represent.

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**Address correspondence to:**

Sandro Rizoli

E-mail: rizolis@smh.ca