# PROPHYLACTIC USE OF CORTICOSTEROIDS IN A SINGLE LONG BONE FRACTURE OF LOWER LIMB TO PREVENT FAT EMBOLISM SYNDROME – A CLINICAL EXPERIENCE

**Prashanth N[1], Neeta PN[2], Amit RU[3,*], Shilpa K[4]**

[1]Senior Resident, Department of Anesthesiology, [2]Assistant Professor, Department of Community Medicine, VIMS, Bellary, Karnataka, India.
[3]Assistant Professor, Department of Microbiology, [4]Assistant Professor, Department of Community Medicine, Azeezia Institute of Medical Sciences, Kerala, India.

***Corresponding Author:**
E-mail address: amitrun9979@gmail.com

**ABSTRACT**

**Background**: *Fat embolism syndrome is commonly associated with long bone fractures and the mortality associated with it is due to cerebral and pulmonary involvement. Recently experimental and clinical data have suggested that the benefit of corticosteroid therapy may be maximized if the treatment is given early as a prophylaxis for the development of the fat embolism syndrome in high risk patients. The aim of our study was to test the efficacy of single dose methyl prednisolone as prophylaxis to prevent Fat embolism syndrome in patients with single long bone fracture of lower limb.*

**Methods**: *We conducted a double blinded randomized control among 44 patients, who showed signs and symptoms of sub clinical fat embolism and fulfilled our inclusion and exclusion criteria over 2years period in a tertiary trauma care centre, Bangalore, Karnataka. These 44 patients were randomly selected and assigned 1 envelope and segregated to respective group. The nursing staffs who were educated about the division of groups administered the drug methyl prednisolone or normal saline accordingly. We were blinded to this allocation of groups and drug administration. The patients were followed up by us in the ICU and wards. At the end of study, the group allocation was disclosed. Among these patients were divided into Control Group A (21 patients), who were given placebo treatment with normal saline and Study Group B (23 patients), who were given a single dose of methyl prednisolone 30mg/kg over one hour.*

**Results**: *Among the 44 patients analyzed, 33.3% of group A and 8.7% of group B patients developed clinical Fat Embolism Syndrome (FES). The mean duration of ventilator support in group A (9.25 days) was higher than in the group B (7.33days). There was significant increase in the vital parameters like heart rate and respiratory rate as well as significant fall of Spo2, in control group than the study group postoperatively. There is no change in the PaCO2, systolic and diastolic blood pressure.*

**Conclusion**: *A Single prophylactic dose of Methyl Prednisolone 30 mg/kg significantly reduces the incidence of Fat Embolism Syndrome. Hence use of Methyl Prednisolone as a Prophylaxisfor Fat Embolism Syndrome in long bone fractures of lower limbs is beneficial.*

**Key words**: *Fat embolism syndrome, Methyl prednisolone, long bone fracture*

## INTRODUCTION

Fat embolism is the most frequent cause of death after fracture of long bones [1].The most common clinical situation in which Fat embolism syndrome may develop is orthopedic or general trauma. A high association with multiple long bone fractures also is found. Although pulmonary fat embolization occurs in almost all patients with long bone fracture [2, 3], only 1% to 30% [4] of patients develop the full, clinical fat embolism syndrome that consists of petechial rash, diffuse pulmonary infiltrates, hypoxemia, confusion, pyrexia, tachycardia and tachypnea, 24 to 48 hour after trauma. Since 1966, several studies have claimed benefit from corticosteroid therapy for this syndrome [5, 6, 7]. However most of these studies have been retrospective.

Recently experimental and clinical data have suggested that the benefit of corticosteroid therapy may be maximized if the treatment is given early as a prophylaxis for the development of the fat embolism syndrome in high risk patients.

A study reported a series of 48 patients with uncomplicated extremity fractures who were randomized into fluid loading, hypertonic glucose, aspirin, steroids or control groups. Methyl prednisolone 30ml/kg every six hours was given to steroid group. They demonstrated

consistently significant improvement in $PO_2$ levels with apparent coagulation mechanism stabilization in steroid group as compared to control [8].

Another study conducted a prospective randomized trial of prophylactic therapy in fat embolism syndrome with three groups treated with (a) Hypertonic glucose (b) Methyl prednisolone and (c) Placebo and showed that methyl prednisolone given prophylactically may reduce the incidence of fat embolism syndrome and can reduce the degree of hypoxemia associated with long bone fractures of lower extremity. In this study the first group received 50% Dextrose; study group received three 1 gm doses of methyl prednisolone every eight hours beginning on admission. Incidence was 21% in glucose group, 0% in steroid group and 29% in control groups [9].

To test the prophylactic value of corticosteroid therapy in patients with fracture, we prospectively administered methyl prednisolone sodium succinate in a randomized double blind study of 44 patient believed to be at risk for fat embolism syndrome and who had no other major injuries that might otherwise predispose them to posttraumatic respiratory failure.

## MATERIALS AND METHODS

The present study was conducted from May 2005 to May 2007, in a tertiary care centre especially for trauma in Bangalore, Karnataka, India. In this period 210 patients with single long bone fracture of lower limb (femur or tibia) fulfilling our criteria were attended in the casualty and evaluated for subclinical fat embolism by peripheral oxygen saturation using pulse oxymeter and arterial blood gases.

Inclusion criteria -

a. Patients with closed fracture long bone in lower limb.
b. ASA – I
c. Age- < 45 years

Exclusion Criteria-

a. Patients with polytrauma.
b. Patients with head injury and sepsis.
c. Patients associated with fracture ribs and lung contusion.
d. Patients with ischemic heart disease, congenital heart disease, hypertension and valvular heart disease.
e. Patients with blunt injury to thorax, abdomen, head and neck.
f. Patients with cervical spine injury and facio-maxillary injuries.
g. Patients with shock – hemorrhagic, septic, cardiogenic and neurogenic.
h. Patients with vascular injuries.
i. Associated with respiratory system and other medical illness like chronic obstructive airway disease, pneumonia (Aspiration) or lower respiratory tract infection.

Among these, total of 44 patients showed signs and symptoms of subclinical fat embolism and were selected for our study and assigned 1 envelope and segregated to respective group. Of selected patients, 21 were in Group A (control) and 23 were in Group B (study) were placed randomly. These 44 patients were subjected to a prospective randomized double blind study to test the efficacy of single dose of Methyl Prednisolone as a prophylactic for fat embolism syndrome development. The nursing staffs who were educated about the division of groups administered the drug methyl prednisolone or normal saline accordingly. We were blinded to this allocation of groups and drug administration. The patients were followed up by us in the ICU and wards. At the end of study, the group allocation was disclosed.

Patients in Control Group A (21 patients), received placebo treatment with normal saline and Study Group B (23 patients), received a single dose of methyl prednisolone 30mg/kg over one hour.

A. Mellor & Neil Soni[10] reviewed several Randomized Controlled Trials which reported beneficial effect of Methyl prednisolone used in doses ranging from 9 – 90 mg/kg. Only three trials reported significantly improved gas exchange. A ten-fold decrease in Fat Embolism Syndrome was seen in one series. One fatality was reported in these trials due to sepsis in a patient receiving Methyl prednisolone. 30 mg/kg of methyl prednisolone is the

recommended therapy for some life threatening conditions.[22]

Institutional ethical committee clearance was obtained and written informed consent was taken from all patients or their relatives. Both groups otherwise received the same supportive treatment like oxygen supplementation, intra venous fluids, antibiotics, antacids, chest physiotherapy, incentive spirometry, etc. All the patients underwent surgical fixation of bones i.e. intramedullary nailing within 12 hours. The patients were followed up and assessed for development of signs and symptoms suggestive of clinical "Fat Embolism Syndrome" using clinical monitoring and serial investigations like pulse oximetry, arterial blood gases, urine fat globules, platelet count, fibrin degradation products (D-Dimer), altered sensorium and chest x ray.

Intra operatively patients were supplied oxygen at 5 lit/min through ordinary mask or $FiO_2$ of 0.4 maintained in general anesthesia. All the patients monitored clinically for fat embolism syndrome. Arterial blood gas analysis was done in some patients who had hypoxia intra operatively and $FiO_2$ increased accordingly.

Post operatively also patients were monitored for 24 hours in similar way. The patients who developed respiratory failure were given ventilator support.

In the study Fat embolism syndrome was described on basis of Lindeque's criteria [10].

1. A sustained $PaO_2$ of less than 8 k.Pa (60mm of Hg) with $FiO_2$ 0.21.
2. A sustained $PaCo_2$ of more than 7.3 k.Pa (55mm of Hg) or pH of less than 7.3
3. A sustained respiratory rate of greater than 35breath/min. even after adequate sedation.
4. Increased work of breathing judged by dyspnoea use of accessory muscles, tachycardia and anxiety.

Any patient with fracture femur and/or tibia showing one or more of these criteria was judged as having Fat Embolism Syndrome.

Data was analyzed and expressed in terms of rates, ratios and percentages. Statistical analysis was done using Pearson's Chi Square test. A probability value (p value) of less than 0.05 was considered as significant.

## RESULTS

The study was conducted in HOSMAT hospital, Bangalore, a tertiary trauma care centre from May 2005 to May 2007. Ethical Clearance was obtained from the Hospital Ethics review committee. The objective was to study the efficacy of methyl prednisolone as prophylaxis for Fat Embolism Syndrome in single long bone fracture of lower limb.

One fatality was reported in the series of trials due to sepsis in a patient receiving Methyl prednisolone of 9-90mg/kg. 30 mg/kg of methyl prednisolone is the recommended therapy for some life threatening conditions.[10,22]

In the study period, all patients coming to the Casualty with single long bone fractures were evaluated. A total of 210 Patients with closed fracture of tibia or femur and without any other major injuries were screened for sub clinical Fat Embolism. Among them, 44 patients (20.95 %) confirmed to the inclusion criteria for Fat Embolism and were hence included for the study after obtaining informed consent. Out of 210 patients, nine developed FES, eight among fracture femur and one among fracture tibia.

These 44 patients were then placed randomly into Group A (control), with 21 patients and Group B (study), with 23 patients. Mean age was 26.95 years for Group A and 28.78 years for Group B. Majority of patients (76.19% Group A & 86.96% Group B) were males. Most of the patients (61.9% of Group A & 73.91% of Group B) showed normal chest X- ray. On admission mean values of vital parameters (heart rate, respiratory rate, systolic and diastolic Blood Pressure as well as $SPO_2$) were within normal limits for both the groups. Arterial blood gas analysis (pH,

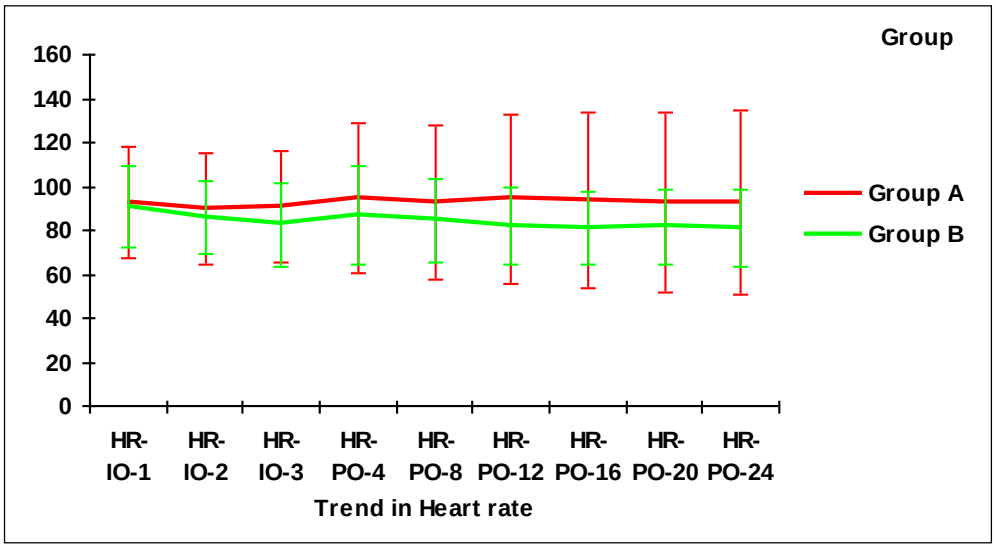
$PaO_2$, P $aCO_2$) of both groups was similar and within normal limits on admission. These data shows that we received both groups of patients in same condition.

At start of surgery, the mean values of $SPO_2$ were 94.38% with s.d of ±1.72 in Group A and 94.74% with s.d of 1.57 in Group B. 24 hours after the surgery the $Spo_2$ was 94±6.53% in Group A and 97.48±3.98% in Group B. There was significant fall in saturation in Group A patients 24 hours after surgery. (Table 1)

**Table.1: Compares the Spo2 readings of patients in two groups at regular intervals.**

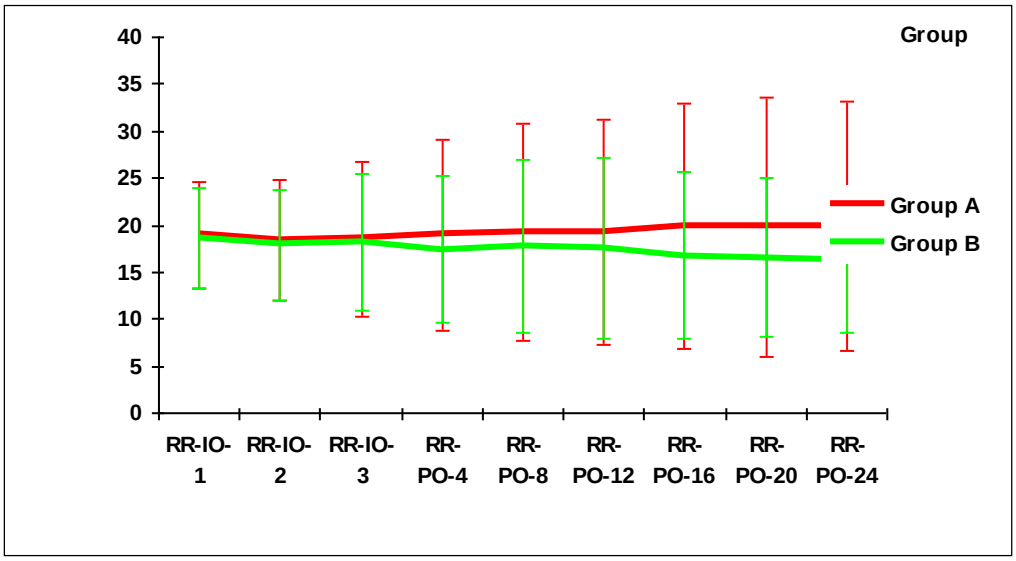
| | Intraop 1st Hour | Intraop 2nd hour | Intraop 3rd hour | Postop 4th hour | Postop 8th hour | Postop 12th hour | Postop 16th hour | Postop 20th hour | Postop 24th hour |
|---|---|---|---|---|---|---|---|---|---|
| Group A (n=21) | 94.38 ±1.72 | 95.19 ±1.40 | 94.86 ±2.39 | 94.10 ±2.77 | 94.57 ±3.79 | 94.29 ±4.81 | 94.33 ±5.50 | 94.19 ±6.22 | 94.10 ±6.53 |
| Group B (n=23) | 94.74 ±1.57 | 95.78 ±1.20 | 95.87 ±1.94 | 94.78 ±2.30 | 95.70 ±2.69 | 96.48 ±2.61 | 97.04 ±3.56 | 97.57 ±3.69 | 97.48 ±3.98 |
| t | 0.72 | 1.49 | 1.53 | 0.89 | 1.13 | 1.86 | 1.92 | 2.16 | 2.05 |
| p-value | 0.48 | 0.14 | 0.13 | 0.38 | 0.27 | 0.07 | 0.06 | 0.04 | 0.05 |
| Statistical significance | N.S. | N.S. | N.S. | N.S. | N.S. | N.S. | N.S. | S. | S. |

The heart rate on admission was 92.90±12beats/min and 90.96±9.23beats/min in Group A and Group B patients respectively. The heart rate was significantly increased in Group A patients i.e. 92.43±20.93beats/min as compared to Group B (80.91±8.93 beats/min), 24 hours after surgery. (Graph 1)




**Graph.1: Shows the trend in heart rate in patients of two groups.**

Before the surgery respiratory rate was around 18breaths/min in both the groups. Whereas 24 hours after the surgery it was increased significantly in Group A Patients i.e. 19±6breaths/min when compared to Group B, i.e.16±3breaths/min. (Graph 2)




**Graph.2: Shows the trend in respiratory rate in patients of two groups.**

The systolic as well as diastolic blood pressure did not show any variation between two groups during pre operative, intra operative or post operative period. The incidence of FES in Group A was 33.3% (7 out of 21), where as in Group B 8.7% (2 out of 23), which is statistically significant (p value = 0.043). The mean duration of ventilator support required was higher in Group A (9.25 days) than in Group B patients (7.33days).

## DISCUSSION

Fat embolism syndrome is fat in circulation associated with an identifiable pattern of clinical symptoms and signs [11]. The lack of definitive diagnostic criteria, the unpredictable course and frequent associated disease have made it difficult to standardize patient population [12].

Fat embolism syndrome can be diagnosed using

1) Gurd´s criteria [13]
2) Lindeque´s criteria [14]

Gurd´s criteria for diagnosis of fat embolism syndrome have been criticized for being unreliable because fat droplets can frequently be found in the blood of healthy volunteers and trauma patients, without clinical evidence of fat embolism syndrome [15]. Lindeque suggested that Gurd´s criteria may under diagnose the syndrome and proposed his criteria based on respiratory parameters [14]. Lindeque´s criteria involved arterial blood gas study which is gold standard for detection of hypoxia. Gurd´s criteria do not use arterial blood gas analysis as criteria.

In our study a total of 210 patients were randomly selected and evaluated in the casualty for hypoxemia with arterial blood gas analysis. The incidence of fat embolism in patients with fracture femur was significantly higher ($p= 3.63 X 10^{-18}$) than that with tibia. The incidence of sub clinical fat embolism was similar to previous studies with involvement of patients with single long bone fracture [16].

In one study Fat embolism occurred within 72 hours in all patients who developed Fat Embolism Syndrome [16]. The syndrome developed within 24 hours in the present study. The interval between the injury and the admission varied widely from one hour to 48 hours in our study. This wide interval could be attributed to the fact that our institution is the only tertiary care referral center for trauma in Bangalore and attracts patients from both within and outside the city.

The mean baseline values in all patients included in the study were: Heart rate of 96 beats/min, respiratory rate 20breaths/min, Systolic BP 115 mm of Hg and Diastolic BP of 76 mm Hg. The $SpO_2$ on Pulse Oximetry showed less than 94 % in all patients with Fat embolism on room air. The Arterial Blood Gas (ABG) values on room air in these patients showed mean

values of $PO_2$ 61 mm Hg, $PCO_2$ 33 mm Hg and pH 7.32. The PO2 values were similar to that obtained by Tachakra et al [17]. This overall picture of Hypoxemia following long bone fracture was suggestive of Fat embolism.

These 44 patients were subjected to prospective double blind study to test efficacy of methyl prednisolone as prophylaxis to fat embolism syndrome. We used single dose of 30mg/kg of Methyl prednisolone administered over one hour as infusion in study group patients soon after admission after being diagnosed to have sub clinical fat embolism. All fractures were surgically stabilized within 12 hrs of admission. They were followed up for a period of 24 hrs for development of signs and symptoms of fat embolism syndrome, which was defined on basis of Lindeques criteria [14].

It is thought that steroids may act by decreasing the edema, increasing vascular integrity, and preventing the inflammatory response to the hydrolyzed products of the lodged fatty acids. Steroids are also thought to exert a general effect on stabilization of lipoid membranes [5].

Methyl prednisolone has been used in different doses from 6mg/kg to 90mg/kg both as a prophylactic and as a treatment modality for fat embolism syndrome by different authors [9, 12, 18, 19, 20, 21, 22]. Another study had used 80-125 mg of methyl prednisolone every six hours for 3 days primarily as treatment for Fat Embolism Syndrome [5]. Methyl prednisolone used as prophylaxis in a dose of 30mg/kg does not increase risk of infection or sepsis [23].

In the present study, the reading at $24^{th}$ hour after surgery showed a statistically significant fall in saturation and a rise in heart rate and respiratory rate in Group A (Control) patients as compared to that in Group B (Study) patients, which is suggestive of Fat Embolism Syndrome in these patients due to fat emboli being released into the systemic circulation secondary to fracture manipulation and reaming of marrow cavity during surgery.

Four out of 21 in control group and three out of 23 patients in study group required ventilator support which was not statistically significant. Only one patient in the control group with Fat embolism syndrome who was on ventilator support died of multi organ dysfunction syndrome.

The incidence of clinical Fat embolism syndrome in study group patients (8.7%) was significantly lower than that in control group patients (33.3%). Our study demonstrated that Methyl prednisolone 30 mg/kg significantly reduces the incidence of Fat Embolism Syndrome when given as a single prophylactic dose. This is in close agreement in the study, where Methyl prednisolone 30 mg/kg was given in divided doses [12].

## CONCLUSION

A Single prophylactic dose of Methyl Prednisolone 30 mg/kg significantly reduces the incidence of Fat Embolism Syndrome. Hence use of Methyl Prednisolone as a Prophylaxisfor Fat Embolism Syndrome in long bone fractures of lower limbs is beneficial.

**CONFLICTS OF INTEREST**: Nil.
**SOURCE OF FUNDING**: None.

**ACKNOWLEDGEMENT**: We thank Dr Thomas A Chandy, Dean and Director of HOSMAT hospital, Bangalore, for giving permission to carry out research.

## REFERENCES:

1. Warthin AS: Traumatic lipemia and fatty embolism. IntClin 1913;4:171-227.
2. Evarts CM: The fat embolism syndrome- a review. SurgClin North America 1970;50:493-507.
3. Emson HE: Fat embolism studied in 100 patients dying after injury. J Clin Path 1958;11:28-35.
   Herndon: The syndrome of fat embolism. South J Med 1975;68;1577-84.
4. Fischer JE, Turner RH, Herndon JH, Riseborough EJ: Massive steroid therapy in severe fat embolism. SurgGynecolObstet 1971 April;24:667-72.
5. Ashbaugh DG, Petty TL: The use of corticosteroids in the treatment of respiratory failure associated with massive fat embolism. SurgGynecolObstet 1966;123:493.

6. Moylan JA, Birnbaum M, Katz A, Everson MA: Fat emboli syndrome. J Trauma 1976;16;341-7.
7. Shier MR, Wilson RF, James RE, Riddle J, Mammen EF, Pedersen HE: Fat embolism prophylaxis - A study of four treatment modalities. J Trauma 1977;17:621
8. Stoltenberg JJ, Gustilo RB: The use of methylprednisolone and hypertonic glucose in the prophylaxis of fat embolism syndrome. Clinic OrthopRelat Res 1979 Sep;143:211–21
9. Gosling HR, Pellengrini VD: Fat embolism syndrome – A review of the Pathology and Physiological basis of treatment. Clinic OrthopRelat Res 1982 May;165:68-82.
10. Mellor A, Soni N. Fat Embolism : Review article. Anaesthesia 2001;56:145–54.
11. Antti A, Kari Saikku, Pekka E, Matti K, Hamalainen M: Corticosteroids in patients with a high risk of fat embolism syndrome. SurgGynecolObstet 1978 Sept;147:358–62.
12. Gurd AR: Fat Embolism; an aid to diagnosis. J Bone Joint Surg 1970;52B:732–7.
13. Lindeque BG, Schoeman HS, Domisse GF, Boeyens MC, Vlok AL: Fat Embolism and Fat Embolism Syndrome – A double blind therapeutic study. Br J Bone Joint Surg 1987; 69:128–31.
14. Nolte WJ, Olofsson T, Schersten T, Lewis DH: Evaluation of the Gurd test for fat embolism. Br J Bone Joint Surg 1974; 56B:417-20.
15. Richard B Ganong: Fat embolism syndrome in isolated fractures of the tibia and femur. Clinic OrthopRelat Res 1993 June; 291:208-14.
16. Tachakra SS, Sevitt S: Hypoxaemia after fractures. J Bone Joint Surg 1975 May;57(2):197-203.
17. Schonfeld AS, Yongyudh P, Ralph D, John DC, Edward M, Dale EH et al: Fat embolism prophylaxis with corticosteroids; a prospective study in high risk patients. Annals of Internal Medicine 1983; 99:438-43.
18. Kallenbach JL, Zaltzman M, Feldman C, Orford A, Zwi S: 'Low dose' corticosteroid prophylaxis against Fat Embolism. J Trauma 1987 Oct:27(10):1173–6.
19. Babalis GA, Yiannakopoulos CK, Karliaftis K, Antonogiannakis E: Prevention of posttraumatic hypoxemia in isolated lower limb long bone fracture with a minimal prophylactic dose of corticosteroids. Injury 2004 Mar;35(3):309–17.
20. Rokkanen PA, Avikainen AV, Karaharaju E, Kataja J, Lahdensuu M, Lepisto et al: The efficacy of corticosteroids in severe trauma. SurgGynecolObstet 1974; 138:69.
21. Shier MR, Wilson RF, James RE, Riddle J, Mammen EF, Pedersen HE: Fat embolism prophylaxis - A study of four treatment modalities. J Trauma 1977; 17:621.
22. Therapeutic index: Anti-inflammatory drugs :URL:http://www.Cipladoc.com