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Articles

Study of Leishmaniasis Disease: A Systematic Review

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Abstract

Sand flies are characterized by their inability to fly continuously and spread over a wide range, as they rarely spread more than one kilometer away from their breeding areas. It was found that wind does not affect the intensity of its spread, but on the contrary, these insects are ineffective when the wind speed is more than one kilometer per second and resort to their homes when the wind blows.

Leishmaniasis has been known for a long time and is still one of the ten most important infectious diseases in the world, in addition to being a public health problem in many countries of Africa, South America, Central and South West Asia and Indian subcontinent. It is also one of diseases endemic in Iraq and parasite has caused a healthy problem to be underestimated in Southern Iraq, especially in Dhi Qar Governorate.

Leishmaniasis is a main careless tropical disease related with high attribution of disability and death. This illness is linked with destitution, which can be reflected in housing housing quality, especially in rural territory. This sickness is transported amidst mammalian hosts through bites of blood sucking vector sand fly. So, Lack of realization among local societies also decrease the efficiency of reservoir host and vector control schemes. Until now parasites transition to mammalian host has never been immediately determined, so this disease has a great impact to public good health of Individuals. The form of protozoan parasite is closely related to pathogenicity. Therefore, many instant actions must done in order to excess scientific information on this disease and higher achievement, of the patients and observation programmers need be carried out by raise realization around the sickness between common public and stringent sharing of local society in surveillance and safeguard actions.

Keywords: *Leishmania*, Epidemiology, diseases, review.

1. Introduction

Leishmaniasis is occasion by a protozoa parasite (that is transmitted by the bite of infected female sand flies) of more than 20 species, the number of sand flies known to transmit *Leishmania* parasites exceeds 90 (Giraud et al., 2019). The disease effects on the poorest people in the world, and is linked to malnutrition, population displacement, poor housing, a weak immune system, and a lack of financial resources (Kimblin et al., 2008). Leishmaniasis is associated with environmental changes such as dams building, deforestation, establishing irrigation systems and urbanization (Kholoud et al., 2018). The number of cases of this disease is estimated between 700,000 and one

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million annually, the disease appears only in a small percentage of infected with parasite will ultimately develop Leishmaniasis (Abdullah et al., 2017). *Leishmania* disease is classified as a parasitic disease of animal origin, man is infected by bite of a female type of mosquito called sand bug, this small-sized insect is silent when flying and lives in the hot humid climate and its activity increases in the summer and feeds on human or animal blood and absorbs this Blood from an infected person or animals (such as dogs and foxes, where these animals are a reservoir for the disease parasite) and this blood is loaded with the disease parasite that multiplies in the stomach of the insect and then reaches its saliva and when it bites a healthy person or animal, it injects these parasites into his body, causing him disease (Giraud et al., 2019). There are three main forms of disease include visceral leishmaniasis (also known as kalaazar, the most serious form of the disease), cutaneous (most common) and mucocutaneous disease (Hendrickx et al., 2020).

2. Results and discussion

Fundamental species of leishmania

It appears in three forms: eastern sorts, diffuse cutaneous and mucocutaneous form. The lesions may take from 2-5 years to heal.

1) Visceral leishmaniasis, also known as kala azar, is fatal in 95 % of cases if left untreated, it is characterized by irregular bouts of fever, weight loss, an enlarged spleen and liver and anemia. This type is often found in people with double infection between leishmaniasis vascular and AIDS .Most of its cases are concentrated in Brazil, East Africa and India. Number of new cases around the world is estimated at between 50,000 and 90,000 annually, of which only 25-45 percent are reported to the World Health Organization. In 2018, more than 95 % of the new cases were concentrated in 10 countries: Brazil, China, Ethiopia, India, Iraq, Kenya, Nepal, Somalia, South Sudan and Sudan (Kholoud et al., 2018).

2) Cutaneous leishmaniasis, which is the most widespread form of leishmaniasis, causes skin lesions, actually ulcers on visible parts of the body, leaving permanent scars, serious disability or eschar. About 95 % of cutaneous leishmaniasis cases occur in the Americas, Middle East and Central Asia. In 2018, more than 85 percent of new cases were concentrated in 10 countries: Afghanistan, Algeria, Bolivia, Brazil, Colombia, Islamic Republic of Iran, Iraq, Pakistan, Syrian Arab Republic and Tunisia. The number of new cases per year is estimated at between 600,000 to one million globally (Hendrickx et al., 2020).

3) Mucocutaneous leishmaniasis, which causes partial or complete damage to mucous membranes of nose, mouth and throat. More than 90 % of mucocutaneous leishmaniasis cases are concentrated in the Plurinational State of Bolivia, Brazil and Ethiopia (Kholoud et al., 2018).

Major risk factors

1) Socio-economic conditions

Poverty increases the risk of leishmaniasis, it may worsen housing conditions and health conditions in homes (such as insufficient waste management or open sanitation) from sand fly breeding and resting sites, as well as the possibility of reaching people. Sand flies are attracted to overcrowded dwellings because they provide a good source of blood that they feed on. Also, human behavior, such as sleeping outside or on the ground, may increase the odds of developing this disease (Okwor, Uzoona, 2016).

2) Malnutrition

Diets that lack protein, energy, iron, vitamin A and zinc increase risk of infection developing into advanced disease (Wijerathna et al., 2017).

3) Population mobility

Epidemics of cutaneous leishmaniasis and epidemics of visceral leishmaniasis are often associated with migration and the movement of unimmunized people to areas with disease transmission cycles. Occupational exposure as well as large-scale deforestation remain important factors (Calderon et al., 2018).

4) Environmental changes

Incidence of leishmaniasis may be affected by changes in civilization and human live into forested areas (Wijerathna et al., 2017).

5) Climate change

Leishmaniasis is a climate-sensitive disease that affects its epidemiological characteristics in many ways, including the following (Ghazanfar, Malik, 2016):

- * Changes in temperature, rainfall and humidity may severely affect the host vectors and reservoirs by changing their distribution and affecting their survival and numbers.

- * Simple fluctuations in temperature may significantly influence the development cycle of the leishmaniasis in sand flies, allowing the parasites to move to areas that were not endemic to the disease.

- * Droughts, famines and floods may lead to mass displacement and migration of people to areas where leishmaniasis is transmitted, and malnutrition may Weaken their immunity.

Shape and life cycle

There are two phases of the parasite, 1)(Amastigote) which is oval in shape and its diameter is (3-5) micrometers and contains one nucleus and has a kinetic structure (Kinoplast) (Sunter, Gull, 2017). As well as the presence of flagella that is present in macrophages and cells of the internal retinal system, which includes liver, spleen and lymph nodes, which enriched the bones 2)(Promastigote), second form, this species is found in the vector insect and is fusiform-shaped and has a length of about (20-30) μm , it has one flagellum at the front of the body, during its life the parasite needs two hosts, one of which is vertebrate and the other is invertebrate (sand fly) and the parasite transforms in the insect's intestine from (Amastigote) to (Promastigote). In fact, it multiplies by longitudinal fission and then migrates after several days (Sunter, Gull, 2017).

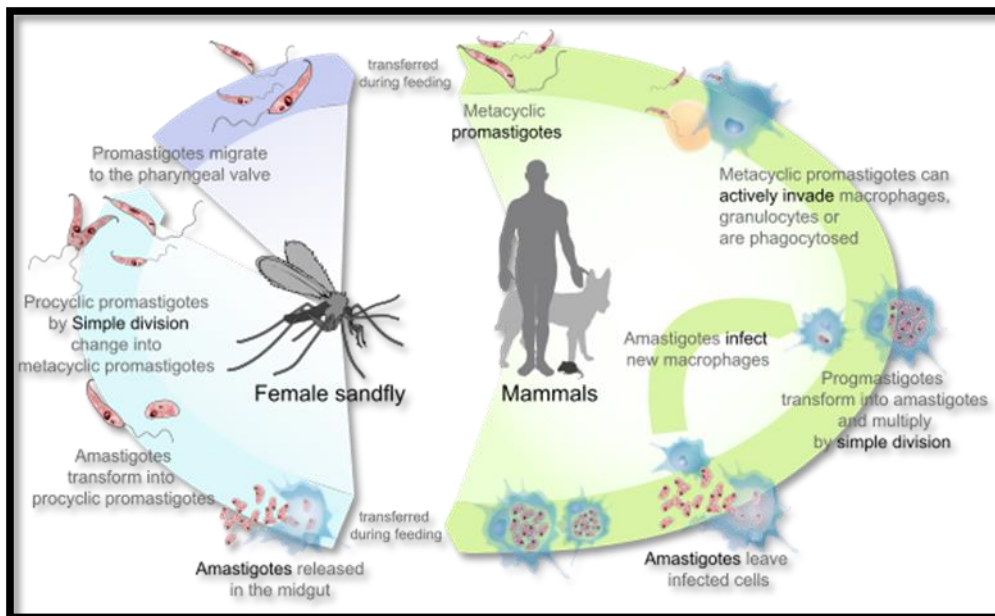


Fig. 1. Life cycle of *leishmania* (Harkins et al., 2016)

Host carrier (Sand fly)

Sand fly is considered the host for the leishmaniasis parasite and this insect is seasonal in its appearance in temperate regions of the world, adults appear only in the summer, that is, the breeding season is confined to the summer season in the tropics, and some species seem almost constant throughout the year, but in other species there may be significant changes to an extent that is considered for the group of adults, especially in the dry and wet climates (Harkins et al., 2016).

In fact, there is no evidence of eggs hatching in nature, and from some studies the eggs hatch within 3-4 days of laying in the summer and the period may increase to (7) days in the winter season so that they lay the female is from (30-40) eggs throughout her life, and the larva is found in the same places where the eggs were laid, and it feeds on the same materials. The duration of the larva is two weeks in the summer, and the period may increase or decrease in the winter season,

in this time, the larva goes through three alienations and has four stages, the number of insects in Iraq increases in two seasons (Blume, Eloi, 2019).

Spring season, the numbers start to increase from the end of the month of March and increase more in the month of April and May, as well as in the first half of June, then their number begins to decrease, and their quantities remain low in the rest of June, July and the first half of the month of August, and then the number begins to increase, reaching a large extent and very high in late September and early October, subsequently the number begins to decrease until the insects fertilize or multiply in late November and for a period of months: December, January and February, and do not start in public places, homes and cities during the winter, and this is not a strange thing (Casanova et al., 2019). Rather, they come to houses to provide warm conditions. Females leave the residence before sunset and then return and enter them at about eleven o'clock in the evening (Kumar et al., 2015). Sand insect is spread in tropical regions, but it does not exist in submerged and cold areas, and its presence is limited between 4 degrees south and 40 degrees north, and in America, Europe and parts of Asia its presence reaches 95 degrees north, and the southern presence is unknown. As for Iraq, it is present in all governorates, but it is few in Basra, which indicates that soil moisture affected its reproduction and there are (16) species of insect, although recent studies have revealed many types of them (Mauldin, Peters, 2016).

The insect's saliva is mixed inside the vertebral host while feeding on it, where it is consumed by the macrophage cells and transformed inside them into (amastigote) , it begins to proliferate within macrophages, after which these cells divide and the parasites are released to be consumed by other phagocytes, thus, reproduction continues when the large macrophage cells split into the body of the vertebral host, and numbers of parasites move through the lymph nodes and body fluids to the internal viscera, such as, liver, spleen and lymph nodes, which subsequently cause these organs to enlarge (Menezes, Madeira, 2016).

Clinical Symptoms of leishmaniasis

Symptoms of cutaneous leishmaniasis have skin ulcers that appear at the site of the bite, usually in the exposed areas of the body include limbs and face, period of parasite harbor lasts from two months to several months, however hosting duration depends on parasite genus and immune response of the infected person , yet, lesions, which are small at first, grow into sores that usually heal themselves after sundry months (up to 24 months), while about skin harm often disappear without any medication, most of the suffering caused by *Leishmania* major recover within 6-12 months. In most cases, symptoms caused by *Lishmania* Tropica will recover within 24 months. But in visceral *leishmania* include regular signs such as fever, depression, weight loss, anemia, enlarged spleen, liver and lymph nodes, these symptoms occur as a result of a weakened immune system of infected person. It also causes leukopenia and thrombocytopenia and shows secondary infection and bleeding tendency (Terio et al., 2018).

Diagnosis and Treatment

Method of diagnosis depends on infection type. In cutaneous leishmaniasis, clinical symptoms are clear, the examiner is isolating parasite from damage skin of known laboratory methods according to the fluids around the skin and cultivated it in the medium, then checked the parasite in a Promastigote stage. while other methods, especially in cases of visceral leishmaniasis, depend on several procedure, inclusive (Kimblin et al., 2008).

1) Laboratory methods that have isolation and diagnosis of parasite when a part of the live tissue (biopsy) is not taken from the iliac bone, thereafter sample is implanted in the culture medium as resemble a cross, and observed parasite in (promstigote phase) after staining the sample directly with *Leishmania* stain , and in this time can viewing parasite in an amasigote phase inside the cells (Abdullah et al., 2017).

2) Serological examinations which comprise (fat, Elisa) and others. These tests depend on specific antibodies presence to leishmaniasis parasite in the serum of patient or suspected person (Obaid, 2018).

3) Possible to use other methods in state of disease progression, such as using X-rays or sonar (ultrasound) to detect cases of enlarged liver and spleen in advanced stages of the illness (Kholoud et al., 2018).

Often cutaneous leishmaniasis infection cures automatically without any treatment, and healing of these ulcers takes a period from one to two years, sometimes it may extend to more than this time (Calderon-Anyosa et al., 2018).

As for the infection with visceral leishmaniasis, it leads to death of patients if it is left untreated, death cause is often an accidental harm with another disease and sometimes injury returns again after complete recovery, these relapses occur even after years of treatment period, but, most cases of visceral leishmaniasis respond well to treatment. There are now several treatments available to cure visceral leishmaniasis disease, but some studies confirmed that the disease is difficult to treat, therefore used antimonial in symptoms appear, but it is not known whether this chemical element directly effect on parasite activity in (Amastigot) stage inside cells, or indirectly, by accelerate macrophages and other elements of the immune system. A recent study about visceral leishmaniasis suggests that work should be done by reducing current levels of cytokines (Giraud et al., 2019).

For treatment of chronic leishmaniasis, use Pentostam, which is sodium stibo glnconate for a period of (6) days. aside from rest, protein and vitamins intake and good care, there are many remediation, such as (Choline to Promastigot), which is new class of inhibitors, whose may be used to treat leishmaniasis and this it completely effective and gives a cure rate of 97 % for 28 days (100 mg/l a day) (Abudallah et al., 2017).

Review in the previous studies carried out of Leishmaniasis

Due to medical prominence of Leishmaniasis, it is a main assembly health issue that can cause dangerous human diseases, as well as, economical damage to the person, family and society, there have been numerous studies on leshmaniasis illness and transact with many portion, subsequent section of these studies:

Kimblin et al. (2008) study on quantification of number Leishmania for main parasites injected inside the ears of living mice within nutrition during persons infected flies. Al-Samarai (2009) study to locate the rang of cutaneous leishmaniasis (C L) in Alhaweja zone and to enquire the subaltern bacterial contamination in C L. Another study which also included ecological agents related with apportionment of visceral leishmania disease (kala-azar) in chronic regions of Bangladesh and which increased morbidity and mortality rates in these areas: design of environmental variables (Abdullah et al., 2017). While other study of Obaid (2018) involved clinical study on Leishmania kinds and distribution areas in Kirkuk city, Iraq, for one year from 2014 to April 2015, conducted on inside and outside patients of Pediatric, Kirkuk General and Azadi Teaching hospitals. As for the study of Kholoud et al. (2018) on epidemiology consequences of leishmaniasis to distinguish advice and define topic recommendations to fight this illness by study climate variation influence on spread and distribution of this disease in Morocco. Other study Calderon-Anyosa et al. (2018) about housing features and Leishmaniasis, these study revealed found that clay walls with puncture and cracks, moist, and dusky houses it hazard agents for leishmaniasis transmission because these factors make suitable places for sand flies nurture and resting as sand fly choose warmth, wet and preservation from sunlight through midday. Finally, (Giraud et al., 2019) conducted on survey of comprehension of transportation strategy by using Real-Time Quantitative (PCR) to quantify contagious Non-metacyclic and metacyclic kinds in mouse lacing from singular sand fly biting to reveals role and prevalence of heterogeneity dose of sand flies.

3. Conclusion

1. Leishmaniasis is a parasitic illness transmitted by the female sand fly G: phleptomas.
2. There are three major kinds of this disease, visceral, cutaneous and Mucocutaneous leishmaniasis.
3. This parasite has two main phases in its life cycle: Amastigote and Promastigote.
4. Leishmaniasis is one of the most widespread diseases in the world, especially in Iraq, for both visceral and cutaneous types.

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Radiofrequency Microneedling for the Treatment of Acne Scar in Iraqi Patients

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Abstract

The study was done to evaluate the role of radiofrequency micro needling as a treatment modality in treating acne scars. This study is a prospective follow up study carried out in a private clinic through the period from 1st of August, 2017 to 31st of July, 2018 on convenient sample of 60 patients with acne scars.

The acne scars were classified and treatment evaluated according to qualitative and quantitative Goodman and Baron's Acne Scarring System. the radiofrequency micro needling treatment outcome of acne scar patients was distributed as followings; minimal (20 %), moderate (31.7 %), good (38.3 %) and very good (10 %) and patients' satisfaction regarding radiofrequency micro needling treatment of acne scar was distributed as followings; 13.3 % no change, 10 % slight improvement 23.3 % moderate improvement, 30 % significant improvement and 23.3 % excellent improvement. The recorded side effects were minor; erythema (20 %), pain (6.7 %), hyperpigmentation (5 %) and edema (3.3 %).

In conclusion: The radiofrequency micro needling treatment modality of acne scar is effective and safe.

Keywords: Acne, scar, micro needling, radiofrequency, Iraqi patients.

1. Introduction

Acne is a common condition with prevalence as high as 80 % among adolescents. All body areas with high concentrations of pilosebaceous glands may be involved, but the commonest affected areas include the face, back and chest. Acne lesions can result in permanent scarring with a marked impact on quality of life. Genetic factors, disease severity and delay in treatment are the main factors influencing scar formation. The prevalence and severity of acne scarring in the population is largely unknown (Gozali, Zhou, 2015).

Scar severity is another important factor in the management of scars. It is used as a tool of identifying a suitable treatment to evaluate outcomes (Goodman, Baron, 2006). Several different modalities have been devised. Such assessments can be objective or subjective examples of such grading scales include the Vancouver Scar Scale (VSS), Goodman and Baron Qualitative and Qualitative grading scales, Patient and Observer Scar Assessment Scale (POSAS), Visual Analog Scale (VAS) and the Patient Satisfaction Score (PSS) (Fearmonti et al., 2010). Furthermore, different treatments was used of acne scar such as Pulsed dye laser (PDL). PDL is the gold-standard for treating scar-associated erythema (Iyer et al., 2005).

Traditional ablative lasers considered the gold standard in acne scarring treatment (Brightman et al., 2009), ablative fractional lasers (Ong, Bashir, 2012), traditional non-ablative lasers, non-ablative fractionated lasers (Maluki, Mohammad, 2012), non-ablative radiofrequency (RF) treatments can be used as a monotherapy or adjuvant therapy with fractional lasers. Radiofrequency delivers a current through the dermis that stimulates dermal remodeling,

producing new collagen and softening scar defects (Simmons et al., 2014). New developments have allowed for more precision in the delivery of RF energy to deeper tissues, with decreased injury to the overlying epidermis. Bipolar RF allows for delivery of a more focused current to the dermis.

Microneedle bipolar RF and fractional bipolar RF treatments offer the best results for acne scarring, particularly icepick and boxcar scars (Min et al., 2015), as well as, radiofrequency and microneedling were subsequently combined in an attempt to enhance the results that could be achieved with either one alone.

The combination technology creates fractional radiofrequency coagulation of dermal collagen and results in immediate collagen contraction. It also stimulates a natural healing response which leads to the replacement of damaged connective tissue with new healthier skin (Garg, Baveja, 2014).

The microneedling Fractional Radiofrequency (MFR) device, which delivers heating in a fractional manner, was introduced for the use in skin treatments including skin rejuvenation, acne scar, axillary hyperhidrosis, and striae alba.

The MFR device delivers uniform heat at a controlled depth to the dermal-hypodermal layers where the sweat glands and hair follicles are present, resulting in thermolysis of the sweat glands and subsequent necrosis (Fatemi et al., 2016). The study was aimed to evaluate the role of radiofrequency microneedling as a treatment modality in treating acne scars.

Patients and methods

Study design, settings and duration

This study is a prospective follow up study carried out in a private clinic (Dr. Wesam Al-Saraf Clinic) through the period from 1st of August, 2017 to 31st of July, 2018.

Population

All patients presented with acne scars to the clinic. With inclusion criteria included Adults (age \geq 20 years) and Acne scars.

Exclusion criteria: it is included the following: previous treatment of acne scars, Laser therapy during treatment or during follow up, Photosensitivity, Pregnancy and lactation, Hypertrophic or Keloid scarring, Patients On isotretinoin treatment or Anticoagulants history, Active herpes infection and Refused to participate.

Sampling

A convenient sample of 60 patients with acne scars presented to private clinic was enrolled in the study after filling the inclusion and exclusion criteria.

Data Collection

The data was collected through direct interview with acne scar patients and fulfilling a prepared questionnaire. The diagnosis of acne scars was confirmed by Dermatologist in the clinic. The questionnaire was prepared by the supervisor and researcher.

The questionnaire included the followings: Demographic characteristics: Age and gender, skin type of patients with acne scars, acne scar types, age at acne and acne scars development, treatment outcome assessment by physicians and Patients' satisfaction in treatment outcomes. After full history and examination of patients by the researcher, the acne scars were carefully examined and classified according to qualitative and quantitative Goodman and Baron's Acne Scarring System (Goodman, Baron, 2006; Al-Hammamy et al., 2015). The acne scars selected in this study were mild to severe acne scars according to grading of Goodman. The treatment plan of acne scar by microneedling and radiofrequency was organized in four sessions lasting for 6 months with a schedule of 1st visit, 2nd month, 4th month and 6th month.

Microneedling and radiofrequency treatment

The equipment used was (Micro-needle and Fractional Radiofrequency tb-88) and the researcher was trained on using this equipment by Dermatologist in the clinic. Before application of treatment, the face was cleansed using non-abrasive detergent and gauzes soaked in 70 % isopropyl alcohol. Additionally, the topical anesthetic cream (EMLA) was used under occlusive dressing for 1 hour duration and then removed. The power and intensity of microneedling and radiofrequency applied is dependent on acne scar grade and depth. The device had dual handpieces and two head tips of different sizes, 25 and 49 pins. The intensity was 7 with active pulse 210 ms, in depth of 1.5 mm at 0.5 sec. interval. The forced air cooling is essential to maintain comfort of patients.

The treatment was administered in four sessions during a period of 6 months in a schedule of 1st visit, 2nd month, 4th month and 6th month.

Follow up and assessment

The acne scars patients were followed up during treatment four sessions and the final assessment was done after completing 6 months or four session's treatment with microneedle and radiofrequency.

Treatment outcomes were assessed by standardized digital photography (SONY-DSC-W300; 13.6 mega pixels) by the patient himself and by the researcher and other Dermatologist. The dermatologists' evaluation was depending on quantitative Goodman and Baron's Acne Scarring System outcome assessment (Goodman, Baron, 2006; Al-Hammamy et al., 2015). This assessment was categorized into four groups as shown in Table 1.

Table 1. Assessment of improvement of acne scar using Goodman and Baron's Acne Scarring System (Goodman, Baron, 2006; Al-Hammamy et al., 2015)

Grades	Improvement status
0-5	Minimal reduction in GSGS score
5-10	Moderate reduction in GSGS score
10-15	Good reduction in GSGS score
>15	Very good reduction in GSGS score

The self-assessment level of improvement of the patients was evaluated using the following five-point scale:

- 0=no change;
- 1=slight improvement (0-25 %);
- 2=moderate improvement (26-50 %);
- 3=significant improvement (51-75 %);
- 4=excellent improvement (>75 %).

The two assessors were blinded to the order of the photographs. The evaluators were asked to perform two actions. First, to identify the photograph that showed better scar appearance. Second, to rate the difference in the severity of the acne scars using the above mentioned scale.

Statistical analysis

All patients' data entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 20 was used. Descriptive statistics presented as (mean \pm standard deviation) and frequencies as percentages. Multiple contingency tables conducted and appropriate statistical tests performed, Fishers exact test was used for categorical variables. In all statistical analysis, level of significance (p value) set at ≤ 0.05 and the result presented as tables and/or graphs. Statistical analysis of the study was done by the community medicine specialist.

2. Results

Age of patients

The present study included 60 patients with acne scars; with mean age of 25.9 \pm 3.9 years, 50 % of them were in age group 20-25 years, 36.7% of them were in age group 26-30 years and 13 % of them were in age group 31-35 years. All these findings were shown in Table 2.

Table 2. Age of acne scar patients

Variable	No.	%
Age mean±SD (25.9±3.9 years)		
20-25 years	30	50.0
26-30 years	22	36.7
31-35 years	8	13.3
Total	60	100.0

Gender of patients

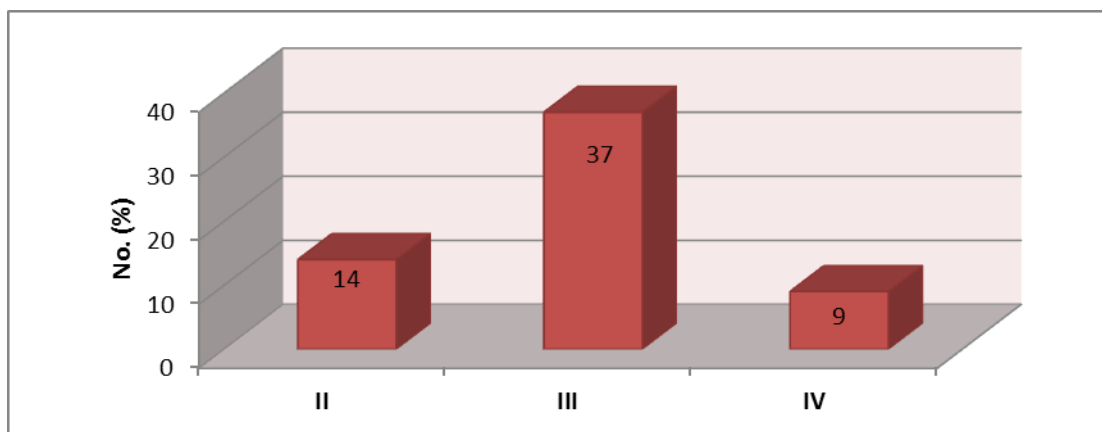
More than two thirds (80 %) of acne scar patients were females and 20% of acne scar patients were males with female to male ratio as 4:1. All these findings were shown in [Table 3](#).

Table 3. Gender distribution of acne scar patients

Variable	No.	%
Gender		
Male	12	20.0
Female	48	80.0
Total	60	100.0

Skin types

The skin types of acne scar patients were distributed as following; 23.3 % type II, 61.7 % type III and 15 % type IV. All these findings were shown in [Figure 1](#).

**Fig. 1.** Skin types**Acne scar types**

The acne scar types for studied patients were distributed as followings; significant rolling (26.7 %), deep boxcar (20 %), shallow boxcar (35 %), and icepick scar (18.3 %). All these findings were shown in [Figure 2](#).

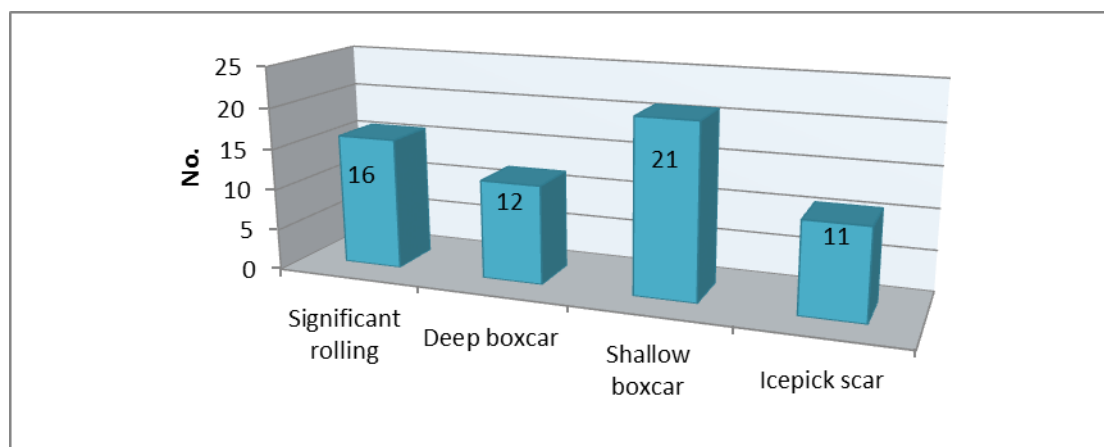


Fig. 2. Types of acne scars

Age at onset

Mean age of patients at onset of acne was 16 ± 1.5 years; 70 % of them had acne at age group 14-16 years and 30 % of them had acne at age group 17-19 years. Mean age of patients at onset of acne scar was 19.6 ± 1.5 years; 46.7 % of them had acne at age group 17-19 years and 53.3 % of them had acne at age of 20 years and more. All these findings were shown in [Table 4](#).

Table 4. Age at onset of acne and acne scar development

Variable	No.	%
Age at acne onset mean\pmSD (16\pm1.5 years)		
14-16 years	42	70.0
17-19 years	18	30.0
Total	60	100.0
Age at acne scar onset mean\pmSD (19.6\pm1.5 years)		
17-19 years	28	46.7
≥ 20 years	32	53.3
Total	60	100.0

Treatment outcome

According Goodman and Baron's Acne Scarring System outcome assessment, the Micro-needling Radiofrequency (MR) treatment outcome of acne scar patients was distributed as followings; minimal (20 %), moderate (31.7 %), good (38.3 %) and very good (10 %). All these findings were shown in [Table 4](#).

Table 5. MR treatment outcome of acne scar by Goodman and Baron's Acne Scarring System

Variable	No.	%
Treatment outcome		
Minimal	12	20.0
Moderate	19	31.7
Good	23	38.3

Very good	6	10.0
Total	60	100.0

Patients satisfaction

The patients' satisfaction regarding MR treatment of acne scar was distributed as followings; 13.3 % no change, 10 % slight improvement 23.3 % moderate improvement, 30 % significant improvement and 23.3 % excellent improvement. All these findings were shown in Table 6.

Table 6. Patients' satisfaction toward MR treatment of acne scar

Variable	No.	%
Patients satisfaction		
No change	8	13.3
Slight improvement	6	10.0
Moderate improvement	14	23.3
Significant improvement	18	30.0
Excellent improvement	14	23.3
Total	60	100.0

Relationship between MR outcome and study variables

As shown in Table 7, there was a significant association between increased age of patients with acne scar and good MR treatment outcome ($p = 0.002$).

Table 7. Distribution of patients' age according to MR treatment outcome

Age groups	Minimal		Moderate		Good		Very good		P
	No.	%	No.	%	No.	%	No.	%	
20-25 years	4	33.3	12	63.2	14	60.9	0	-	0.002* Significant
26-30 years	8	66.7	6	31.6	3	13.0	5	83.3	
31-35 years	0	-	1	5.3	6	26.1	1	16.7	

*Fishers exact test

As shown in Table 8, no significant differences were observed between acne scar patients with different MR outcomes regarding patients gender ($p = 0.2$).

Table 8. Distribution of patients' gender according to MR treatment outcome

Gender	Minimal		Moderate		Good		Very good		P
	No.	%	No.	%	No.	%	No.	%	
Male	4	33.3	5	26.3	2	8.7	1	16.7	0.2* Not significant
Female	8	66.7	14	73.7	21	91.3	5	83.3	

*Fishers exact test

As shown in Table 9, no significant differences were observed between acne scar patients with different MR outcomes regarding patients skin types ($p = 0.7$).

Table 9. Distribution of patients' skin types according to MR treatment outcome

Skin type	Minimal		Moderate		Good		Very good		P
	No.	%	No.	%	No.	%	No.	%	
II	2	16.7	6	31.6	5	21.7	1	16.7	0.7* Not significant
III	7	58.3	11	57.9	14	60.9	5	83.3	
IV	3	25.0	2	10.5	4	17.4	0	-	

*Fishers exact test

As shown in Figure 3, there was a significant association between significant rolling acne scar and very good MR treatment outcome (p = 0.001).

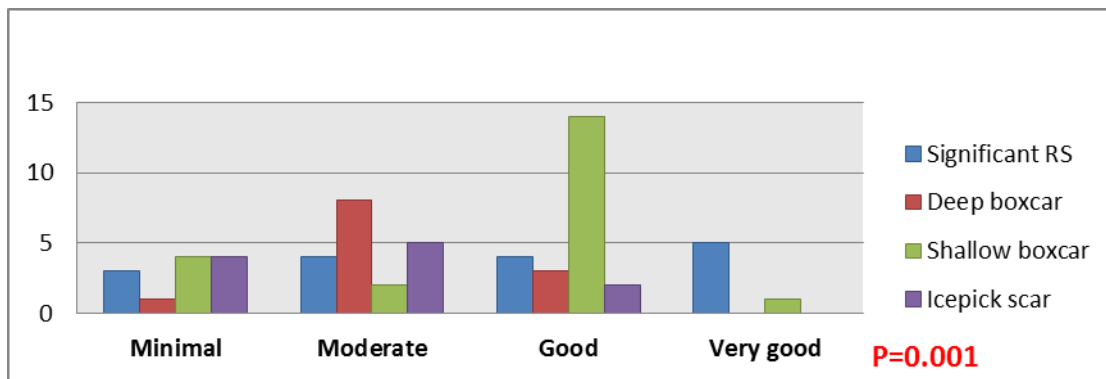


Fig. 3. Distribution of MR outcome according to acne scar types

MR post-treatment side effects

As shown in Figure 4, no side effects were observed after MR treatment of acne scars among 39 (65 %) patients, while the present side effects included erythema (20 %), pain (6.7 %), hyperpigmentation (5 %) and edema (3.3 %).

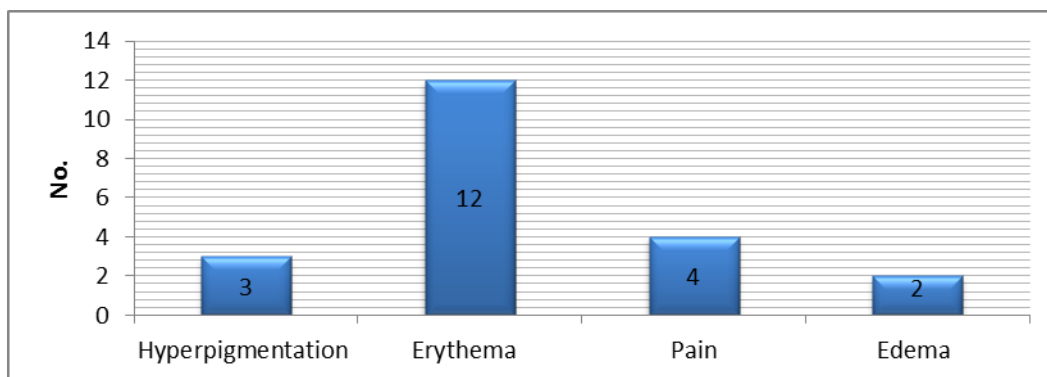


Fig. 4. Side effects of acne scar treatment by MR



Fig. 5. Male patient with acne scar; Left pre-treatment, Right post-treatment (anterior view)

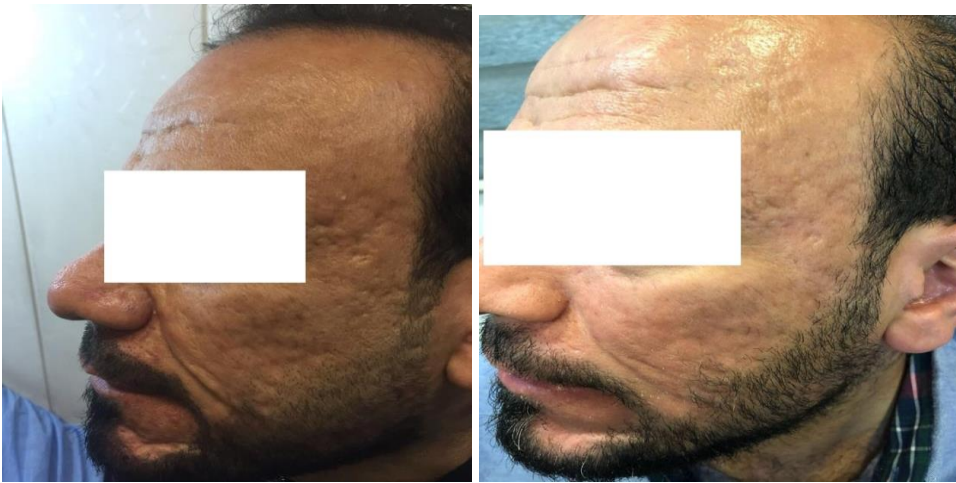


Fig. 6. Male patient with acne scar; Left pre-treatment, Right post-treatment (lateral view)



Fig. 7. Female patient with acne scar; Left pre-treatment, Right post-treatment (lateral view)



Fig. 8. Female patient with acne scar; Left pre-treatment, Right post-treatment (anterior view)

3. Discussion

The current study showed that outcome of using microneedling and radiofrequency in treating after four sessions resulted in 20 % minimal improvement, 31.7 % moderate improvement, 38.3 % good improvement and 10 % very good improvement according Goodman and Baron's Acne Scarring System outcome assessment. These outcome results are better than results of Chandrashekar et al. (2014). Study in India which evaluated the outcome of four session's microneedling fractional radiofrequency for 6 months in treatment of acne scars and ended in 29 % minimal improvement, 58 % moderate improvement, 9 % good improvement and 3 % very good improvement. In Iraq, a study conducted by Al-Hammamy et al. (2015), revealed that subcision and microneedling are safe and effective treatment procedure for acne scars with long term outcome. A study conducted in South Korea by Min et al. (2015), evaluated the microneedling and radiofrequency modality in comparison to bipolar radiofrequency in treating acne scars and showed that microneedling radiofrequency had higher efficacy and safety for treatment of acne scars. The micro-needling is the public choice in treating the facial atrophied acne scars. In a review of literatures conducted by Harris et al. (2015), in Australia, there was moderate evidence confirming the effectiveness and safety of microneedling in treating the facial acne scars. The action of microneedling is aiming to re-establishment and building up new collagen fibers, elastin and capillaries (Singh et al., 2016). Current Egypt study revealed that microneedling application for acne scar treatment causes a rising in collagen fibers after 6 sessions. Enhancing new synthesis of percutaneous collagen by microneedling refresh the skin and influence the youthful expression of skin through lowering fine lines and wrinkles, decreasing pore size, increase in suppleness and more elastic texture. Adding the radiofrequency to microneedling would create radiofrequency thermal zones without epidermal injury that lead to increase the thickness of skin dermis by new skin dermis organization, new collagen and elastin fibers (Chandrashekar et al., 2014).

Current study found that satisfaction of patients with acne scars regarding outcome of microneedling and radiofrequency in treating acne scars was significant to excellent in more than half of patients, while 13.3 % of patients had perceived no change, 10 % perceived slight improvement and 23.3 % of them perceived moderate improvement. These findings are better than results of Saeed et al. (2016), study in Iraq which evaluated the outcome of microneedling radiofrequency alone or in combination with platelets-rich plasma and found that satisfaction of patients toward outcome of microneedling radiofrequency alone was distributed as followings; 4.5 % no improvement, 27.3 % mild improvement, 27.3 % moderate improvement, 27.3 % good improvement and 4.5 % excellent improvement (Saeed et al., 2016).

In present study, the side effects were not observed in 65 % of acne scars patients treated with microneedling and radiofrequency. This finding is consistent with results of Min et al. (2015), study in South Korea and Hussain (2018). In Pakistan which documented minor side effects of post treatment of acne scars with microneedling radiofrequency. The common side effects reported in our study were erythema, pain, hyperpigmentation and edema. These findings are similar to results of Elawar and Dahan (2018), in France which evaluated the outcome of microneedling

radiofrequency in treating the acne scars and found that this treatment modality was highly effective with high patients' satisfaction and minimum side effects like erythema and pain. In Thailand, Vejjabhinanta et al. (2014), carried out a study evaluation the role of microneedling radiofrequency in treatment of acne scars and reported that main adverse effects occurred after treatment were pain, erythema, scabbing and pigmentary alterations.

Our study showed a significant association between increased age of patients with acne scar and good microneedling radiofrequency treatment outcome ($p = 0.002$). This finding coincides with results recorded by O'Daniel (2011) in USA. In China Gozali and Zhou (2015) reported that microneedling is effective in treating acne scars of aging face as it replaces the atrophied scars with neo collagen fibers specifically for elderly age women. Present study showed also a significant association between significant rolling acne scar and very good microneedling radiofrequency treatment outcome ($p = 0.001$). This finding is similar to results obtained by Kravvas and Al-Naimi (2017), who stated that boxcar acne scars are difficult to be treated while the rolling acne scars are easily treated. However, many authors clarified the effectiveness of microneedling and radiofrequency modality in treating the acne scars generally and rolling acne scars specifically (Chandrashekar et al., 2014).

4. Conclusion

The study concluded, the microneedling radiofrequency treatment modality of acne scar is effective and safe and satisfactory for patients with acne scars. microneedling radiofrequency have adverse side effects including erythema, pain, hyperpigmentation and edema. As well as, the improvement rate of acne scars treated with microneedling and radiofrequency is more likely to be affected by age of patients and type of acne scar.

Declaration of competing interest

None.

Funding

None.

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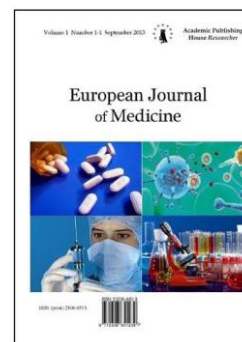
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Acid-Base and Gas Status of Blood in COVID-19 Patients with “Quiet Hypoxia”

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Abstract

An observational prospective study was conducted, during which 50 patients of both sexes with severe COVID-19 and moderate manifestations of acute respiratory failure were examined. The study included patients who showed a decrease in transcutaneous saturation of less than 93 %, with a respiratory rate of no more than 25 per minute, who did not have complaints of dyspnea and impaired consciousness, but required, according to temporary clinical recommendations for the treatment of patients with COVID-19, correction of respiratory disorders. We determined the values of transcutaneous saturation using pulse oximetry, studied the acid-base state and gas composition of arterial and venous blood, and also took into account complaints of respiratory disorders, respiratory rate, the presence of forced breathing, heart rate, the "white spot" symptom and blood lactate level. The selected methods of treatment of respiratory disorders, necessary for the correction of acute respiratory failure, and the results of hospitalization were also taken into account. Based on the data obtained, it was concluded that in patients with COVID-19 "silent hypoxia" is associated with the development of moderate compensated arterial hypoxemia without the development of hypercapnia, tissue hypoxia and acidosis. Arterial hypoxemia in patients with "silent hypoxia" is compensated by known compensatory mechanisms – an increase in the delivery and utilization of oxygen to the tissues and an increase in the alkaline reserve. Moderate arterial hypoxemia without tissue hypoxia is corrected by pron-position and oxygen therapy, and does not require conversion to artificial ventilation.

Keywords: arterial hypoxemia, hypercapnia, acidosis, tissue hypoxia, “silent hypoxia”.

1. Введение

У пациентов с тяжёлым течением COVID-19 часто развиваются дыхательные нарушения с различной степенью клинических проявлений – от минимально выраженной до тяжёлого острого респираторного дистресс-синдрома (ОРДС) (Xu et al., 2020, Wilcox, 2020).

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При этом выделяется категория пациентов, имеющих клинические симптомы лёгкой или умеренной степени нарушений дыхания, но с непривычно низкими значениями транскутанной сатурации (SpO₂) (Wang et al., 2020, Fauci et al., 2020).

Такое различие между клинической картиной острой дыхательной недостаточности (ОДН) и транскутанной десатурацией получил название «тихой» или «счастливой гипоксии» (happy hypoxia) (Ottestad et al., 2020, Couzin-Frankel, 2020).

Как известно, тканевая десатурация может быть вызвана артериальной гипоксемией, нарушениями микроциркуляции, повреждением эритроцитов и гемоглобина или с сосудистым микротромбозом (Moroz et al., 2020, Nardelli, Landoni, 2020).

Вместе с тем, вне зависимости от механизмов десатурации, итогом микроциркуляторных нарушений, артериальной гипоксемии и гиперкапнии, а также повреждений эритроцитов и гемоглобина является развитие тканевой гипоксии и ацидоза (Matthay et al., 2019, Wilcox, 2020).

Понимания сути феномена «тихой гипоксии» и её специфических особенностей крайне важно, поскольку позволяет решить вопрос выбора необходимых методов лечения у пациентов с COVID-19 и симптомами ОДН: позиционной терапии, лечения кислородом, СРАР-терапии или инвазивной искусственной вентиляции лёгких (ИВЛ) (Ding et al., 2020; Gattinoni et al., 2020, Клинические рекомендации..., 2020).

Вместе с тем, кислотно-основное состояние, газовый состав крови и выраженность гипоксии тканей у пациентов с «тихой гипоксией» при COVID-19 пока ещё не изучены должным образом.

В связи с указанным, интерес к изучению особенностей кислотно-основного состояния, газового состава крови и выраженности гипоксии тканей у пациентов с умеренно-выраженными симптомами ОДН при COVID-19 имеет большое практическое значение, поскольку позволяет принять верное и своевременное решение о выборе метода коррекции дыхательных нарушений.

Цель исследования: изучить особенности КОС и газового состава крови у пациентов с COVID-19 при умеренно-выраженной острой дыхательной недостаточности

2. Материалы и методы

Было проведено многоцентровое проспективное наблюдательное исследование, в ходе которого обследованы 50 пациентов обоего пола (23 мужчины и 27 женщин) с тяжёлым течением COVID-19, сопровождающегося клиникой ОДН, госпитализированных в инфекционные стационары Университетской клиники ПИМУ Минздрава России, Городской больницы №33, Городской клинической больницы №3 г. Нижнего Новгорода. Диагноз COVID-19 устанавливался на основании критериев, изложенных во Временных клинических рекомендациях Министерства здравоохранения Российской Федерации (МЗ РФ) (Профилактика, диагностика и лечение..., 2020). Средний возраст пациентов составил 70 (58;77) лет.

В исследование были включены пациенты, у которых выявлялось снижение транскутанной сатурации менее 93 %, с частотой дыхания не более 25 в минуту, не имевших жалоб на диспноэ и нарушения сознания но, требовавшие, согласно Временным клиническим рекомендациям МЗ РФ и международным клиническим рекомендациям по лечению пациентов с COVID-19, коррекции дыхательных нарушений (Профилактика, диагностика и лечение..., 2020).

В исследование не включали пациентов, которые на момент обследования имели клинику сепсиса, шока, синдрома полиорганной недостаточности, комы.

Определяли значения транскутанной сатурации методом пульсовой оксиметрии, частота дыхания (ЧД), частота сердечных сокращений (ЧСС) с помощью прикроватных мониторов Dreger, Cardex, Mindrey, Triton.

Кислотно-основное состояние (КОС), газовый состав в венозной и артериальной крови и уровень лактата крови оценивали с помощью анализаторов Radiometer Medical. Также учитывались выбранные методы лечения дыхательных нарушений, необходимые для коррекции ОДН и результаты госпитализации.

3. Методы статистического анализа

Статистическая обработка материала проводилась программами Microsoft office Excel и Statistica 6.0. Для описания и представления анализируемых данных были применены следующие методы описательной статистики. Для определения выборок на нормальность распределения использовали критерий Шапиро-Уилка. С учётом асимметрии выборок, значения дискретных и непрерывных количественных показателей представлены в виде медианы и процентилей – Me(P25;P75).

4. Результаты исследования

Было установлено, что ЧД была в диапазоне от 16 до 25, в среднем 22(20;24) в минуту, ЧСС была в диапазоне от 84 до 99, в среднем 90 (87;95) в минуту, SpO₂ была в диапазоне 83-93 %, в среднем 85(84;90) %. В венозной крови рН регистрировали в диапазоне 7,34-7,46, в среднем 7,39(7,37;7,41), рСО₂ – в диапазоне 35-40, в среднем 37(35;39), ВЕ – в диапазоне 2-12 ммоль/л, в среднем – 6(4;9), рО₂ определялось в диапазоне 40-47 мм рт ст, в среднем – 42(40;44), SO₂ был в диапазоне 62-77 %, в среднем – 67(64;70), в артериальной крови рО₂ определялось в диапазоне 67-85 мм рт ст, в среднем – 74(71;77), SO₂ в диапазоне 83-93 %, в среднем – 86(87;90), рСО₂ в диапазоне 33-46 мм рт ст, в среднем 37(34;39).

Симптом белого пятна был менее 3 сек. у всех пациентов, что свидетельствовало об отсутствии нарушений микроциркуляции. Повышение уровня лактата в крови не выявлено. При проведении оксигенотерапии потоком 2-15 л/мин в прон-позиции все показатели становились нормальными. В дальнейшем подключения к аппаратам механической вентиляции не потребовалось. Все пациенты были выписаны из стационаров.

5. Обсуждение

Как следует из представленных результатов, у обследованных пациентов имела место транскутанной десатурацией до 83 %, которая сопровождалась развитием умеренной артериальной гипоксемии, но при этом не развивались гиперкапния и ацидоз.

В связи с тем, что доставка кислорода к тканям была удовлетворительной (рvO₂ более 40 мм рт ст, SvO₂ более 60 %), артериальная гипоксемия не сопровождалась развитием тканевой гипоксии, а компенсировалась за счёт увеличения транспорта и утилизации кислорода.

Кроме того, развитию ацидоза препятствовало наличие щелочного резерва (компенсаторное увеличение ВЕ), также позволявшего нивелировать влияние кислых факторов на КОС. Таким образом, для «тихой гипоксии» характерно развитие умеренной артериальной гипоксемии без развития гиперкапнии и тканевой гипоксии.

Ранее подобные изменения КОС и газового состава крови были описаны в условиях гипоксической гипоксии у здоровых людей ([Ottestad, Søvik, 2020](#)).

Артериальная гипоксемия, а также тканевая десатурация корригировалась прон-позицией и кислородотерапией потоком от 2 до 15 л/мин. Это позволяет предположить, что причина развития ОДН у пациентов с «тихой гипоксией» была связана с развитием микроателектазов лёгких и увеличением «мёртвого пространства» в дорсальных отделах лёгких, что в свою очередь обусловлено диффузным повреждением лёгких – интерстициальной инфильтрацией (отёком) лёгочной ткани ([Xu et al., 2020](#), [Tian et al., 2020](#)).

Поэтому простое изменение положения тела (прон-позиция) позволяло открыть спавшиеся альвеолы и улучшить аэрацию дорсальных отделов лёгких, в которых сохранялась хорошая перфузия. В результате улучшения вентиляционно-перфузионных соотношений увеличивалась оксигенация артериальной крови и состояние пациентов улучшалось, что согласуется с ранее представленными данными ([Caputo et al., 2020](#), [Elharrar et al., 2020](#)).

Безусловно, исследования в этом направлении следует продолжать.

6. Заключение

У пациентов с COVID-19 «тихая гипоксия» ассоциирована с развитием умеренной компенсированной артериальной гипоксемии без развития гиперкапнии, тканевой гипоксии и ацидоза. Артериальная гипоксемия у пациентов с «тихой гипоксией» компенсируется за счёт увеличения доставки и утилизации кислорода к тканям и

увеличения щелочного резерва. Умеренно-выраженная артериальная гипоксемия без тканевой гипоксии корригируется прон-позицией и кислородотерапией, и не требует подключения к аппарату для ИВЛ.

7. Финансирование исследования

Работа не финансировалась никакими источниками.

8. Конфликт интересов

Не отмечено.

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Кислотно-основное состояние и газовый состав крови у пациентов COVID-19 с «тихой гипоксией»

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Аннотация. Было проведено наблюдательное проспективное исследование, в ходе которого были обследованы 50 пациентов обоого пола с тяжёлым течением COVID19 и умеренными проявлениями ОДН. В исследование были включены пациенты, у которых выявлялось снижение транскутанной сатурации менее 93 %, с частотой дыхания не более 25 в минуту, не имевших жалоб на диспноэ и нарушения сознания, но требовавшие, согласно временным клиническим рекомендациям по лечению пациентов с COVID19, коррекции дыхательных нарушений. Определяли значения транскутанной сатурации с помощью пульсовой оксиметрии, изучали кислотно-основное состояние и газовый состав крови артериальной и венозной крови, а также учитывали жалобы на дыхательные нарушения, частоту дыхания, наличие форсированного дыхания, частоту сердечных сокращений, симптом «белого пятна» и уровень лактата крови. Также учитывались выбранные методы лечения дыхательных нарушений, необходимые для коррекции острой дыхательной недостаточности и результаты госпитализации. На основании полученных данных сделано заключение о том, что у пациентов с COVID 19 «тихая гипоксия» ассоциирована с развитием умеренной компенсированной артериальной гипоксемии без развития гиперкапнии, тканевой гипоксии и ацидоза. Артериальная гипоксемия у пациентов с «тихой гипоксией» компенсируется за счёт известных компенсационных механизмов – увеличение доставки и утилизации кислорода к тканям и увеличения щелочного резерва. Умеренная артериальная гипоксемия без тканевой гипоксии корригируется проп-позицией и кислородотерапией, и не требует перевода на искусственную вентиляцию лёгких.

Ключевые слова: артериальная гипоксемия, гиперкапния, ацидоз, тканевая гипоксия, «тихая гипоксия».

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