akademik acil tıp dergisi

A Novel Experimental Bilateral Blunt Chest Trauma Model on Rabbits and its Effects in Lung

Tavşanlarda Deneysel İki Taraflı Yeni Künt Göğüs Travması Modeli ve Akciğere Etkileri

Halil Kaya[1], Mehmet Ertuğrul Kafalı[2], Kemal Aydın[3], Mustafa Şahin[2], Arif Duran[4], Ayşegül Bayır[5], Hatice Toy[6], Özgür Söğüt[1]
[1]Department of Emergency Medicine, Faculty of Medicine, Harran University, Sanliurfa, Turkey
[2]Department of General Surgery, Selcuklu Medical Faculty, Selcuk University, Konya, Turkey
[3]Department of Emergency Medicine, Diskapi Education and Research Hospital, Ankara, Turkey
[4]Department of Emergency Medicine, Faculty of Medicine, Abant Izzet Baysal University, Bolu, Turkey
[5]Department of Emergency Medicine, Selcuklu Medical Faculty, Selcuk University, Konya, Turkey
[6]Department of Pathology, Meram Medical Faculty, Selcuk University, Konya, Turkey

Abstract

Objective: Blunt chest trauma (BCT) is an important problem in emergency services and Intensive Care Unit (ICU) due to high morbidity and mortality. Some aspects of pulmonary contusion of BCT have not been evident. We aimed to investigate the effects of BCT on the blood gas, biochemical parameters and microscopic and macroscopic level of lung by using a novel trauma model.

Materials and Methods: The rabbits were separated into two cohorts of seven. (trauma and control groups). Standardized blunt force was applied to the thorax of animals in the trauma group. Calculated energy via Newton Law was focused on the chest. Blood pressure, heart rate, respiratory rate, arterial blood gases and biochemical levels were recorded. Histopathological examinations of the lungs were performed.

Results: The cardiovascular response to the injury was tachycardia in the trauma group. Pulmonary responses observed in the trauma group relative to control animals were a decrease in SO_2, PO_2 and an increase in CO_2. Biochemical injury markers found to be elevated in the experimental group. After the in vivo phase of the study, histological assessment confirmed features characteristic of pulmonary contusion. No signs of abdominal injury were observed in experimental animals on necropsy.

Conclusion: We suggest that this model is an alternative way for clinical investigation of different drugs effective in bilateral blunt chest trauma. Our developed model is practical, cheap and useful and the experimental values can be changed easily. *(JAEM 2011; 10: 103-9)*

Key words: Bilateral blunt chest trauma, pulmonary effects, lung contusion, Newton Law

Received: 05.01.2011 **Accepted:** 23.03.2011

Özet

Amaç: Künt göğüs travması yüksek morbiditesi ve mortalitesi nedeniyle Acil Servis ve yoğun bakım ünitelerindeki önemli problemlerden biridir. Künt göğüs travmasına bağlı akciğer kontüzyonunun bazı yönleri aşikar değildir. Biz, yeni bir travma modeli kullanarak tavşanlarda iki taraflı künt göğüs travmasının kan gazları, biyokimyasal parametreler ve akciğerin mikroskobik ve makroskobik düzeyi üzerine etkilerini araştırmayı amaçladık.

Gereç ve Yöntemler: Tavşanlar her biri 7'şerli olmak üzere travma ve kontrol diye iki gruba ayrıldı. Standardize edilmiş künt travma, travma grubuna uygulandı. Newton Yasası'na göre hesaplanan enerji tavşanların göğüs kafesine uygulandı. Kan basıncı, kalp hızı, solunum sayısı, arteryel kan gazları ve biyokimyasal markerler kaydedildi. Akciğerin histopatolojik incelemesi yapıldı. Tavşanlar her biri 7'şerli olmak üzere travma ve kontrol diye iki gruba ayrıldı. Standardize edilmiş künt travma, travma grubuna uygulandı. Newton Yasası'na göre hesaplanan enerji tavşanların göğüs kafesine uygulandı. Kan basıncı, kalp hızı, solunum sayısı, arteryel kan gazları ve biyokimyasal markerler kaydedildi. Akciğerin histopatolojik incelemesi yapıldı.

Bulgular: Travma grubunda kardiyovasküler olarak taşikardi görüldü. Pulmoner bakımdan PO_2, SO_2 düşerken CO_2 düzeyinde artış görüldü. Histolojik değerlendirmede pulmoner kontüzyon izlendi. Abdominal yaralanma bulguları gözlenmedi.

Sonuç: Bu modeli bilateral künt göğüs travmasında farklı ilaçların klinik değerlendirmesi için önerebiliriz. Geliştirdiğimiz model pratik, ucuz ve kullanışlıdır ve çalışma verileri kolaylıkla değiştirilebilir.
(JAEM 2011; 10: 103-9)

Anahtar kelimeler: Bilateral künt göğüs travması, akciğer etkilenmesi, akciğer kontüzyonu, Newton Yasası

Alındığı Tarih: 05.01.2011 **Kabul Tarihi:** 23.03.2011

Correspondence to / Yazışma Adresi: Yard. Doç. Dr. Halil Kaya, Department of Emergency Medicine, Faculty of Medicine, Harran University, Sanliurfa, Turkey
Phone: +90 505 443 19 73 e.mail: drhalilkaya@gmail.com
doi:10.5152/jaem.2011.020

Introduction

The study of LC is certainly relevant to the traumatologist. Twenty-five percent of civilian trauma deaths per year results from chest trauma mainly caused by motor vehicle accidents (1). Despite the improved treatment methods, chest traumas cause high rate morbidity and mortality.

Crash Injury Research and Engineering Network's (CIREN) recent reports demonstrated that two significant predictors of LC are an instantaneous change in velocity (delta V) of more than 45 (miles per hour) mph (odds ratio=1.9) and a frontal crash into a fixed object (odds ratio=1.8) (2). Near-side lateral impact during a vehicular crash has also been implicated as an important mechanism leading to this lesion (2, 3).

The vast majority of chest traumas occur due to blunt injuries (4). In a study of trauma patients, the incremental hospital expenditure per patient with ALI or ARDS ($36,713 or $59,633, respectively) was much higher than for patients without ALI/ARDS ($24,715) in 2004 year (5).

LC and blunt chest trauma's pathophysiology includes inflammation, increased alveolocapillary permeability and pulmonary edema, ventilation/perfusion mismatching, increased intrapulmonary shunting, and a loss of compliance (6).

These reasons emphasize us the important role of lung trauma for the prognosis of chest trauma patients. Consequently, unfortunately there are no satisfying treatment modalities for this type of injury. To facilitate experimental work in this area, an adequate model for studying LC is required. Bilateral BCT model described below, was adapted and optimized to induce an isolated blunt and bilateral chest trauma in rabbits.

Materials and Methods

This study was performed in the Animal Research Laboratory of the Selcuk University Meram, Medical Faculty. Ethics committee's permission of the Selcuk University Medical Faculty was obtained before the study. For the study 14 female NZW rabbits weighing 1600-4100 (Average 3050) gr. were used. The weight of the rabbits: 2980gr, 3250 gr, 3200 gr, 3100 gr, 3011 gr, 3010 gr, 1600 gr, 2900 gr, 3100 gr, 3200 gr, 3100 gr, 3035 gr, 3150 gr, 4100 gr. The rabbits have been choosen about 3050 gr.

The rabbits were divided into trauma group and control groups, with seven rabbits in each group. The rabbits were anesthetized with intramuscular xylazine HCl (Rompun® flakon, Bayer) 15 mg/kg and ketamine HCl (Ketalar® flakon, Pfizer) 50 mg/kg. After the anesthesia, all the subjects were monitorized and systolic, diastolic and average arterial pressure (AAP), respiration number and pulse were controlled. To the chest of the monitorized subjects, energy was applied bilaterally and calculated according to Newton Law E = m x g x L x (1-cosα). We applied energy to the same region to all the animals in study. Ozel et al., emphasized that it is important. Different thoracic regions may respond differently to the same traumatic stress, and this may be related to the biomechanical properties of the thoracic cage. Lung parenchyma seems to be badly affected after trauma to the posterolateral thoracic wall (7).

We didn't entubate rabbits. All rabbits were fed with standard rabbit feed during the study. Our BCT model was essentially made up from three components (Figure 1).

Cannula was placed in ear artery and veins. Blood samples were taken from the subjects at 0, 3rd, 24th, 96th hours to define blood gases and biochemical measurements levels. In the blood gas, PO2, pH, PCO_2, SO_2; and as biochemical measurements Na^+, K^+, Ca^+2, $HCO3^-$, urea, creatinine, LDH, SGOT, SGPT, CPK, CK-MB, troponin were measured. All the subjects were sacrificed at 96th hour with decapitation.

Macroscopic and microscopic analysis

Histopathological evaluations were blinded and were performed by an experienced laboratory pathologist. For histological assessments of pulmonary tissue, the lungs were gradually inflated with 1% formalin, and tissue sections were stained with hematoxylin and eosin (H&E). The specimens were embedded in paraffin and cut by a microtome into 1-mm sections. Histopathology of evolving tissue injury in rabbits with isolated LC. A, Hematoxylin-eosin (H&E)-stained section of lung tissue. (magnification 10x). Microscopic evaluation of lung samples revealed severe atalectazia, emphysema, bleeding, edema, septum damage, septum thickening, septum bleeding, septal hyperemia, lymphocyte, neutrophil widespread, neutrophil infiltration, bronchial macrophage in trauma groups, whereas lung specimen from control animals were considered intact. A typical example of the microscopic findings is presented in Figure 2. Macroscopically abdominal organs were always found unaffected and intact. The findings were recorded with SPSS 10.0 and statistical analysis was done with Kruskal-Wallis, Mann-Whitney U, and Chi-Square tests.

Results

No statistical difference was defined at 3rd , 24th , 96th hour systolic and diastolic arterial pressure levels between trauma and control groups (p>0.05). Both trauma and control groups systolic and diastolic arterial pressure measured between 95±15 / 65±10 mmHg.

No statistical difference was defined respiration number levels between trauma and control groups (p>0.05). In trauma group respiration number measured 158±14/min, 144±28/min, 126±21/min at 3rd, 24th , 96th hours respectively. In control group respiration number measured 122 ±12/min at 3rd , 24th , 96th hours.

No statistical difference was defined pulse levels between trauma and control groups (p>0.05). In trauma group pulse measured 297±19 beat/min, 224±22 beat/min, 184±16 beat/min at 3rd , 24th , 96th hours respectively. In control group 175±18 beat/min, 172±12/min, 174±10/min at 3rd , 24th , 96th hours respectively.

Macroscopic and microscopic evaluations of blunt chest injury induced damage to the lung tissue were conducted to estimate reproducibility of the insult. Pulmonary and liver tissue were obtained from rabbits over a 96-h period after bilateral chest trauma (Figure 2 and 3: Macroscopic and microscopic analysis). PO_2/FiO_2 rate decreased fewer than 300 at 24th hour after trauma and continued during study (Figure 4).

No statistical difference was defined liver histopathology between trauma and control groups (p>0.05). There were significant differences between checked wet lung weight, dry lung weight and wet/dry lung weight rate as seen in Figure 5. pH level decreased after trauma and acidosis developed and continued during study (Figure 6). No statistical difference was defined at 3rd, 24th, 96th hour PO_2, PCO_2, SO_2 levels between trauma and control groups (p>0.05). In trauma group PO_2 and SO_2 decreased at 3rd, 24th, and 96th hours and PCO_2 increased during these hours (Figure 7-9).

Figure 1a and b. Schematic of rabbit model of isolated bilateral blunt chest trauma. Our BCT model was essentially made up from three components. First component is 65 cm long two wires and wire stabilization parts, second component is support table and third component is metal weights including of 700 grams. Rabbits were placed in supine position over the trauma model's support part. Metal weights were dropped from 65 cm length, and with 900 angle onto rabbit's chest. We applied bilateral BCT on rabbits' chest calculating Newton Law. The same intensity trauma was applied rabbits' chest. Applied energy was calculated by that formula:

E: m.g.l. (1-cosα), E: trauma energy, (joule) m: weight (gr), g is gravitational acceleration (9.8 m/s2), L: length of wire (meter), α: angle between wire and middle point. We used m=700 gr= 0.7 kg, l=0.65 m, α=900 (cos 900=0), E= 0.7*9.81*0,65*(1-cos 900), E= 4,4635 Joule energy was bilaterally applied to rabbits chest

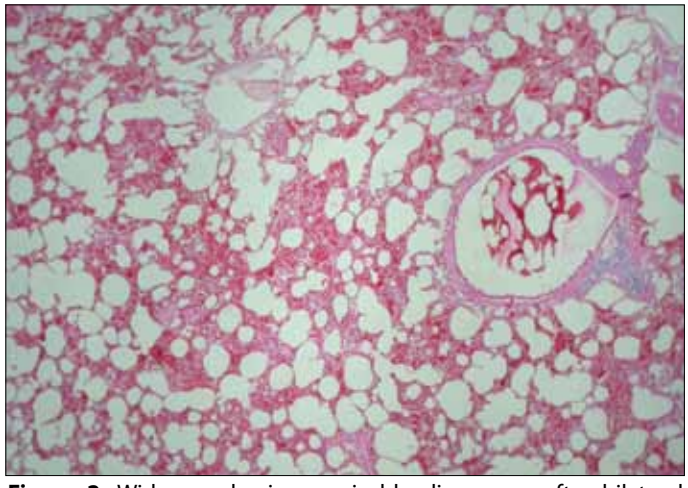

Figure 2. Widespread microscopic bleeding areas after bilateral blunt chest trauma at 96th hour. Histopathology of evolving tissue injury in rabbits with isolated lung contusion. A, Hematoxylin-eosin (H&E)-stained section of lung tissue. (magnification 10x)

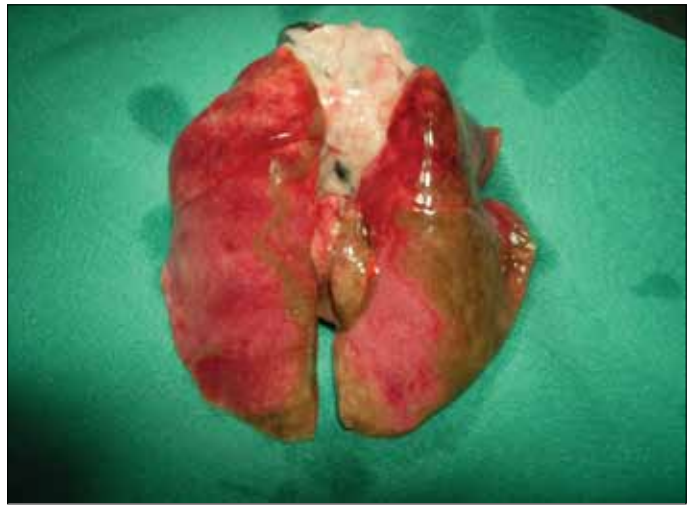

Figure 3. Macroscopic appearance of right and left lung after bilateral blunt chest trauma at 96th hour: Bilateral edema, bleeding and color changing are seen

No statistical difference was defined CK-MB, Tn and LDH levels between trauma and control groups (p>0.05). Statistically significant difference was defined CPK levels between trauma and control groups (p<0.05) (Table 1).

No statistical difference was defined glucose, urea, creatinin, SGOT, SGPT levels between trauma and control groups (p>0.05) (Table 1).

Statistically significant difference was defined atalectazia, emphysema, bleeding, edema, septum damage, septum thickening, septum bleeding, septal hyperemia, lymphocyte, neutrophil widespread, neutrophil infiltration, bronchial macrophage (p<0.05) (Table 2).

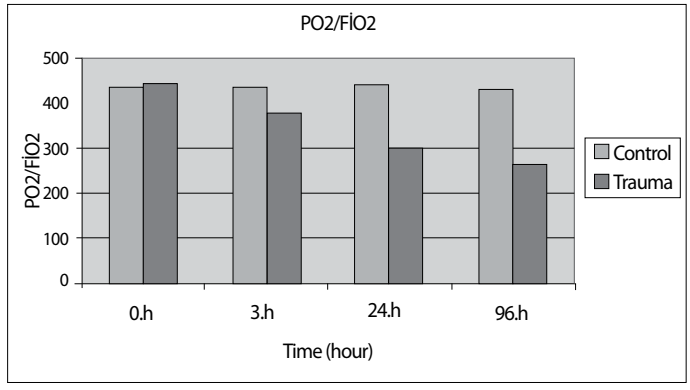

Figure 4. PO_2/FiO_2 rate decreased fewer than 300 at 24th hour after trauma and continued during study. ALI developed animals

Discussion

Unfortunatelly traumas are still a very important problem in modern life. Blunt chest trauma is a common problem in the care of

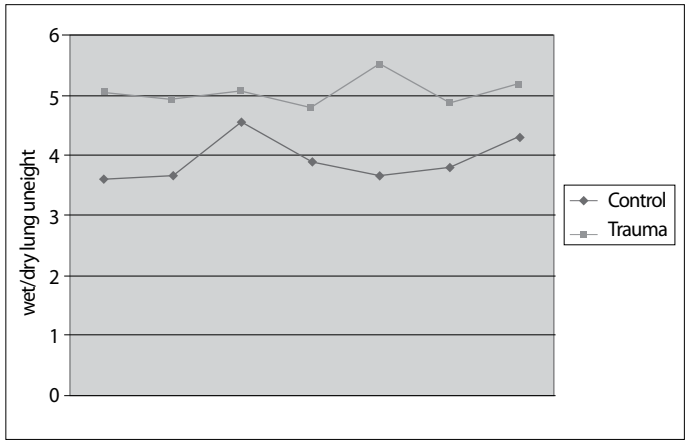

Figure 5. Wet/dry lung weight. When the subjects were sacrificed, by applying thoracotomy a segment was removed from left lung lower lobe for histopathological examination and right lung was totally removed and wet weight was measured. After weighing the lung was kept in 80°C incubator, for 24 hours, was dried and weighed again. The lungs and liver of sacrificed rabbits were examined microscopically and macroscopically

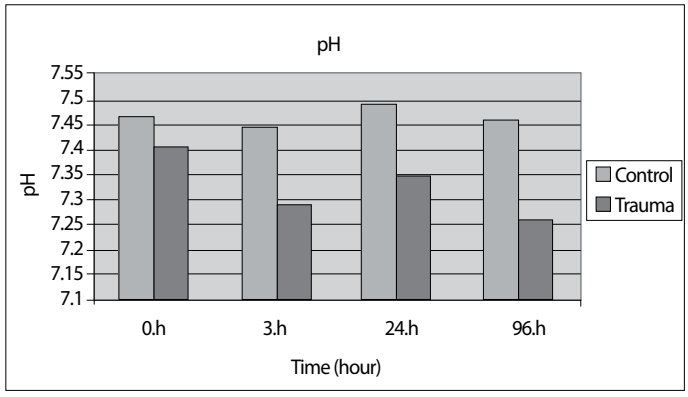

Figure 6. pH level decreased after trauma and acidosis developed at 3rd hour and continued during study

critically ill trauma patients (8), and thoracic trauma accounts for 20%-25% of adult deaths caused by trauma (9). BCT is one of the most important leading causes of morbidity and mortality around the world. Various large-animal models for LC have been developed, including studies in canines, swine, and monkeys (10).

The understanding of physiopathology and the relationship between time and physiopathology of chest trauma will decrease morbidity and mortality and clarify diagnosis and treatment process.

LC is the most frequently diagnosed intrathoracic injury resulting from blunt trauma (11, 12), and is an important risk factor for the development of other conditions such as pneumonia and ALI/ARDS (12).

Behnia et al. didn't entubate the rabbits because both intubation and ventilation per cause considerable alterations in lung (13). We didn't entubate the rabbits lest inflammatory changes occur. In this study, rabbits were not ventilated before, during, or after bilateral BCT.In this study we easily constituted a bilateral BCT model useful on rabbits.

The BCT is always associated with cardiac changes. Forces applied to the chest wall may cause cardiac rhythm disorders and also may result in a sudden death. Bradycardia, hypotension and apnea after trauma were also reported in two studies (14, 15). In our

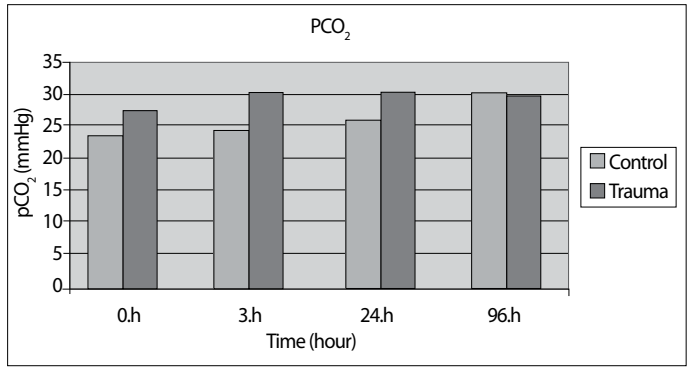

Figure 7. PCO_2 level increased after trauma at 3rd hour and continued during study

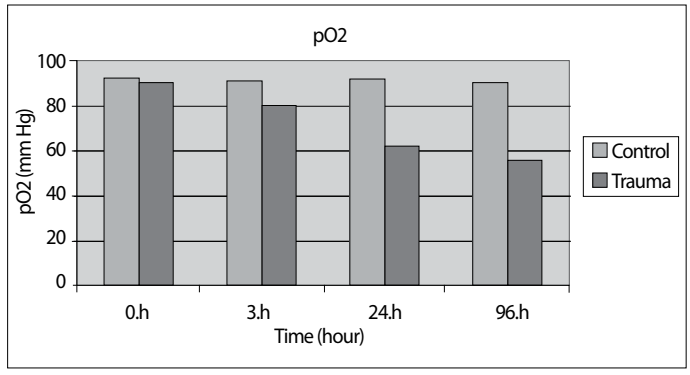

Figure 8. PO_2 level decreased after trauma at 3rd hour and this decreasing continued increasingly during study

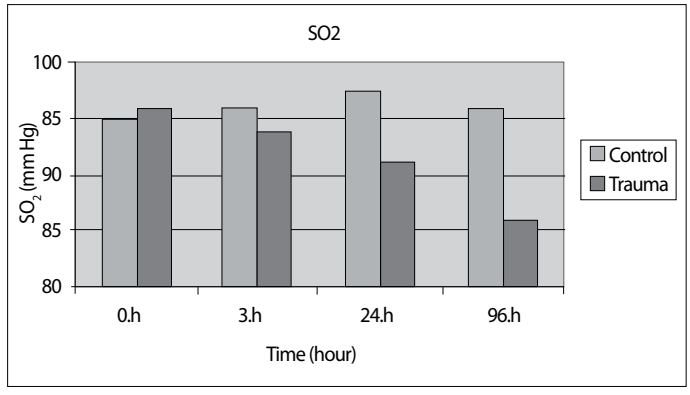

Figure 9. SO_2 level decreased after trauma at 3rd hour and this decreasing continued during study

study we reported apnea in one of the rabbits, bradycardia in one and tachycardia in five of them.

Mirua et al. have found LC of 49% in their study with BCT in their series containing 161 patients (16). PO_2/FiO_2 rate decreased fewer than 300 at 24th hour after BCT and continued during study. PO_2/FiO_2 rate decreased fewer than 300 at 24th hour after trauma and continued during study. ALI developed animals. (Figure 4: PO_2/FiO_2 rate).

Tranbaugh et al. measured lung water in 16 trauma patients in shock (mean arterial pressure <40 mm Hg). Lung water increased after resuscitation in the four patients with LC but was not found in patients with hemorrhagic shock who had no lung trauma (17).

American-European Consensus Conference (AECC) members proposed the following diagnostic criteria for ALI and ARDS: a) Acute

Table 1. The values of biochemical parameters and blood gas

Valuable	0. h Mean±SD	3. hr Mean±SD	24. hr Mean±SD	96 .hr Mean±SD	Statistical significance*
pH C	7.46±0.02	7.44±0.03	7.49±0.05	7.46±0.07	NS
pH Tr	7.40±0.02	7.28±0.01	7.34±0.03	7.26±0.03	NS
PCO_2 C (mmHg)	23.57±3.95	24.57±2.3	25.85±2.54	30.57±1.79	NS
PCO_2 Tr (mmHg)	27.57±2.38	30.57±1.81	29.85±3.35	29.71±2.64	NS
PO_2 C (mmHg)	92.71±1.11	92±1.25	93±2.69	91.14±3.21	NS
PO_2 Tr (mmHg)	92.28±0.69	80.57±1.11	62±1.15	56±1.45	NS
SO_2 C (mmHg)	95.71±0.75	96±1.97	97.42±1.77	96.28±1.69	NS
SO_2 Tr (mmHg)	96±1.06	93.85±1.29	91.57±0.89	85±1.26	NS
PO_2/FiO_2 C	441±23	438±21	442±28	434±33	NS
PO_2/FiO_2 Tr	442±14	383±23	295±24	266±30	NS
CPK C (u/L)	374±242	583±380	649±480	672±390	p<0.05*
CPK Tr (u/L)	862±496	4691±400	5300±470	3039±350	p<0.05*
CK-MB C (ng/ml)	1.257±0.74	0.828±0.40	3.1±1.74	2.628±1.62	NS
CK-MB Tr (ng/ml)	0.485±0.33	0.7±0.38	0.74±0.20	1.414±0.25	NS
Tn C (ng/ml)	0.031±0.02	0.25±0.02	0.058±0.013	0.072±0.028	NS
Tn Tr (ng/ml)	0.012±0.03	0.034±0.016	0.061±0.044	0.048±0.02	NS
LDH C (u/L)	214±195	244±116	283±214	315±224	NS
LDH Tr (u/L)	305±123	827±312	729±325	592±256	NS
Urea C (u/L)	36.85±14	36.2±8	31.57±17	36.28±11	NS
Urea Tr (u/L)	40.71±23	60.57±15	48.28±13	57.28±18	NS
Creatinin C (u/L)	1.27±0.23	1.2±0.47	1.14±0.38	1.27±0.29	NS
Creatinin Tr (u/L)	1.51±0.39	1.9±1.1	1.31±0.36	1.64±0.27	NS
SGOT C (u/L)	32.71±17	26.42±13	38.14±19	42.14±21	NS
SGOT Tr (u/L)	26.85±16	47.42±23	46.71±21	51.28±18	NS
SGPT C (u/L)	62.42±26	60±24	58.14±18	67±25	NS
SGPT Tr (u/L)	71±28	80.57±33	76.42±29	78.71±32	NS

NS: non significant; SD: Standart deviation; C: control; Tr: trauma, Parameters X± SD: Standart deviation, *Mann-Whitney U test

onset, b) Bilateral chest radiographic infiltrates (We found bilateral macroscopic and microscopic lung damage), c) Pulmonary artery occlusion pressure of <18 mmHg or no evidence of left atrial hypertension, d) $Pa0_2$ / $Fi0_2$ ratio of<300 mmHg for ALI (18).

We accepted ALI for acute onset, bilateral chest radiographic infiltrates (We found bilateral macroscopic and microscopic lung damage), no evidence of left atrial hypertension, $Pa0_2$ / $Fi0_2$ ratio of <300 mmHg for ALI in our study.

In our study ALI developed, not ARDS and we didn't find meaningful difference between checked wet lung weight, dry lung weight and wet/dry lung weight rate (p>0.05). In our study the lung water and weight significantly increased in trauma applied rabbits. But there wasn't statistical difference between trauma and control groups (Figure 5: wet/dry lung weight).

Histological analysis showed that the characteristic landmarks of LC in all specimens such as intraalveolar and subpleural hemorrhage and the microscopic estimation of hemorrhage distribution revealed a comparable pattern to the macroscopic results. The microscopic findings are in line with reports from Jaffin and coworkers (19). We found intraalveolar hemorrhage in our study, as well.

Table 2. Histopathological features resulting from chest trauma in rabbits

Histopathological Values	Statistical significance*
Atalectazia	p<0.05*
Emphysema	p<0.05*
Bleeding	p<0.05*
Edema	p<0.05*
Septum damage	p<0.05*
Septum thickening	p<0.05*
Septum bleeding	p<0.05*
Septal hyperemia	p<0.05*
Lymphocyte	p<0.05*
Neutrophil widespread	p<0.05*
Neutrophil infiltration	p<0.05*
Bronchial macrophage	p<0.05*

*Mann-Whitney U test

Ulrich et al. reported bilateral pulmonary injury in all trauma animals with extensive hemorrhage on the ventral as well as the dorsal surface of the lung. There were no intra-abdominal lesions or injuries to the chest wall itself. Histologic analyses revealed subpleural and alveolar hemorrhage in all animals subjected to the blast injury. No such damage was detected in control animals. There were no morphologic differences in liver tissue between any of the groups (20). In our study we found bilateral pulmonary injury in all trauma animals with hemorrhage on the ventral as well as the dorsal surface of the lung, and didn't find difference liver histopathology between trauma and control groups. Our study is well-matched with this report.

Knoferl MW et al. reported arterial blood gas analysis was performed at 180 min post injury. PO_2 values of all trauma groups regardless of the blast exposure distance were significantly diminished when compared with sham animals. PCO_2 values showed a significant increase in the 1.5 cm and 2.5 cm nozzle-thorax distance groups whereas at 2.0 cm the tendency towards hypercarbia did not reach statistical significance (21). At 180 min after chest trauma, there were no significant differences in arterial pH values between trauma and sham groups (21). In our study pH level decreased after trauma and acidosis developed and continued during study. (Figure 6: pH Level). PCO_2 values showed increase from 3rd hour to 24th hour and didn't change from 24th hour to 96th hour. (Figure 7: PCO_2 level).

In a study PO_2 level sharply decreased after trauma. Decreasing of oxygenating started 6 hours after trauma and this value was statistically significant and continued during study (21). In our study arterial blood gas PO_2 values of all trauma groups decreased from 3rd hour to 96th hour. After 24th hour it started to decrease significantly. In our study PO_2 level decreased after trauma and decreasing of oxygenating started 3 hours after trauma and this table continued during study, but no meaningful difference was detected (Figure 8: PO_2 level). In our study SO_2 level decreased after trauma and this decrease continued at 3rd, 24th and 96th hours. These values show us that ventilation was deteriorated due to edema and bleeding in trauma deteriorated ventilation and perfusion (V/Q) values (Figure 9: SO_2 level).

In addition, experiments with both rat and murine models of isolated LC indicate that hypoxia is effectively reversed by about 48 hr (21). Although, even at 96th hour in our study hypoxia didn't reverse before trauma. This may be the result of the fact that pathology related to trauma detoriate the ventilation of the subjects. This may be related with the strength of the trauma. A significant decrease was seen in SO_2 after trauma due to deteriorated ventilation and perfusion (V/Q) value. Deterioration in V/Q occurred at the beginning of trauma and got worse during the next period. It is very important in clinical practice for the patients with chronic obstructive pulmonary disease and children whose defense mechanism has not developed yet.

In our study all rabbits survived until 96th hour and we decapitated subjects at the end of the study; therefore life-span of the subjects hasn't been compared. Markus W. Knöferl et al. reported abdominal organs were always found unaffected and intact. Microscopic evaluation of lung samples revealed severe intraalveolar, intrabronchial, and subpleural hemorrhage, interstitial edema and atalectasis in all trauma groups, whereas lung specimen from sham animals were considered intact (21).

In our study we detected alveolar and intrabronchial hemorrhage in trauma group. The rat model of isolated bilateral LC injury developed by Raghavendran and co-workers (22, 23). Their model involves dropping a cylindrical weight at a well-defined energy impact level onto a mobile lexon platform positioned over the chest to minimize associated cardiac trauma. In our rabbit model energy level was well-defined too.

Although many specifics of the inflammatory response in LC injury remain to be clarified, it is clear that physiological dysfunction in this condition is related in part to the significant acute inflammation. One important feature of the current rat model is that it involves isolated (or at least relatively isolated) LC injury without substantial cardiac or abdominal trauma. Wang et al. (24) reported an animal model of thoracic trauma without protection of the heart in which mortality was primarily associated with blunt myocardial injury. In our model cardiac trauma was minimized. In our study statistically significant difference was defined in CPK ($p<0.05$), but no statistical difference was defined CK-MB, Tn and LDH levels between trauma and control groups ($p>0.05$). CPK level increased fivefold at 3rd hour after trauma. This increase occurred eight fold at 24th hour and this value decreased three fold at 96th hour. CK-MB level increased three fold at 3rd hour after trauma. This value occurred four fold at 24th hour and decreased two fold at 96th hour. Tn level didn't increase at 3rd hour after trauma however this level increased five fold at 24th hour and this value decreased three fold at 96th hour. LDH level increased two fold at 3rd hour after trauma and this level occurred 2.5 fold at 24th hour and this value decreased 1.5 fold at 96th hour. These values becoming resemble to normal values after 96th hour but the values of blood gases not recovering significantly shows that lungs are more sensitive than heart and lungs are affected much more than heart. Our study is well-matched with the other studies.

The hypoxemia and pulmonary hemodynamic changes (specifically acute reactive pulmonary hypertension) associated with lung injury have been shown in many animal studies. These changes have shown that cardiac function is affected seriously (25, 26).

Krishnan Raghavendran et al. emphasized the technical variables and basic characteristics of the rat model of isolated LC rather than on detailed mechanistic investigations of pathophysiology (27). The results display several features consistent with other forms of acute inflammatory pulmonary injury in animals. The results in rats reported there, support the paradigm that a severe but isolated LC could lead to transient injury with a relatively rapid recovery. Many patients with blunt chest trauma experience a transient clinical course with rapid recovery, whereas others exhibit disease that is severe and progressive (28-30). As we decapitated all the subjects at 96th hour, we could not evaluate the recovery process.

In a study at 24 hr post-contusion, atalectasis was reported, and there were increased numbers of leukocytes (predominantly neutrophils) within the alveoli and interstitium. At 48 hr, neutrophilic infiltration continued to be prominent, and alveolar lining tissue was thickened with an increase in alveolar macrophage infiltration and cellular debris (23). Similar histological findings in LC injury have been reported by others (31). Because we decapitated all rabbits at 96th hour, we don't know when atalectasis happened in our study. We reported atalectasis in all trauma group rabbits at 96 hour post BCT.

At 48^{hr}, neutrophilic infiltration continued to be prominent, and alveolar lining tissue thickened with an increase in alveolar macrophage infiltration and cellular debris (23). Similar histological findings in LC injury have been reported by others (32). We reported similar histological findings at 4 days post-BCT.

At 7 days post-contusion, evidence of fibrosis especially around the bronchioles was also observed (23). No statistical difference was defined in fibrosis between trauma and control groups in our study at 96 hours post BCT. Leiner et al (33) have reported increased alveolar epithelial apoptosis following blunt chest trauma, and Seitz et al. have documented increased type II cell apoptosis at 48 hr following LC injury (34). But we didn't find apoptosis in our study at 96th hours. We reported apoptosis only one rabbit's lung.

Conclusions

The long-term consequences of LC of BCT have not been clearly defined and the management of LC is primarily supportive. Blunt chest trauma is a true medical emergency that can be fatal if not properly and promptly treated. The properly treatment can be developed by making useful experimental model. Our model is an alternative to other models. This model is practical, cheap and useful and the experimental values can be changed easily. Surviving of the all rabbits till the end of the study provided us adequate time to examine the blood gases, biochemical values and histopathological examinations. In our model minimal cardiac trauma was observed and no abdominal trauma was observed. Our model is an alternative way for clinical investigation of different drugs effective in bilateral blunt chest trauma. As a result this study has established a useful model for the study of bilateral blunt chest trauma in rabbits.

Conflict of Interest

No conflict of interest was declared by the authors.

References

1. Aufmkolk M, Fischer R, Voggenreiter G, Kleinschmidt C, Schmit-Neurburg KP, Obertacke U. Local effect of lung contusion on lung surfactant composition in multiple trauma patients. Crit Care Med 1999; 27: 1441-6.[CrossRef]
2. O'Connor JV, Kufera JA, Kerns TJ, Stein DM, Ho S, Dischinger PC, et al. Crash and occupant predictors of pulmonary contusion. J Trauma 2009; 66: 1091-5. [CrossRef]
3. Gayzik FS, Martin RS, Gabler HC, Hoth JJ, Duma SM, Meredith JW, et al. Characterization of crash-induced thoracic loading resulting in pulmonary contusion. J Trauma 2009; 66: 840-9.[CrossRef]
4. Battistella F, Benfield JR. Blunt and penetrating injury of the chest wall, pleura and lungs. In Schields TW. General Thoracic Surgery. Malvem, Williams and Wilkins 1994; 767-83.
5. Treggiari MM, Hudson LD, Martin DP, Weiss NS, Caldwell E, Rubenfeld G. Effect of acute lung injury and acute respiratory distress syndrome on outcome in critically ill trauma patients. Crit Care Med 2004; 32: 327-31. [CrossRef]
6. Cohn SM, Zieg PM. Experimental pulmonary contusion: review of the literature and description of a new porcine model. J Trauma 1996; 41: 565-71. [CrossRef]
7. Ozel SK, Ozel HB, Colakoğlu N, Ilhan N, Arslan N, Ozan E. Protective effect of the thoracic cage on parenchyma in response to trauma direction in blunt thoracic trauma: an experimental study. Ulus Travma Acil Cerrahi Derg 2010; 16: 287-92.
8. Shorr RM, Crittenden M, Indeck M, Hartunian SL, Rodriquez A. Blunt thoracic trauma: analysis of 515 patients. Ann Surg 1987; 206: 200-5.[CrossRef]
9. Lo Cicero J, Mattox KL. Epidemiology of chest trauma. Surg Clin North Am 1989; 69: 15-9.
10. Moomey CB Jr, Fabian TC, Croce MA, Melton SM, Proctor KG. Cardiopulmonary function after pulmonary contusion and partial liquid ventilation. J Trauma 1998; 45: 283-90.[CrossRef]
11. Miller PR, Croce MA, Bee TK, Qaisi WG, Smith CP, Collins GL, et al. ARDS after pulmonary contusion: accurate measurement of contusion volume identified high risk patients. J Trauma 2001; 51: 223-8. [CrossRef]
12. Cohn SM. Pulmonary contusion: review of the clinical entity. J Trauma 1997; 42: 973-9. [CrossRef]
13. Behnia R, Molteni A, Waters CM, Panos RJ, Ward WF, Schnaper HW, et al. Early markers of ventilatory-induced lung injury in rats. Ann Clin Lab Sci 1996; 26: 437-50.
14. Guy R, Watkins PE. Cardiopulmonary, histological, and inflammatory alterations after lung contusion in a novel mouse model of blunt chest trauma. Shock 2004; 21: 190-1.[CrossRef]
15. Irwin RJ, Lerner MR, Bealer JF, Brackett DJ, Tuggle DW. Cardiopulmonary physiology of primary blast injury. J Trauma 1997; 43: 650-5. [CrossRef]
16. Miura H, Taira O, Hiraguri S, Uchida O, Hagiwara M, Ikeda T, et al. Blunt thoracic injury. Jpn J Thorac Cardiovasc Surg 1998; 46: 556-60. [CrossRef]
17. Tranbaugh RF, Elings VB, Christensen J, Lewis FR. Determinants of pulmonary interstitial fluid accumulation after trauma. J Trauma 1982; 22: 820-6. [CrossRef]
18. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 1994; 149: 818-24. [CrossRef]
19. Jaffin JH, McKinney L, Kinney RC, Cunningham JA, Moritz DM, Kraimer JM, et al. A laboratory model for studying blast overpressure injury. J Trauma 1987; 27: 349-56. [CrossRef]
20. Liener UC, Knoferl MW, Strater J, Barth TF, Pauser EM, Nussler AK, et al. Induction of apoptosis following blunt chest trauma. Shock 2003; 20: 511-6. [CrossRef]
21. Knoferl MW, Liener UC, Seitz DH, Perl M, Bruckner UB, Kinzl L, et al. Cardiopulmonary, histological, and inflammatory alterations after lung contusion in a novel mouse model of blunt chest trauma. Shock 2003; 19: 519-25.
22. Raghavendran K, Davidson BA, Huebschmann JC, Helinski JD, Hutson AD, Dayton MT, et al. Superimposed gastric aspiration increases the severity of inflammation and permeability injury in a rat model of lung contusion. J Surg Research 2009; 155: 273-82. [CrossRef]
23. Raghavendran K, Davidson BA, Woytash JA, Helinski JD, Marschke CJ, Manderscheid PA, et al. The evolution of isolated, bilateral lung contusion from blunt chest trauma in rats: Cellular and cytokine responses. Shock 2005; 24: 132-8. [CrossRef]
24. Wang ND, Stevens MH, Doty DB, Hammond EH. Blunt chest trauma: an experimental model for heart and lung contusion. J Trauma 2003; 54: 744-8. [CrossRef]
25. Schuster DP, Perez JE, Trulock EP, Williamson JR, Biello DR, Kenzora JL, et al. Cardiac dysfunction during acute lung injury induced by oleic acid in dogs. Am Rev Respir Dis 1986; 133: 519-25. [CrossRef]
26. Teplinsky K, O'Toole M, Olman M, Walley KR, Wood LD. Effect of lactic acidosis on canine hemodynamics and left ventricular function. Am J Physiol 1990; 258: 1193-9.
27. Raghavendran K, Davidson BA, Helinski JD, Marschke CJ, Manderscheid P, Woytash JA, et al. A rat model for isolated bilateral lung contusion from blunt chest trauma. Anesth Analg 2005; 101: 1482-9. [CrossRef]
28. Fulton RL, Peter ET. The progressive nature of pulmonary contusion. Surgery 1970; 67: 499-506.
29. Kollmorgen DR, Murray KA, Sullivan JJ, Mone MC, Barton RG. Predictors of mortality in pulmonary contusion. Am J Surg 1994; 168: 659-63. [CrossRef]
30. Schreiter D, Reske A, Scheibner L, Glien C, Katschert S, Josten C. The open lung concept: clinical application in severe thoracic trauma. Chirurg 2002; 73: 353-9. [CrossRef]
31. Hoth JJ, Hudson WP, Brownlee NA, Yoza BK, Hiltbold EM, Meredith JW, et al. Toll-like receptor 2 participates in the response to lung injury in a murine model of pulmonary contusion. Shock 2007; 28: 447-52. [CrossRef]
32. McAuley DF, Frank JA, Fang X, Matthay MA. Clinically relevant concentrations of beta2-adrenergic agonists stimulate maximal cyclic adenosine monophosphate-dependent airspace fluid clearance and decrease pulmonary edema in experimental acid-induced lung injury. Crit Care Med 2004; 32: 1470-6.. [CrossRef]
33. Liener UC, Knoferl MW, Strater J, Barth TF, Pauser EM, Nussler AK, et al. Induction of apoptosis following blunt chest trauma. Shock 2003; 20: 511-6. [CrossRef]
34. Seitz DH, Perl M, Mangold S, Neddermann A, Braumuller ST, Zhou S, et al. Pulmonary contusion induces alveolar type 2 epithelial cell apoptosis: role of alveolar macrophages and neutrophils. Shock. 2008; 30: 537-44. [CrossRef]