

## Реферати

**ОСОБЛИВОСТІ ПЕРЕБУДОВИ КЛІТИННОГО СКЛАДУ СЛИЗОВОЇ ОБОЛОНКИ ПОРОЖНИНИ РОТА НА ТЛІ ТЮТЮНОПАЛІННЯ**

Гасюк Н.В., Єрошенко Г.А., Майстрюк П.О.

В статті приведені результати комплексного морфологічного дослідження слизової оболонки порожнини рота у курців, отримані шляхом комплексного цитологічного та статистичного вивчення. Приведені результати, дають можливість характеризувати описані зміни, як «дискератозні» або «проліферативні», які в собі несуть цитологічні ознаки дискератозу у вигляді порушення зроговіння епітелію даної анатомічної ділянки. Аналіз запропонованих нами схем патогенезу, і наявність спільних складових, в його ланках, дає можливість розглядати приведену цитологічну перебудову – «запальний» тип цитограм та «дискератозний» як два автономних процеси, які виникли на слизовій оболонці порожнини рота за умов впливу нікотину, так і ланки одного і того ж патогенетичного механізму на етапі передпухлинної трансформації.

**Ключові слова:** слизова оболонка, епітелій, клітини, ядро, цитоплазма.

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**ОСОБЕННОСТИ ПЕРЕСТРОЙКИ КЛЕТОЧНОГО СОСТАВА СЛИЗИСТОЙ ОБОЛОЧКИ ПОЛОСТИ РТА НА ФОНЕ ТАБАКОКУРЕНИЯ**

Гасюк Н.В., Єрошенко Г.А., Майстрюк П.О.

В статье приведены результаты комплексного морфологического исследования слизистой оболочки полости рта у курильщиков, полученные путем комплексного цитологического и статистического изучения. Данные результаты, дают возможность характеризовать описанные изменения, как «дискератозные» или «пролиферативные», которые в себе несут цитологические критерии дискератоза в виде нарушения ороговения эпителия данной анатомической области. Анализ предложенных нами схем патогенеза, и наличие общих составляющих, в его звеньях, дает возможность рассматривать приведенную цитологическую перестройку – «воспалительный» тип цитограм и «дискератозный» в виде двух автономных процессов, которые возникли на слизистой оболочке полости рта в условиях курения, так и звенья патогенетического механизма на этапе предопухоловой трансформации.

**Ключевые слова:** слизистая оболочка, эпителий, клетки, ядро, цитоплазма.

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L.M. Zaiats, U.V. Kur

HSEE "Ivano-Frankivsk National Medical University", Ivano-Frankivsk

**PATHOMORPHOLOGICAL CHANGES OF RESPIRATORY DEPARTMENT OF LUNGS DUE TO MULTIPLE SKELETAL TRAUMA WITH THE USE OF INTRAMEDULLARY OSTEOSYNTHESIS IN THE EXPERIMENT**

E-mail: ulynakuz@gmail.com

Experimental study was carried out on 90 white male Wistar line rats and defined microscopic and ultrastructural changes of the respiratory department of the lung due to multiple skeletal trauma with intramedullary osteosynthesis use in dynamics (6, 24, 72, 168 hours) by lightoptical and electron microscopic methods. It was proved that intramedullary osteosynthesis of the femoral bones bring on severe changes of the structural organization of all components of the respiratory department of the lungs during the first 24 hours after the trauma. In the respiratory department there was both dystrophic-destructive and compensatory-adaptive changes during 72-168 hours of the study.

**Key words:** lungs, respiratory department, experimental multiple skeletal trauma, intramedullary osteosynthesis.

*The study is a fragment of the research project «Pathogenetic mechanisms of development changes in the organs of the respiratory, endocrine and nervous systems in the various pathological models and their correction» (state registration No. 0117U001758).*

Polytrauma is a complex of completed biochemical and immune reactions that cause homeostasis disorders, multiple organ failure syndrome (MOFS), acute lung injury (ALI), sepsis and high mortality as well [1, 3, 5, 7, 8].

Prevalence of multiple injuries is 5.5-35 % of all traumas [2].

Researches of the most appropriate tactic of treatment of bone and joint system injuries are getting from the second half of the XX century until now. It is very important if needed to make surgery, especially long bones osteosynthesis. The best method of treatment of the long bone fractures is intramedullary osteosynthesis, but there are contraindications of its use, as risk of AII and MOFS [9, 10].

**The purpose** of the experimental study was to determine microscopic and ultrastructural changes of the respiratory department of the lung due to multiple skeletal trauma with intramedullary osteosynthesis use in dynamics.

**Materials and methods.** Study was made on 90 white male Vistar rats with bodyweight 180-230 g. Animals were distributed on three groups: I – modeling of multiple skeletal trauma (40 animals), II – modeling of multiple skeletal trauma + intramedullary osteosynthesis (40 animals) and III – intact (10 animals). All animals in group I and II were done modeling of multiple skeletal trauma – osteotomy of the both femur bones in the middle part according to the own technique [4]. Animals of the II group accept of

modeling of multiple skeletal trauma was done intramedullary osteosynthesis by Kirschner wire 3 hours after trauma modeling. All manipulations were done under Tiopental anesthesia 60 mg/kg. All animals in I and II group received appropriate analgesia by Diclophenac sodium 10 mg/kg 3 times per (in the day of surgery 2 times).

Lung tissue sampling for light microscopic and electron microscopic study was made under Tiopental anesthesia 6, 24, 72, 168 hours after trauma by general methods. Paraffin sections for histological study, size 5-8 microns, were stained with Hematoxylin and Eosin. Lung tissue samples for electron microscopic study were fixed in the glutaraldehyde 2,5% solution and further postfixation by osmium tetroxide 1% solution. Samples after dehydration were embed in the epon-araldit. Sections were done by ultramicrotome "Tesla BS-490" and studied by electronic microscope "ПЕМ-125K".

**Results of the study and their discussion.** The light microscopic analysis of the lung respiratory department in animals of the 1<sup>st</sup> experimental group showed that 6 hours after beginning of the study in some alveoli was spotted increasing of alveolar macrophages (AM). There was hyperemia of haemocapillaries in some alveolar partitions.

There were mostly reactive changes of the lung respiratory department components detected on the ultrastructure level. It was defined mitochondria with mild electronic-optical density matrix, enlarged ribosome-rich cisterns of the rough endoplasmic reticulum (RER) in the alveolar epithelial cells, endothelial cells of haemocapillaries and AM. There were increase numbers of the lamellar bodies (LB) in the alveolar cells type II (A-II). In the peripheral part A-I and endothelial cells of haemocapillaries was showed intensification of micropinocytosis process. Nowever some endothelial cells of haemocapillaries were with cytoplasm lightening, nuclear deformities, rare vacuole-transformed mitochondria and fragmented membranes of RER. Inside those haemocapillaries was seen the rise of white blood cells number, their aggregation and adhesion.

During 24 hours it was microscopically defined increasing the number of AM, some red blood cells and white blood cells in the alveoli. Electronic microscopy showed that in the cytoplasm of the huge number of AM there were lots of osmiophilic inclusions with irregular size, shape and density. Sometimes it was found AM with giant phagosomes that included destroyed fragments of cells.

The alterations in the A-I, A-II and endotheliocytes normal structure were tend to intracellular swelling and disorders of smooth organization of organelles. Accumulation of swelling fluid was showed also in interstitial tissue.

During the 72 hours after beginning of the study in the A-I, A-II and endotheliocytes was noticed lightening of cytoplasm. The number of LB in the A-II was decreased. The interstitial tissue was swelling. It was found platelets and leucocytes aggregation in the haemocapillaries. Macrophages during this period of study had got irregular morphology.

Electronic microscopy data received during 168 hours showed that severity and amplification of swelling of the lung respiratory department components was less than during the previous stage of the study. However there were some lung respiratory department cells whose ultrastructural organization had included changes considered with increase their functional capacity.

The light microscopic analysis of the lung respiratory department in animals of group 2 showed that 6 hours after the beginning of the study in lots of alveoli increasing of AM number was observed. There was thickening of alveolar partitions due to haemocapillary hyperemia.

The electron microscopic analysis showed that in the alveoli between macrophage pull with increased functional capacity were detected some of them with dystrophic and destruction changes.

The nucleoplasm of A-I was filled by small-grain matrix. Chromatin granules mostly were situated regularly along whole nuclear area. The nuclear membrane had got twisted contours and made smooth invaginations. There were rare mitochondria, some of them with lightened matrix. Cisterns and canals of smooth and rough endoplasmic reticulum were enlarged. Basement membrane was locally thickened. In the peripheral part of A-I was increased number of micropinocytosis vesicles. There were some microvilli on the surface of some A-I turned toward alveolar space.

Nuclei of A-II were round shape, generally with moderate electronic-optical density matrix. Nuclear membrane was with mild indentations and prominences. Mitochondria were irregular size and shape with moderate electronic-optical density matrix. However there were some enlarged mitochondria with solitary and reduced cristae. Components of of smooth and rough endoplasmic reticulum were extended. There were in some LB irregular light electronic spaces between osmiophilic plates. Basement membrane was diffusively thickened. There were some small microvilli on the apical surface.

The interstitial tissue diffusively extended because of swelling fluid accumulation.

Nuclei of endothelial cells were irregular shape because of indentations and prominences of nucleolemma. Perinuclear space was slight extended. Mitochondria were with low electronic-optical density matrix. It was also partial destruction of mitochondria. There was extension of smooth endoplasmic reticulum (SER) and fragmentation of RER. Numbers of ribosomas on the membranes of the last one were

reduced. The basement membrane was thickened with irregular contours. There were big vacuoles in the peripheral departments of endotheliocytes. It was found disorders of integrity of the luminal membrane of endotheliocytes in some haemocapillaries. There were erythrocyte sludge, aggregation and adhesion of leucocytes in some haemocapillary space (fig. 1).

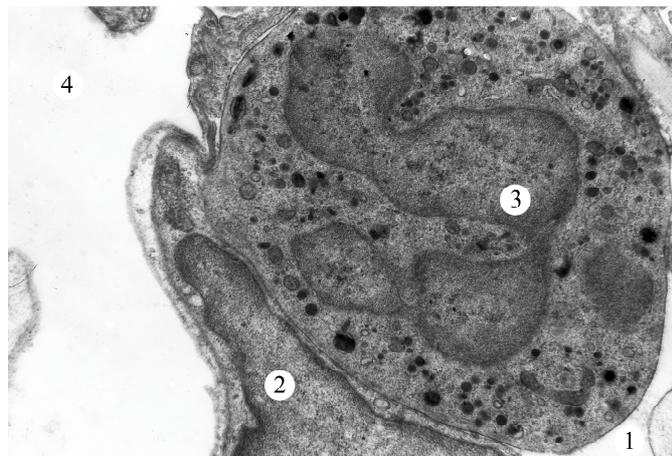


Fig. 1. Adhesion of leucocyte to the haemocapillary endotheliocyte of the lung alveolar wall 6 hours after beginning of study (multiple skeletal trauma and osteosynthesis). 1 – haemocapillary space; 2 – endotheliocyte; 3 – leucocyte; 4 – alveolar space. Microelectronic picture. x8000.

The microscopic study during 24 hours showed increase number of AM, red blood cells, white blood cells and also desquamated cells of the alveolar epithelium in the alveoli.

The electronic microscopy defined lots of macrophage elements with dystrophic and degenerative changes in the alveolar space. Cell nuclei had got low electronic-optical density nucleoplasm. The perinuclear space was extended. Mitochondria were swelling with solitary short cristae. SER was represented by solitary enlarged cisterns and valuoles. Canals of RER were fragmented, on the outer surface of their membranes lack of ribosomes. The cytoplasm the number of

AM was low electronic-optical density, where were defined solitary lysosomes and big phagosomes with irregular osmiophilic material.

Prominent changes of ultrastructural organization during this period of study were detected in the A-I and A-II. Cell nuclei were with low electronic-optical density matrix. The electronic light cytoplasm included not numerous, severe damaged organelles. Lots of A-I had got sail-like prominence of their peripheral part into the alveolar space (fig. 2). The number of LB in the A-II was strongly reduced. Sometimes instead LB there were vacuoles with odds of the membrane. The apical surface of the A-II was smoothed due to reduction of microvilli.

The interstitium of alveolar partitions was sharply extended because of swelling and infiltration by cell elements mostly neutrophyls and mononuclears. The interstitial swelling was especially prominent in departments that close to areas with destroyed endothelium capillaries integrity.

The progressive nature of changes was detected in the haemocapillaries of the alveolar partitions. Endotheliocytes nuclei with nucleoplasm were low electronic-optical density. Perinuclear space was enlarged. Mitochondria were swelling with light matrix and reduced cristae. In some cells there was swelling with complete lysis of cristae and tearing of outer membrane. Cisterns and canals of SER and RER mostly were fragmented. Often inside haemocapillaries were lysis areas of the luminal plasmolemma of the endotheliocytes that led to going intracellular content inside the microvascular space. There was also desquamation of endothelial cells inside the haemocapillary space and bare of basement membrane. There were adhesion and aggregation of white blood cells and platelets and red blood cells sludge in the lots of haemocapillary spaces (fig. 3).

Microscopically during 72 hours after modeling of the - multiple skeletal trauma in the lung respiratory department rotation in atelectasis areas of emphysematous enlarged alveoli was defined. There was prominent hyperemia of haemocapillaries in some alveolar partitions.

Submicroscopically, at this stage of study, there were still swelling events of the components of the lung respiratory department. The cytoplasm of A-I and A-II was with low electronic-optical density matrix. There is inside the cytoplasm swelling mitochondria, enlarged and partially fragmented components of the SER and RER. It was defined solitary ribosomes on the outer surface of the RER membrane. There were decrease numbers of LB in A-II. Interstitial tissue had low electronic-optical density of the connective tissue matrix.

There were also hyperhydration events in haemocapillary endotheliocytes with disorders of structure of their organelles. The most of capillaries had got extended space with various shape erythrocytes inside, adhesion and aggregation of leucocytes and platelets.

Inside the alveolar space it was a decrease of active phagocyte capacity AM. The most of macrophage elements had got dystrophic and destructive changes.

The extension of swelling events during 168 hour of study was less. Nevertheless, there were detected alveolar epithelial cells with signs of increased functional activity. Inside the cytoplasm of those cells there were mitochondria with moderate electronic-optical density matrix, canals of RER were enlarged, ribosomes rich. The number of LB in the A-II were saved.

Hyperhydration of the interstitial tissue had got more local character. Among Swelled connective tissue matrix of the alveolar wall sometimes were defined fibroblasts with increased amount of collagen fibers.

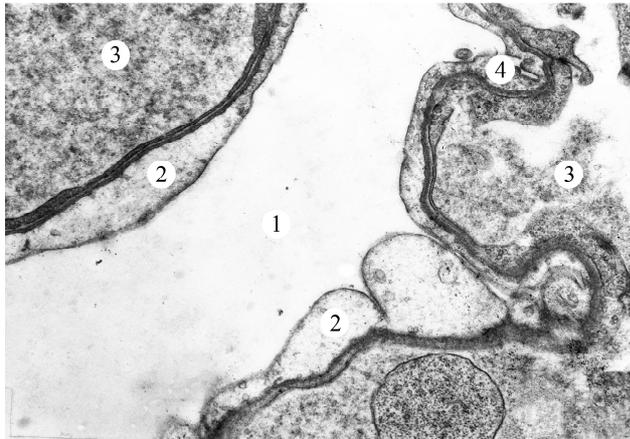


Fig. 2. Respiratory department of lungs 24 hours after beginning of study (multiple skeletal trauma and osteosynthesis). 1 – alveolar space; 2 – sail-like prominence of the peripheral part of the alveolocyte I type inside alveolar space; 3 – haemocapillary space; 4 – peripheral part of the alveolocyte I type. Microelectronic picture. x4800.



Fig. 3. Ultrastructural changes of the haemocapillaries of the alveolar wall of the lungs during 24 hours after beginning of study (multiple skeletal trauma and osteosynthesis). 1 – haemocapillary space; 2 – platelet; 3 – erythrocyte; 4 – peripheral part of the haemocapillary endotheliocytes; 5 – alveolar space. Microelectronic picture. x8000.

Intracellular swelling of endotheliocytes had place during this stage of the study, but it was less prominent than during previous stages of the study.

Submicroscopically there are huge heterogeneity in the alveoli of AM. It was detected cells with signs of increased functional activity and also ones with dystrophic and degenerative changes. In the space of some alveoli were found conglomerates of AM with big phagosomes and polymorphous osmiophilic material.

The study showed that multiple skeletal trauma is considered with morphological changes of submicroscopic structure of the components of the lung respiratory department. However, it is suggested that intramedullary osteosynthesis of the femur fracture increase as severity changes of structure of the components of the lung respiratory department, as well extension of them. It is defined that osteosynthesis of fractures by intramedullary device during the first 24 hours after trauma cause systemic effect, which was called the «second hit» (the first one is the initial trauma) [12, 13, 14]. Surgery triggers the release of lots of proinflammatory cytokines, which stimulates recruitment of polymorphonuclear leucocytes and haemocapillary endothelium damage [6, 11, 15, 17]. Submicroscopic morphology damage of the endotheliocytes of the lung haemocapillaries, overaccumulation of activated neutrophils due to intramedullary osteosynthesis of femur fractures was also proved by our study.

### Conclusions

1. Our study showed that intramedullary osteosynthesis in case of multiple skeletal trauma cause to submicroscopic morphology damage of all components of the lung respiratory department.

2. The most prominent changes of ultrastructure of alveolar cells I type, alveolar cells II type, interstitial tissue, haemocapillaries and alveolar macrophages occur during 24 hours of study.

*The prospects of further studies lie in the correction of structural changes in the components of the lung respiratory department due to multiple skeletal trauma with intramedullary osteosynthesis.*

### References

1. Kopytchak IR. Morphofunctional changes in the lungs in isolated and coupled injury. Hospital Surgery. 2014; 1: 36-9. [in Ukrainian]
2. Kovalchuk OL, Kulyanda IS, Smorshchok YUS, Kulyanda OO. Assisting victims with polytrauma at dominative skeletal trauma. Hosp Sur. 2011; 4: 72-4. [in Ukrainian]
3. Kozak DV, Volkov KS. Electronically microscopic state of liver by experimental polytrauma. World of Medicine and Biology. 2014; 2(44): 126-8. [in Ukrainian]
4. Kuz UV, Sulyma VS, Zaiats LM, Kovalyshyn TM. Model of multiple skeletal trauma in small animals. Rationalization proposition №14/2729. 2014 Nov 11. [in Ukrainian]
5. Alberdi F, Azaldegui F, Zabarte M, García I, Atutxa L, Santacana J et al. Epidemiological profile of late mortality in severe polytraumatism. Med Intensiva. 2013; 37(6): 383-90.
6. Bhatia M, Zemans RL, Jeyaseelan S. Role of chemokines in the pathogenesis of acute lung injury. American Journal of Respiratory Cell and Molecular Biology. 2012; 46(5): 566-72.
7. Chen C, Shi L, Li Y, Wang X, Yang S. Disease-specific dynamic biomarkers selected by integrating inflammatory mediators with clinical informatics in ARDS patients with severe pneumonia. Cell Biol Toxicol. 2016; 32: 169-184.
8. Chen X, Song Y, Liu Z, Zhang J, Sun T. Ultrastructural lung pathology following brain injury combined with femur shaft fracture in a rat model. Journal of Trauma and Acute Care Surgery. 2015; 78(3): 558-64.

9. Howard BM, Kornblith LZ, Hendrickson CM, Redick BJ, Conroy AS, Nelson MF et al. Differences in degree, differences in kind: characterizing lung injury in trauma. *J. Trauma Acute Care Surg.* 2015; 78(4): 735–741.
10. Husebye E, Lyberg T, Opdahl H, Aspelin T, Stoen R, Madsen J, Riosse O. Intramedullary nailing of femoral shaft fractures in polytraumatized patients. A longitudinal, prospective and observational study of the procedure-related impact on cardiopulmonary- and inflammatory responses. *Scandinavian journal of trauma, resuscitation and emergency medicine.* 2012; 20:2.
11. Mare TA, Treacher DF, Shankar-Hari M, Beale R, Lewis SM, Chambers DJ et al. The diagnostic and prognostic significance of monitoring blood levels of immature neutrophils in patients with systemic inflammation. *Critical Care.* 2015; 19(1): article 57.
12. Namas R, Ghuma A, Hermus L, Zamora R, Okonkwo D, Billiar T et al. The Acute Inflammatory Response in Trauma / Hemorrhage and Traumatic Brain Injury: Current State and Emerging Prospects. *The Libyan Journal of Medicine.* 2009; 4(3): 97–103.
13. Perl M, Hohmann C, Denk S, Kellermann Ph, Lu D, Braumüller S et al. Role of activated neutrophils in chest trauma-induced septic acute lung injury. *Shock.* 2012; 38(1): 98-106.
14. Stubljär D, Skvarc M. Effective strategies for diagnosis of Systemic Inflammatory Response Syndrome (SIRS) due to bacterial infection in surgical patients. *Infectious Disorders: Drug Targets.* 2015; 15(1): 53-6.
15. Williams A, Chambers R. The mercurial nature of neutrophils: still an enigma in ARDS? *Am J Physiol Lung Cell Mol Physiol.* 2014; 306: 217-30.

#### Реферати

#### ПАТОМОРФОЛОГІЧНІ ЗМІНИ РЕСПІРАТОРНОГО ВІДДІЛУ ЛЕГЕНЬ ПРИ МНОЖИННІЙ СКЕЛЕТНІЙ ТРАВМІ ІЗ ЗАСТОСУВАННЯМ ІНТРАМЕДУЛЯРНОГО ОСТЕОСИНТЕЗУ В ЕКСПЕРИМЕНТІ

Заяць Л.М., Кузь У.В.

У досліджах на 90 білих щурах-самцях лінії Вістар світлооптичним та електронномікроскопічним методами вивчено в динаміці (6, 24, 72, 168 год.) мікроскопічні та ультраструктурні зміни компонентів респіраторного відділу легень при множинній скелетній травмі із застосуванням інтрамедулярного остеосинтезу в експерименті. Встановлено, що інтрамедулярний остеосинтез стегнових кісток, проведений впродовж перших 24-х годин після травми супроводжується вираженими змінами структурної організації всіх компонентів респіраторного відділу легень. Зі збільшенням терміну дослідження (72-168 год.) в респіраторному відділі спостерігаються як дистрофічно-деструктивні так і компенсаторно-приспосувальні зміни.

**Ключові слова:** легені, респіраторний відділ, експериментальна множинна скелетна травма, інтрамедулярний остеосинтез.

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#### ПАТОМОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ РЕСПИРАТОРНОГО ОТДЕЛА ЛЕГКИХ ПРИ МНОЖЕСТВЕННЫХ СКЕЛЕТНЫХ ТРАВМАХ С ИСПОЛЬЗОВАНИЕМ ИНТРАМЕДУЛЯРНОГО ОСТЕОСИНТЕЗА В ЭКСПЕРИМЕНТЕ

Заяц Л.М., Кузь У.В.

В опытах на 90 белых крысах-самцах линии Вистар светооптическим и электронномикроскопическим методами изучено в динамике (6, 24, 72, 168 ч.) микроскопические и ультраструктурные изменения компонентов респираторного отдела легких при множественной скелетной травме с применением интрамедулярного остеосинтеза в эксперименте. Установлено, что интрамедулярный остеосинтез бедренных костей, проведенный в течении первых 24-х часов после травмы сопровождается выраженными изменениями структурной организации всех компонентов респираторного отдела легких. С увеличением срока исследования (72-168 ч.) в респираторном отделе наблюдаются как дистрофически-деструктивные так и компенсаторно-приспособительные изменения.

**Ключевые слова:** легкие, респираторный отдел, экспериментальная множественная скелетная травма, интрамедулярный остеосинтез.

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T.I. Krytskyy, N.V. Pasyechko  
I.Ya. Horbachevsky Ternopil State Medical University, Ternopil

#### SPECIFICITY OF HORMONAL AND METABOLIC STATUS IN PRIMARY HYPOTHYROIDISM MEN

E-mail: krytskyy\_t@ukr.net

The purpose of this study was to compare hormonal, anthropometric and metabolic parameters in men with hypothyroidism. Totally 60 males with primary hypothyroidism were studied. It has been established that hypothyroidism is accompanied by an increase in serum concentrations of cholesterol and low density lipoprotein when compared with the control group (25 men without hypothyroidism) and indicating metabolic disturbance. Our results have been shown the significant effect of hypothyroidism on testosterone and follicle stimulating hormone (FSH) serum concentration, but not on luteinizing hormone and estradiol levels. Patients with hypothyroidism had lower circulating testosterone and higher FSH level in comparison with the control group. The reproductive hormone changed in men with hypothyroidism which can result in deleterious effects on sexual functions including erectile dysfunction, reduced libido and alteration in spermatogenesis.

**Keywords:** hypothyroidism, reproductive hormones, testosterone, metabolic status, men.

The hypothyroidism negatively affects well-being, activity and reproductive status in human [1, 2]. Hypothyroidism is often accompanied by dyslipidemia, arterial hypertension, cardiovascular disease, type 2 diabetes, osteoarthritis, decreased fertility, and other pathology [3]. The effects of hypothyroidism