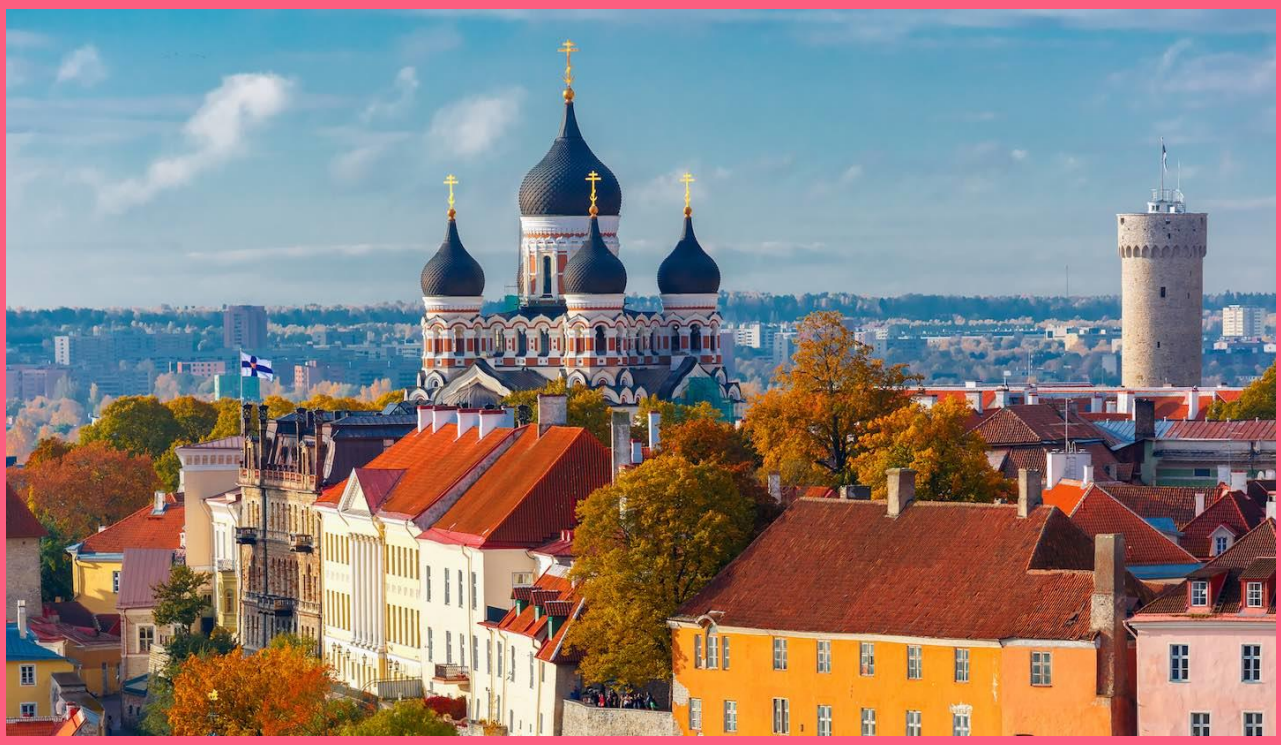

THE SIXTH INTERNATIONAL SCIENTIFIC – PRACTICAL VIRTUAL CONFERENCE IN MODERN MEDICINE AND HEALTH: PROGNOSIS, ACHIEVEMENT AND CHALLENGES."

CONFERENCE PROCEEDINGS

AZERBAİJAN-ESTONIA-KAZAKHSTAN-TURKEY

ESTONIA, TALLINN FEBRUARY 25-26, 2022

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TALLINN 2022

Organizer of the conference:

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Tbilisi State Medical University. Head of International Students Academic Department, Associate Professor. PhD in HNA.
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Gulmira Zhurabekova
Department of fundamental Medicine, Higher School of Medicine. Al Farabi Kazakh National University. Associate Professor.
Irada Sultanova
AMU. Department of Obstetrics and Gynecology I. PhD in Medicine. Associate Professor.
Irma Buchukuri
Doctor of Medicine, Professor of Petre Shotadze Medical Academy.
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Tbilisi State Medical University. The First University Clinic. Dermato-Venereologist. Assistant Professor. PhD in DAPS.
Melis Gonulal
University of Health Sciences, İzmir Tepecik Training and Research Hospital, Associate Professor. PhD in Medicine.
Mina Qarashova
AMU. Department of Obstetrics and Gynecology I. PhD in Medicine. Associate Professor.
Namig Isazade
International Research, Education & Training Center. MTÜ. PhD in Business Administration.
Nigar Kamilova
AMU. Department of Obstetrics and Gynecology I. Doctor of Medical Sciences. Professor.
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Doctor of Theoretical Medicine in Pharmaceutical and Pharmacological Sciences, Professor of Millennium University, Head of The International English Pharmacy Program, Head of The Division of Pharmacology.
Rafig Mammadhasanov
AMU. Head of the Department of Internal Medicine II. Doctor of Medical Sciences. Professor.
Saadat Safarova
AMU. Department of Obstetrics and Gynecology I. PhD in Medicine. Associate Professor.
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AMU. Department of Internal Medicine II. PhD in Medicine. Associate Professor.
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AMU. Department of Internal Medicine II. PhD in Medicine. Associate Professor.
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Associate Professor, PhD in Medicine, Head of the Department of Normal and Topographic Anatomy, Kyrgyz State Medical Academy.
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PROGRAM AT A GLANCE

First day	25 February 2022
Moderators	Namig Isazade, Ekaterine Lomia
Opening ceremony	Namig Isazade
19.00-19.20	**Ekaterine Lomia** Teaching University Millennium. Georgia.
	Melis Gönülal University of Health Sciences, İzmir Tepecik Training and Research Hospital.
	Gulmira Zhurabekova Al-Farabi Kazakh National University. Kazakhstan.
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21.40-22.00	Closing ceremony

ABSTRACTS AND THESES

THE SCIENTIFIC DISCUSSION OF WORLDWIDE CHALLENGES OF COVID-19 EPIDEMIC AND GENERAL DRUG THERAPY APPROACHES TO COMBAT THE COVID-19 DISEASES

Nodar Sulashvili[1], Luiza Gabunia[2], Levan Ratiani[3], Nana Gorgaslidze[4], Ketevan Ghambashidze[5], Elena Varazi[6], Natia Antia[7]

[1]MD, PhD, Doctor of Theoretical Medicine in Pharmaceutical and Pharmacological Sciences, Professor of Millennium University, Head of The International English Pharmacy Program, Head of The Division of Pharmacology, Georgia.
[2]MD, PhD, Doctor of Medical Sciences, Professor, Director of the Scientific Research-Skills Center. Professor, Georgia.
[3]MD, PhD, Doctor of Medical Sciences, Professor, General Director of the First University Clinic. Head of the Department of Emergency Medicine, Reanimatology and Anesthesiology. Georgia.
[4]MD, PhD, Doctor of Pharmaceutical Sciences, Professor. Georgia.
[5]MD, PhD, Doctor of Medical Sciences, Associate Professor
[6,7] Scientific Skills Center, Tbilisi State Medical University, Tbilisi, Georgia.
E-mail: n.sulashvili@ug.edu.ge

ABSTRACT

A new type of coronavirus (COVID-19) SARS-CoV-2 originated in Wuhan, China and has caused a global pandemic. COVID-19 is a newly emerging infectious disease caused by SARS-CoV-2 and is known as SARS. By July 1, 2020, more than 10 million people worldwide will be infected with SARS-CoV-2. Typical manifestations of COVID-19 are fever, sore throat, fatigue, cough, and shortness of breath combined with recent exposure. Most COVID-19 patients have mild to moderate illness; however, 5 to 10% have a serious and even life-threatening illness. The death rate is around 2-3%. Therefore, there was an urgent need for a specific and effective antiviral treatment. Supportive measures such as oxygenated ventilation and fluid handling remain the standard of care today. Several clinical studies are ongoing to determine the most effective drug or combination for this disease and it is highly recommended that patients be included in ongoing studies. The safety and effectiveness of antiviral drugs could only be demonstrated in randomized clinical trials. Several active ingredients such as chloroquine, hydroxychloroquine, favipiravir, monoclonal antibodies, antisense RNA, corticosteroids, convalescent plasma and vaccines were currently being evaluated. A variety of therapeutic interventions were aimed at determining the most effective regimen. The purpose of this article is to describe the treatment strategies that have been used for patients with COVID-19 and to review all available literature.

According to WHO, effective pharmacotherapy options for COVID-19 have been summarized, and nonsteroidal use has been declared controversial. anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs). In accordance with the recommendations, a combination of drugs against COVID 19 was used. Some of the more promising drugs include chloroquine phosphate and hydroxychloroquine, which are both antimalarial drugs, remdesivir, lopinavir-ritonavir with or without a combination, according to a preliminary WHO study. interferon, which is an anti-HIV drug and plasma pharmacotherapy for convalescents. However, some antiviral drugs (Rideliver, favipiravir) and antimalarial drugs (chloroquine, hydroxychloroquine) have emerged as potential drugs. Pharmacotherapy evidence of efficacy and continuous research have been developed in the article. In addition, data were obtained regarding the inflammatory pathogenesis of this virus, leading to a cytokine storm in susceptible

individuals. Thus, cytokine anti-inflammatory drugs such as Anakinra and Tocilizumab are undergoing numerous trials and some of the results are encouraging. Likewise, the use of anti-inflammatory cytokines such as IL-37 and IL-38 is believed to be beneficial and under investigation. Several clinical trials are currently underway that test the efficacy of single and combination pharmacotherapy using the drugs advertised in this review, and new drugs are being monitored, developed, developed and improved [1-5].

SARS-CoV-2 virus entered into the target cells by binding with the hACE2 receptors. Spike glycoprotein promotes the entry of the virus into host target cells [6]. Literature reported a significant mutation in receptor binding sites and membrane proteins of the previous SARS-CoV to turned as SARS-CoV-2 virus, responsible for most dreadful pandemic COVID-19 [7]. These modifications may be the probable reason for the extreme transmission and pathogenicity of the virus. A hasty spread of COVID-19 throughout the world is highly threatening, but still, scientists do not have a proper therapeutic measure to fight with it. Scientists are endeavoring across the world to find effective therapy to combat COVID 19 [8-9]. Several drugs such as Remdesivir, Hydroxychloroquine, Chloroquine, Ribavirin, Ritonavir, Lopinavir, Favipiravir, Interferons, Bevacizumab, Azithromycin, etc. are currently under clinical trials. Vaccine development from various pharmaceutical companies and research institutes is under progress, and more than ten vaccine candidates are in the various phases of clinical trials. This review work highlighted the origin, emergence, structural features, pathogenesis, and clinical features of COVID-19. We have also discussed the in-line treatment strategies, preventive measures, and vaccines to combat the emergence of COVID-19 [10-11]. Thus, treatment approaches that are currently being studied include antiviral and anti-inflammatory cytokines, anti-infective and life-sustaining therapy, monoclonal antibodies, and passive immunotherapy, especially in patients with severe illness. However, while a therapeutic strategy against the disease is important, the most important way to prevent the spread of the virus is to develop a widely available effective and safe vaccine. In the future, it will be wise to choose a personalized medication to choose the best treatment along with an effective dose with minimal side effects. Various studies are currently underway to evaluate vaccines against SARS-CoV2. However, due to genetic changes in viral nucleic acid in different hosts, these specific vaccines may not have a clear preventive effect [12-14].

Keywords: Worldwide, therapy, treatment, covid-19 diseases, epidemic.

MANIFESTATIONS OF SARS-COV-2-INDUCED COVID-19 ON THE SKIN AND ORAL MUCOSA

Nodar Sulashvili[1], Kakhaber Robakidze[2], Irma Buchukuri[3], Lela Grigolia[4]

[1]MD, PhD, Doctor of Theoretical Medicine in Pharmaceutical and Pharmacological Sciences, Professor of Millennium University, Head of The International English Pharmacy Program, Head of The Division of Pharmacology, Georgia.

[2]MD, PhD, Doctor of Medical Sciences, Professor of Caucasus International University, Invited Professor of Millennium University, National Health Center named after Academician O. Gudushauri, Georgia;

[3]MD, PhD, Doctor of Medicine, Professor of Petre Shotadze Medical Academy, Georgia;

[4]MD, PhD, Doctor of Medical Sciences, Professor of Caucasus International University, Georgia;

Email:n.sulashvili@ug.edu.ge

ABSTRACT

A Over the past centuries, it is difficult to find diseases similar in resonance to the corona-virus infection COVID-19 caused by SARS-CoV-2. From the day of manifestation of the infection, it has become the dominant nosology, and its etiological agent has dramatically changed, in its favor, the species spectrum of anthropogenic pathological microorganisms. The review is devoted to the skin manifestations of new coronovirus infection (SARS-CoV-2), information about which is constantly updated. However, this information has not been systematized yet. The purpose of this review is to analyze the dermatological manifestations of a new coronavirus infection. On average, 12.5—20.4% of patients with confirmed COVID-19 have developed skin manifestations. The question of whether the skin symptoms are a secondary consequence of a respiratory infection or a primary infection of the skin itself remains open at the moment. The possible mechanisms of development of skin lesions and the role of diseases of complement system and blood hypercoagulation in the pathogenesis of the disease are discussed in the article. The review also provides descriptive and clinical examples of skin manifestations in COVID-19. Since COVID-19 tends to be asymptomatic within 14 days, skin manifestations can be an indicator of infection, which leads to the timely diagnosis. In addition, doctors' awareness about skin symptoms associated with COVID-19 infection plays a big role in preventing misdiagnosis of the disease.
Keywords: COVID-19, SARS-CoV-2, Skin, Oral Mucosa.

MODERN SCIENTIFIC RESEARCH DEVELOPMENT ISSUES OF HIGHER PHARMACY EDUCATION, SCIENCE, INNOVATION AND PERSPECTIVES TOWARDS ON UNIVERSAL PHARMACIST' PROFESSION GLOBALLY

Nodar Sulashvili[1], Nana Gorgaslidze[2], Luiza Gabunia[3], Ketevan Ghambashidze[4], Irine Zarnadze[5], Shalva (Davit) Zarnadze[6]

[1]MD, PhD, Doctor of Theoretical Medicine in Pharmaceutical and Pharmacological Sciences, Professor of Millennium University, Head of The International English Pharmacy Program, Head of The Division of Pharmacology, Georgia.
[2]MD, PhD, Doctor of Pharmaceutical Sciences, Professor of Tbilisi State Medical University, Department of Social and Clinical Pharmacy, Georgia.
[3]MD, PhD, Doctor of Medical Sciences, Professor, Director of the Scientific Research-Skills Center at Tbilisi State Medical University, Professor of the Department of Medical Pharmacology at Tbilisi State Medical University, Georgia.
[4]MD, Ph.D, Doctor of Medical Sciences, Professor of Department of Pathophysiology and Professor/Lecturer of the Scientific Research-Skills Center at Tbilisi State Medical University, Georgia;
[5]MD, PhD, Doctor of Medical Sciences, Professor of Tbilisi State Medical University, Department of Public Health, Health Care Management, Policy and Economy, Georgia.
[6]MD, PhD, Doctor of Medical Sciences, Professor of Tbilisi State Medical University, Head of the Department of Nutrition and Ageing Medicine, Georgia.
Email: n.sulashvili@ug.edu.ge

ABSTRACT

The main objective of the study was to analyze the modern scientific research development issues of higher pharmacy education, science, innovation and perspectives towards on universal pharmacist' profession Globally. The study was a quantitative investigation and analysis of the characteristics of pharmaceutical vocational inquires and challenges in the direction on pharmacists' profession, role, problems, perspectives and innovations in pharmaceutics and medicine in Georgia by using questionnaires. Were conducted a survey study. The in-depth interview method of the respondents was used in the study. The 7 types of approved questionnaires were used (Respondents were

randomly selected): Questionnaire for chief pharmacists: 410 chief pharmacists participated in the study. Questionnaire for patients: 1506 patients (customers of drug-stores) participated in the study. Questionnaire for the employed pharmacy faculty-student: 222 employed pharmacy faculty students participated in the study. Questionnaire for health-care specialists: 307 public health specialists participated in the study. Questionnaire for pharmacist specialist, 810 pharmacist specialists participated in the study. Were used methods of systematic, sociological (surveying, questioning), comparative, mathematical-statistical, graphical analysis. The data were processed and analyzed with the SPSS program. We conducted descriptive statistics and regression analyses to detect an association between variables. Statistical analysis was done in SPSS version 11.0. A Chi-square test was applied to estimate the statistical significance and differences. We defined $p< 0.05$ as significant for all analyses. According to the study results, the level of basic training of pharmacists should be in compliance with the contemporary requirements. The pharmacist should have deep knowledge in pharmacology, in pharmacotherapy, in toxicology, in pharmaceutical care, in clinical pharmacy, in pharmacokinetics, in pharmacodynamics, in basic of medicine and in other pre-clinical and clinical directions. Such knowledge can be obtained only in the higher pharmaceutical education institutions. Therefore, pharmacist working in pharmacy must have only higher pharmaceutical education. It is necessary to provide a deep cooperation between pharmacists and physicians on the issues of pharmacotherapy and healthcare to ensure the patients' health state effective improvement, and also to provide the best feedback regulation and revision in the healthcare specialists' team work. Pharmacists also should be responsible for registration of the drugs' side effect, as well as be attentive in case of improperness and professional defects of drugs they provide. To achieve that it is necessary to raise awareness of specialists on the essence of pharmacists' profession and functions among the medical personnel and general public [1-12].

Keywords: scientific, pharmacist, pharmacy, profession, medicine, pharmaceutics, education.

MORPHOLOGICAL RESEARCH USAGE OF BIOPLAST - DENT IN EXPERIMENT

Nodar Sulashvili, Tamar Okropiridze

[1]MD, PhD, Doctor of Theoretical Medicine in Pharmaceutical and Pharmacological Sciences, Professor of Millennium University, Head of The International English Pharmacy Program, Head of The Division of Pharmacology, Georgia.
[2]MD, PhD, Doctor Medical Sciences, Professor. Teaching University Geomedy, Department of Dentistry, Georgia.
Email: n.sulashvili@ug.edu.ge

Introduction: One of the urgent problems of modern dentistry is the search for the most effective means and methods of bone grafting [1, 2, 3]. These funds should optimize and at the same time stimulate the processes of reparative osteogenesis [4,5,6,7]. Osteoplastic materials are used in the surgical treatment of dental diseases accompanied by bone tissue destruction: chronic periodontitis, periodontitis, jaw bone cysts, etc [8,9,10,11,12,13].

The work represents experimental and morphological studies of regeneration of damaged areas of maxillo-facial bones. Time course of healing of induced defects in the low jaw bone filled with bioplast - dent and was studied in experimental rabbits. On days 7, 14, 21 and 28 four rabbits from each group were killed and the defect investigated by X-ray and histological methods. We stained the micropreparations ith hematoxilineeosine. Bioplast - dent granulate exerted the best effect on bone repair. In experiments with bioplast - dent, bone regenerate replaced up to one half of the area of defect by day 28.

Aim of the research: the aim of the study was to conduct a comparative analysis of the dynamics and nature of the bone reparative process in standard experimentally reproduced bone defects filled with osteoplastic material - bioplast - dent.
Material and methods: The experiments were carried out on chinchilla rabbits weighing up to 2 kg (n=32). In animals under general Calipsol anesthesia, a standard defect with a diameter of 4-5 mm was created on the lower jaw bones. At the end of the operation, the wounds were sutured with silk thread. In control animals (n=16), bone defects were left to heal under a blood clot, and in animals of the main group (n=16), bioplast-dent granules were injected into the bone defect. The animals were decapitated under anesthesia on the 7th, 14th, 21st and 28th days after the bone wound was applied. There were 4 rabbits per observation point in each group. The bone fragments were fixed in formalin, decalcified in Trilon-B, and embedded in paraffin. Sections were stained with hematoxylin and eosin.
Results and discussion: In the group of observations with bioplast - dent granulate, on the 7th day from the start of the experiment, the animals in the area of experimental exposure had extensive bone defects filled with tightly lying mineral granules, represented by a part of oxyphilic particles of accumulations of small dark crystals in the central sections of defects between bioplast - dent particles . Thin strands of a weakly oxyphilic homogeneous protein substance were located in these areas. Cellular elements were completely absent. The bone wall had a space free from granulate, filled with cellular-fibrous connective tissue, with a loose structure, high cellularity and a low level of collagenization. In the centripetal direction, there was a tendency for cellular elements to grow into bioplast-dent deposits. The strands from young fibroblasts penetrated to the periphery into the deposits of the mineral between its granules.
Conclusion: Bioplast - dent granules, being germinated tissue elements of the regenerate, provide the closest contact between cells penetrating into the pores and bioplast - dent crystals, as a result of which optimal conditions are created for its interaction with the tissue environment and stimulation of reparative osteogenesis. The action of bone growth factors, carried out through increased proliferation, differentiation and synthetic function of bone cells. The presence of a phage in an osteoplastic preparation determines its anti-inflammatory properties and, thus, accelerates reparative osteogenesis. Thus, the bioplast-dent osteoplastic material can be recommended for large-scale use in dental practice.
Keywords: Osteogenesis stimulation, reparative regeneration, morphological, X-ray.

ИЗМЕНЕНИЯ ТРАХЕОБРОНХИАЛЬНЫХ ЛИМФАТИЧЕСКИХ УЗЛОВ БЕЛЫХ КРЫСЯТ ПРИ ЭКСПЕРИМЕНТАЛЬНОЙ ХРОНИЧЕСКОЙ ВНУТРИУТРОБНОЙ ГИПОКСИИ В РАННЕМ ОНТОГЕНЕЗЕ

[1]Т.А. Адайбаев, [2]М.К. Жаналиева, [3]А.Ы. Алмабаева, [4]Н.Д.Айтенова, [5]Е.М.Серкеш
[1]д.м.н., профессор кафедры анатомии человека НАО «Медицинский университет Астана», Казахстан.
[2]к.м.н., профессор кафедры анатомии человека НАО «Медицинский университет Астана», Казахстан.
[3]д.м.н., профессор кафедры анатомии человека НАО «Медицинский университет Астана», Казахстан.
[4]к.м.н., профессор кафедры анатомии человека НАО «Медицинский университет Астана», Казахстан.
[5]преподователь кафедры анатомии человека НАО «Медицинский университет Астана», Казахстан.

РЕЗЮМЕ

Актуальность. Реакция лимфатических узлов в экстремальных условиях является одним из показателей адаптивных потенций организма к поддержанию тканевого гомеостаза [1]. Лимфатические узлы разной локализации у плодов обладают неодинаковым набором популяции лимфоцитов и имеют свои функционально-морфологические особенности [2-7].

Кроме того при жизни плодов и новорожденных непосредственное наблюдение за изменениями структурно-функциональных свойств лимфоидной ткани оказывается затрудненными, а имеющиеся в литературе данные о клеточном составе лимфатических узлов у плодов разноречивы. Эти противоречия, возможно, связаны с различием и несовершенством методик, эпидемиологическими и экологическими особенностями, с биоритмом и большой вариабельностью физиологической нормы, с характером питания и др. Следовательно, для выяснения указанных вопросов требуется проведение экспериментальных исследований.

Морфофункциональные преобразования лимфатических узлов при гипоксическом состоянии организма плодов и новорожденных в раннем онтогенезе изучены очень слабо.

Анализируя изложенные данные, необходимо отметить актуальность исследования морфологии лимфатических узлов экспериментальных животных при внутриутробной гипоксии в раннем онтогенезе.

Цель исследования: Изучить динамику морфологических изменений микроанатомической организации и клеточного состава трахеобронхиальных лимфатических узлов белых крысят при экспериментальной хронической внутриутробной гипоксии в антенатальном и постнатальном периодах онтогенеза.

Материал и методы исследования: Материалом для морфологического исследования явились 60 трахеобронхиальные лимфатические узлы плодов и новорожденных белой крысы.

Модель хронической внутриутробной гипоксии плода и новорожденного достигалась следующим образом: экспериментальные животные (крысы-самки) с массой 180-200 гр, на фоне малобелкового рациона питания (количество белка по калорийности составляет 7%), вместо питьевой воды получали 0,13% раствора аптечного таннина. В начале и в конце опыта исследовали кровь животных. Через два месяца у животных развивается анемия: число эритроцитов у них составляет 3 млн. в мкл (в контрольной - 5,78 млн в мкл); содержание гемоглобина в крови - 70 г/л (в контрольной - 154 г/л); цветной показатель - 0,60 (в контрольной - 0,92). После получения анемии, самок животных спаривали с самцами из расчета 2 самки на одного самца. Первым днем беременности считали день обнаружения сперматозоидов в вагинальных мазках. Каждой группе экспериментальных животных соответствовала параллельная группа контрольных животных, у которых беременность протекала в условиях физиологической жизнедеятельности организма. Все группы, как опытных, так и контрольных, животных наблюдались в течение одного сезона с марта по июль.

Результаты исследования и их обсуждение: Трахеобронхиальные лимфатические узлы начинают формироваться в те же сроки, что и у контрольных животных (15-16 сутки антенатального развития). Форма и топография лимфатических узлов не отличается от таковых у контрольных.

В течение I-III этапов, т.е. до 4 суток жизни, паренхима трахеобронхиальных лимфатических узлов остается диффузной – клеточные элементы распределены равномерно, так же, как и у контрольной группы. Дифференцировка паренхимы на корковое и мозговое вещества в

условиях опыта происходит лишь к концу IV этапа, т.е. на 7 сутки жизни, в то время как в контрольной группе – у 5 суточных крысят. Выявлены запаздывание дифференцировки выстилки синусов и задержка формирования ретикулярной стромы узлов.

Выводы: 1. Проведенные исследования позволяют лучше понять закономерности строения и развития органов иммуногенеза, позволяя стандартизировать морфологические данные в процессе физиологического онтогенеза, а также онтогенеза в условиях гипоксии.

2. Полученные данные могут быть использованы морфологами, иммунологами, патологоанатомами, судмедэкспертами для оценки состояния периферических лимфоидных органов при воздействии на организм различных экстремальных дестабилизирующих факторов.

3. Полученные морфологические данные являются теоретическим обоснованием для своевременного начала иммунопрофилактических мероприятий у плодов и новорожденных, страдающих хронической внутриутробной гипоксией.

POST-COVID 19 ENCEPHALITIS IN PATIENT WITH DE NOVO MUTATION IN THE SCN1A GENE, A CASE REPORT

Nonkulovski Danilo[1], Duma Filip[1], Alili-Ademi Learta[1],Sofijanova Aspazija[1], Muaremoska-Kanzoska Ljelja[1], Zhivkovska Liljana[1], Koskarova Malinkova Elena[1]

[1]University Clinic for pediatric diseases, Department of neurology, Skopje, North Macedonia

Email: dr.learta.alili@gmail.com

ABSTRACT

Seizures are defined as a transient occurrence of signs and symptoms due to an abnormal, excessive or synchronous neuronal activity in the brain, characterized by abrupt and involuntary skeletal muscle activity. The presence of cephalgic syndrome, infectious-toxic encephalopathy, hypo- and anosmia and ageusia are pathognomonic conditions in COVID-19 infected patients.

Post-Covid 19 encephalitis develops to encephalopathy in children with epilepsy. Based on the clinical appearance and the parameters that showed past Covid-19 infection, a diagnosis of post-COVID19 encephalopathy was confirmed. To confirm the diagnosis, clinical examinations, MRI of the brain, electroencephalography, lumbar puncture, laboratory tests (including CBC, CRP, basic metabolic panel, liver panel, hemostasis with D-dimer) are necessary. Based on the brain changes registered on the EEG record, the physical findings and the presence of SARS CoV 2 IgG antibodies, it was concluded that a child with an initial diagnosis of epilepsy, developed encephalopathy after asymptomatic COVID 19 infection.

Keywords: Post-COVID19 complications, encephalitis, Dravet syndrome, epilepsy, de novo mutation, children

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BARIATRIC SURGERY INDUCED WEIGHT LOSS RELATION TO PERIPHERAL NEUROPATHY BY SUDOSCAN: CLINICAL CASE STUDY

[1]**Ana Kopaleishvili**, MD, [2]**Ramaz Kurashvili**, MD, PhD, Prof., [3]**Tinatin Akhobadze**, MD, PhD, [4]**Tamar Maghradze**, MD, [5]**Elena Shelestova**, DN, CD

[1,2,3,4]DiabArgo, Millenium University, [3]National Center for Diabetes Research,Georgia

Objective: Obesity is a risk factor for peripheral neuropathy(PN). PN is found in subjects with diabetes, pre-diabetes and metabolic syndrome. Bariatric surgery (BS), a most successful obesity treatment, results in stable weight loss (WL). Though, BS impact on PN is unknown.
A**im:** To investigate impact of WL on PN in type 2 diabetes (T2DM) post-BS by Sudoscan.
Methods: Male, 51yrs, diabetes duration 8yrs**;** pre-operative examination results: weight-145kg, BMI-42kg/m², HbA1c-10.2%, T/A -150/90mmHg (on ACE/Amlodipine); vitamins D/B12 –within the normal range. Patient was on intensive insulin therapy (sol. Glulisine, short-acting insulin/SAI+ sol.Glargine, long-acting insulin/LAI): LAI - 24 IU/at bedtime; SAI-12x12x12 IU/ before main meals. Neuropathy tests/BNT(monofilament, tip-term, vibration tests) were moderately positive; Sudoscan revealed moderate PN (scores 50 feet/48 hands).Diagnosis: T2DM, diabetic neuropathy, obesity class III, AH II. Treatment: BS (sleeve-gastrectomy) was performed; post-operatively - dietary therapy, multivitamins, calcium citrate, iron, vitamins D/B12.
Results: Post-operatively WL and glycemic profile improved, insulin doses gradually reduced, finally insulin/antihypertensive therapy were stopped. Post-operative examinations (month 3): HbA1c-6.7%, BMI-33.2kg/m², T/A -130/80 mmHg; no symptoms of high ABP and/or hyperglycemia. Neuropathic complains/test scores improved: BNT- weak positive; by Sudoscan – moderate neuropathy (scores 55 feet/50 hands). Vitamins D/B12 and ionized calcium - within normal range. High physical activity. Dietary therapy/physical activity continued. Examination results (month 6): HbA1c-5.9%, BMI-28.9kg/m², T/A - 120/70 mmHg. BNT results - weak positive; by Sudoscan- moderate neuropathy (scores 68 feet/56 hands).Treatment: dietary therapy, physical activity, calcium citrate, vitamins D/B12, multivitamins. Examination results (month 12): HbA1c-5.4%, BMI-26.5kg/m², T/A -125/70 mmHg; general condition - satisfactory, mood/motivation – high; no PN symptoms; WL continued. BNT - near normal; no neuropathy by Sudoscan (scores 75 feet/68 hands).
Conclusion: Our studyshows positive impact of WL on glycemia control, ABP and PN. Some research data indicate positive effect of WL on diabetic/non-diabetic PN. Further studies are required to approve these findings.
Keywords: obesity, peripheral neuropathy, diabetes mellitus, bariatric surgery, weight loss

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INSULIN THERAPY IN PATIENTS WITH BREAST CANCER

[1]Ramaz Kurashvili, [2]Maia Nishnianidze, [3]Gia Nemsadze
[1]National Center for Diabetes Research, DiabArgo, Millenium University; MD, PhD, Prof.
[2]National Center for Diabetes Research, Institute of Clinical Oncology; MD
[3]Institute of Clinical Oncology, MD, PhD, Prof., Georgia

Background: Diabetes Mellitus (DM) - chronic progressive disease, associated with short-/long-term complications. Relation between DM and malignancies (OD) was revealed in 1930-ies. According to ADA 8-18% of onco-patients have DM. Women with T2DM have statistically increased risk of breast cancer (BC); their mortality due to malignancy is significantly higher than in women without DM. Hyperglycemia/hypoglycemia and glycemia variability are associated with progression, poor prognosis and outcomes of OD.
Objectives: To achieve long and stable normal or close-to-normal glycemia using new generation ultra-long acting insulin analogue Degludec (ULAIA), and study its effect on outcomes in OD patients with T1, T2 and steroid-induced DM (SIDM) on chemotherapy

Methods: Totally, 108 women with BC and T1DM, T2DM, SIDM were enrolled in the study. All women were receiving chemotherapy. Patients' mean age - 58±6yrs, BMI– 31 ± 4.1kg/m² , HbA1c – 9.8± 4.5%. Ketonuria and glucosuria were registered in 89% of patients. Treatment: At admission T2DM patients were on combination therapy (oral hypoglycemic agents+basal insulin); T1DM patients were receiving short-acting and basal insulin. In all patients basal insulin was replaced by ULAIA. In SIDM treatment was initiated with ULAIA. Insulin doses were titrated individually.
Results: One month post-ULAIA initiation reduction in HbA1c, glycemia normalization and minimal glucose variability were observed in all patients. Patients reported of improved general condition**.** Two month post-ULAIA initiation both objective/subjective indices were improved: HbA1C – 7.3±1.2%, better general condition/quality of life, readiness to continue chemotherapy. Patients on Degludec practically had no hypoglycemia episodes and glucose variability was low.
Conclusion: Based on our results we may suggest that use of ULAIA in oncological patients significantly more effectively normalizes glycemia control than basal and short-acting insulins used previously. Stable good glycemia control leads to improvements in general condition, quality of life, that positively influenced the healing process and OD prognosis in these patients.
Keywords: type 2 diabetes mellitus, type 1 diabetes mellitus, steroid-induced diabetes mellitus, breast cancer, insulin therapy, new generation ultra long-acting insulin analogue.

EFFECT OF HYPERTRIGLYCERIDEMIA ON DIABETIC PERIPHERAL NEUROPATHY (DPN) DEVELOPMENTIN PATIENTS WITH TYPE 2 DIABETES MELLITUS IN GEORGIA

[1]Tamar Maghradze, [2]RamazKurashvili, [3]Liana Tsutskiridze, [4]Elena Shelestova
[1,2,4]National Center for Diabetes Research, [3]Tbilisi Heart Center, Georgia

Background: Diabetic peripheral neuropathy (DPN) is the widespread complications of type 2 diabetes (T2DM) that leads to foot ulcer, gangrene or amputation. The risk of developing DPN increases with age, diabetes duration and poor glycemia control. About 60% to 70% of all people with diabetes will develop DPN. Hypertiglyceridemia is a typical lipid disorder in patients with poorly controlled DM.
Objective of this study was to assess the effect of hypertiglyceridemia on DPN in Georgian patients with T2DM.
Methods: Sixty two T2DM patients with DPN (49 men/45 women) comprised Study Group/SG, their mean age was 56±7yrs, diabetes duration -5 to 10yrs. All SG patients had hypertiglyceridemia. Fifty age, sex and diabetes duration matched patients without DPN and with normal triglyceride level were used as controls (CG). HbA1c in SG and CG was 8,1±1,2% and 7,7±1,1%, respectively. According to current Recommendations DPN was assessed using following battery of neuropathy tests (BNT): 10-g monofilament test, tip-term/temperature test, vibration test with 128-Hz tuning fork, prick tests; neurological examination with Sudoscan was also performed (method for non-invasive assessment of small fiber function, Impeto Medical,France). Results of BNT in SG were positive, and Sudoscan revealed presence of small fiber neuropathy. In CG patients BNT were negative, while Sudoscan revealed small fiber damage. Association between hypertiglyceridemia and DPN was assessed: SG patients had elevated serum triglycerides levels (STR) (mean STG 299± 45mg/dl in SG vs 100±20mg/dl in CG).

Results: Data received showed that DPN in SG comprised 65,9% (62cases). TG concentration was significantly higher in patients with DPN, than without DPN and normal TG levels (P=0,005). Elevated STR were associated with DPN (p<0,044).
Discussion: This study shows that increased levels of STR may play important clinical role in development of DPN in T2DM patients in Georgia. The problem needs further investigation with other important parameters included.
Keywords: Diabetes Mellitus, Diabetic Peripheral Neuropathy, Hypertiglyceridemia, Battery of Neuropathy Tests, Sudoscan, Georgian Patients with Type 2 Diabetes

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PARASITIC PLANTS OF THE GENUS CUSCUTA IN GEORGIAN MEDICAL LITERATURE

Nino Qurashvili[1], Medea Chikava[2], Nodar Sulashvili[3]
[1]Professor, Department of Pharmacy, University of Georgia, Tbilisi, Georgia, Email: n.qurashvili@ug.edu.ge
[2]Professor, Department of Pharmacy, Georgian Technical University, Tbilisi, Georgia, Email: medeachikava@gmail.com
[3]Professor, Department of Pharmacy, The Millennium University, Email: n.sulashvili@ug.edu.ge

ABSTRACT

Objective: to collect and analyze literature data on parasitic plant Cuscuta that has been used in Georgian folk medicine for centuries.
Methods: The material of the article was literature data which were processed by methods of generalization and systematization.
Results: *Cuscuta* L, commonly known as dodder, is a genus of over 201 species of yellow, orange, or red (rarely green) parasitic plants. *Cuscuta* species C. europaea, C. arvensis, and C.epithymum are widely spread across Georgia that is confirmed by its different names according to regions of Georgia: in Kakheti it was called Saponela, Gvelis Becheda, Sapovnela, Kapuna, Tkapuna; Tusheti – Gvelismdziva; Meskheti – Gablandula; Racha – Gvelivenakhi, Butsava; Lechkhumi – gvelidzafa, etc. [1]. According to Botanical Dictionary, its name is Abreshuma and finally, in ancient Georgian Medical handbooks it was mentioned as Aptimoni and Iarsachi [7].
Aptimoni was first mentioned as a medical remedy in XI century Georgian medical handbook "Ustsoro (Incomparable) Karabadini"[2]. In combination with other herbs, Aptimoni was successfully used for treating severe headaches caused by neurological disorders or sometimes, by fasting, healing herpes virus (pesumably, *simplex*), and liver disorders [3].
Saponela,one of the names of Cuscuta, is stemmed from its foaming property due to saponins contained in the plant. For this property, it has been used as a soap and a face and hands whitener [2].
As mentioned in the 15th century compendia of medical arts, Karabadini, by well-known Georgian healer, Zaza Panaskerteli-Tsitsishvili, Aptimoni was used for treatment of neurological and psychic disorders as well as for treatment of melancholy, liver failure, face freckles and psilosis. It was successfully used in the treatment of gout [5]. For its cathartic property, Aptimoni is one of the ingredients of Kuskutina, a cathartic medicine [4].
Aptimoni in a medical herb blend has been used for treatment of chronic pyelonephritis and urinary tract inflammationsas well [6].

Conclusion: Cuscuta has successfully been used for healing various diseases for many centuries. However, due to unknown reasons, its use has been ceased. Renewing research on this unique plant, in our opinion, would open new opportunities to use well tested natural remedies in medicine.
Keywords: Cuscuta, Aptimoni, Kapura, Saponela, Folk medicine, Medical Handbooks.

ОСОБЕННОСТИ НЕПСИХОТИЧЕСКИХ ПСИХИЧЕСКИХ РАССТРОЙСТВ У БЕРЕМЕННЫХ

Вагабова Шарифа[1], Асадова шафаг[1], Асадов Билал[2], Аббасова Фарида[1], Амирасланова Шефа[1]
[1]Кафедра акушерства и гинекологии, АМУ , [2]Кафедра психиатрии АМУ.
Emails: [1]s_vahabova@mail.ru, [1]shefeg.asadova@gmail.com, [2]bilal_44@mail.ru

Актуальность проблемы: Высокий уровень цивилизации, интенсивность производственных процессов, усиливающийся поток информации сказываются на всех областях деятельности человека. Известно, что даже физиологически протекающая беременность оказывает определенное влияние на психику женщины, а некоторые авторы рассматривают ее даже как кризисную ситуацию [1, 2]. Описаны психологические реакции при физиологическом течении беременности. Некоторые беременные особенно уязвимы для воздействия психо-травмирующнх факторов, причем вследствие переоценки прежней системы отношений наблюдается психотравматизация теми конфликтными ситуациями, которые в прошлом не были для нее актуальными. До настоящего времени отсутствуют сведения о влиянии различных факторов на развитие непсихотических расстройств в генерационный период, о динамике развития психических заболеваний в различные триместры беременности. Недостаточно разработана систематизация нозологических и донозологи-ческих психопатологических состояний у данного контингента. Беремен-ность является особым этапом в жизни женщины, во время которого формируются бинарные образования "мать-плод". Особенно уязвимым в данной системе является нейрогуморальное звено [3, 4]. В этот период психосоматическое состояние женщины неразрывно связано с потенциальным здоровьем ребенка.
Как показывают эпидемиологические исследования, женщины подвержены депрессиям в 2 раза чаще, чем мужчины. Поэтому не удивительно, что депрессия является частым осложнением во время беременности и в послеродовом периоде. Различные психические нарушения встречаются в 29–80% случаев от общего количества родов. Однако есть точка зрения, что нормально протекающие беременность и роды могут оказывать положительное влияние и даже купировать некоторые проявления преморбидно существующих симптомов. Многие исследователи полагают, что беременность и роды могут стать провоцирующими факторами в развитии уже имеющихся скрытых нарушений [5, 6].
Цель и задачи исследования: Целью работы является изучение различных психических расстройств , возникающих у беременных при нормальном течении беременности.
Методы исследования: Анкетирование (опрос), пихометрическая шкала депрессии Hamiltonun-a [HADS], шкала депрессии Бека, шкала тревои Spilberqer-a.
Результаты исследования и обсуждение: В связи с поставленной целью исследования нами было обследовано 100 беременных женщин с нормально протекающей беременностью. Были изучены различные демографические показатели: возраст, образование, длительность замужества, условия жизни, социальный статус.

При исследовании возраста беременных было установлено, что наибольшее числ о составили беременные в возрасте 20-25 (23,0%) и 26-30 (33,0 %) лет (табл. 1). Это указывает на тот факт, что данный возрастной диапазон совпадает с наиболее репродуктивным периодом женщины, о чем свидетельствует малое число беременных в возрасте до 20 и 36-40 лет.

Факторы риска: Остается до конца не ясным, почему во время беременности некоторые женщины становятся подвержены невротическим расстройствам и депрессиям. Возможные этиологические факторы могут взаимодействовать друг с другом. К ним относятся гормональные сдвиги, нейроэндокринные и психосоциальные изменения. Систематический обзор 57 исследований (из 1361 предварительно отобранных) выявил строгую доказательность для следующих факторов: стресс, негативные события жизни; отсутствие социальной поддержки; домашнее насилие. Другие факторы риска с меньшим уровнем доказательности: депрессии, которые предшествовали беременности; нежеланная беременность; низкий уровень дохода; низкий уровень образования; курение; незамужний статус; сложный уровень взаимоотношений; отсутствие социальных гарантий; дородовые и послеродовые депрессии в личном или семейном анамнезе; прекращение лечения или уменьшение доз антидепрессантов во время беременности. Сам факт возникновения беременности создает определенные психологические проблемы. При изучении эмоционального реагирования женщин в динамике физиологической беременности был обнаружен возрастающий по мере роста срока беременности уровень личностной тревожности. Некоторые исследователи [1, 4, 6], основываясь на представлении о физиологических рамках, границы которых определены “гомеостатической целесообразностью”, а именно рождением здорового потомства, рассматривают тревогу при беременности как процесс адаптивный, т. е. физиологически необходимый. Совсем другое дело, когда речь идет о тревожных синдромах, достигающих уровня психического расстройства. Как правило, панические, генерализованные тревожные, обсессивно-компульсивные расстройства обнаруживают коморбидность с депрессивными расстройствами у беременных женщин.

Заключение: Высокая распространенность невротических и депрессивных расстройств у беременных свидетельствуют о необходимости проводить скрининг расстройств настроения во время беременности для своевременного применения стратегий профилактики, чтобы свести к минимуму заболеваемость и смертность, ассоциированные с перинатальными психическими расстройствами. Ведение беременных женщин с невротическими расстройствами и расстройствами настроения, которые ранее не принимали психотропные препараты, должно начинаться с психотерапии с использованием интерперсональных и когнитивно-поведенческих техник. При проведении когнитивно-поведенческой психотерапии пациенты изучают, как их мысли влияют на клиническую картину болезни и как следует позитивно изменить свое мышление. Все это сопровождается использованием соответствующих поведенческих техник. Данный вид психотерапии очень полезен как для беременных женщин, так и для женщин, уже родивших детей. В фокусе интерперсональной психотерапии находится подготовка женщины к ее новой роли матери. Женщина узнает новую информацию о развитии ребенка, уходе за ним, важная роль отводится образовательным программам, касающимся возникновения депрессивных расстройств во время беременности и в послеродовом периоде. Проведение интерперсональной психотерапии достоверно улучшает эмоциональное состояние женщин и взаимоотношения между матерями и их новорожденными детьми. Групповая психотерапия также эффективна

для уменьшения депрессивных расстройств у беременных и родивших женщин. Поскольку семейные проблемы часто являются причиной депрессивных расстройств, даже чаще, чем собственно перинатальные расстройства настроения, возрастает роль семейной психотерапии. Стабильные внутрисемейные взаимоотношения позволяют семейной паре наилучшим образом адаптироваться к новым условиям и проблемам, которые создает рождение ребенка. Нарушенные внутрисемейные взаимоотношения являются одним из психологических предикторов перинатальной депрессии и тревоги. Проведение семейной психотерапии, которая позволяет решать самые интимные проблемы женщины, включая проблему домашнего насилия, вносит неоценимый вклад в лечение расстройств настроения у данной категории больных. Наряду с этим необходимо разработать и внедрить психогигиеническую службу для беременных, направленную как на профилактику, так и лечение психических расстройств непсихотического уровня в различные сроки беременности.

ХАРАКТЕРИСТИКА ЭХОГРАФИЧЕСКИХ ПОКАЗАТЕЛЕЙ ШЕЙКИ МАТКИ У БЕРЕМЕННЫХ С ИСТМИКО-ЦЕРВИКАЛЬНОЙ НЕДОСТАТОЧНОСТЬЮ

Шарифа Вагабова, Шафаг Асадова, Фарида Аббасова, Шефа Амирасланова
Кафедра акушерства и гинекологии I Азербайджанского Медицинского Университета
Emails: [1]s_vahabova@mail.ru, [2]shefeg.asadova@gmail.com

Цель исследования: Определение клинических и эхографических критериев ИЦН.
Материал и методы исследования: Обследовано 50 беременных с отягощенным акушерским анамнезом. Средний возраст обследованных женщин составил 26,08±0,52 лет и колебался в пределах от 19 до 40 лет. Проведен сбор анамнестических сведений, включающий перенесенные ранее заболевания, возраст менархе, среднее число предыдущих беременностей, гинекологический анамнез. Всем беременным, с предполагаемой ИЦН, проводили тщательное клиническое обследование, включая бимануальное исследование и осмотр шейки матки в зеркалах, определение степени чистоты влагалища. С ранних сроков беременности проводилось ультразвуковое исследование вагинальным датчиком. При обследовании беременных диагностику ИЦН проводили по шкале Штейнберга (Shteynberq). При этом оценивались. длина влагалищной части шейки матки, проходимость цервикального канала, расположение и консистенция шейки матки.
Результаты исследования: При проведении настоящего исследования была изучена частота субъективных ощущений, наблюдаемых у беременных с ИЦН, которые проявлялись чувством страха за исход беременности, слизистыми выделениями из влагалища, тянущими болями в пояснице и надлобковой области. У 64% беременных отмечалось укорочение шейки матки, у 36% длина шейки матки была менее 1,5 см. Исследование состояния цервикального канала позволило выявить у 76% беременных частичную проходимость цервикального канала, у 16% - проходимость цервикального канала на 1 палец. Только у 8% беременных наружный зев цервикального канала был закрыт. Для достаточно четкой диагностики ИЦН мы считаем важным неоднократное проведение оценки состояния шейки матки по шкале Штейнберга, в динамике беременности. В результате проведенного исследования было установлено, что у беременных с ИЦН средний показатель оценки состояния шейки матки по шкале Штейнберга 6,0±0,8 (5,0-8,0) баллов. Нашими исследованиями подтверждено, что УЗИ вагинальным датчиком является достаточно

информативным скрининговым методом диагностики ИЦН. Данный метод исследования позволяет наиболее точно определить длину влагалищной части шейки матки, проходимость цервикального канала, расположение шейки матки. Увеличение проходимости цервикального канала более 1 см создает реальную угрозу прерывания беременности и является показанием для проведения неотложной коррекции ИЦН: применения разгружающего акушерского пессария. Всем 50 беременным с ИЦН был применен акушерский разгружающий пессарий, применение которого является неинвазивным, эффективным средством коррекции недостаточности шейки матки, которое можно применять в амбулаторных условиях. Применение пессария позволило продлить срок беременности в среднем до 37,42±0,19 (34-39) недель.

Заключение: Клинико-эхографическое исследование состояния шейки матки позволило выявить, что наиболее оптимальным сроком проведения коррекции истмико-цервикальной недостаточности методом применения влагалищного разгружающего пессария является 12-15 недель беременности, что, по нашему мнению, существенно повлияет на благополучный исход беременности, состояние плода и новорожденного.

Ключевые слова: истмико-цервикальная недостаточность, шкала Штейнберга, акушерский пессарий, шейка матки, беременность, ультрасонические параметры шейки матки.

AORTIC VALVE NEOCUSPIDIZATION WITH GLUTARALDEHYDE-TREATED AUTOLOGOUS PERICARDIUM (OZAKI PROCEDURE) IN GEORGIA, 5 YEARS OF EXPERIENCE,CASE STUDIES

[1]Gyorgy Bokeria, [2]Zviad Bakhutashvili
[1]Chapidze Emergency Cardiology Center, 5-year Medical student, Ivane Javakhishvili Tbilisi State University, Email: [1]Giorgibokeria24@gmail.com
[2]Head of cardiac surgery at Chapidze Emergency Cardiology Center, Prof. MD. PhD. Ivane Javakhishvili Tbilisi State University.

ABSTRACT

Objective: We would like to report in this great conference, the 5 years experience of aortic valve reconstruction with autologous pericardium using Ozaki's procedure in Georgia performed in our clinic by head of surgical department Zviad Bakhutashvili. The study included consecutive patients with isolated aortic valve disease who underwent Ozaki's procedure in our hospital between June 2016 and August 2021.

Aortic valve disease is the most common cause of cardiovascular death in nations. Surgical aortic valve (AV) interventions for Rheumatic and infective Valve Disease , especially in adult and children, have proven problematic with graft failure, relapse, and poor compliance with anticoagulation. A novel technique involving neocuspidization of the aortic annulus using autologous pericardium to construct new AV leaflets (the Ozaki procedure) has shown promising outcomes in young adult and children. Aortic valve infective endocarditis with annular abscess is associated with high mortality rate and surgery is usually the choice of treatment. Plasty or reconstruction of aortic valve is being performed more widely.

In this case studies, aortic valve neocuspidization (AVNeo) has emerged as another option, which can be applied to a wide spectrum of aortic valve diseases. Despite the promising results, this

procedure is not widely spread among cardiac surgeons yet. Spurred on by the last publications, we went on to write an overview of the current practice of state-of-the-art AVNeo and its results.

Methods: Discussion and Description: Demographic Data: Number of Patients 101; Age-57.7 ± 9.3(18-78); Height-167.7 ± 7.9; Kg-81.1 ± 12.3; M/F- 52/41; NYHA- 2.7 ± 0.9;

PREOPERATIVE ECHOCARDIOGRAPHY RESULTS: Mean grad.(mm hg.)- 51.9 ± 7.1; Effective Valve Area (cm2)- 0.78 ± 0.12; EF (%)-53.9 ± 7.8; LVEDD (cm)- 5.04 ± 0.52;

Pahtology: Total: 101; (Stenosis-63; Regurgitation-7; Stenoregurgitation -31;)

Types of Aortic Valve: Tricuspid AV-73; Bicuspid AV-26; Unicuspid AV-2;

Types of Surgical Intervention:Only AVNeo-56; AVNeo+CABG-24; AVNeo + Asc.Ao+ CABG -1; AVNeo+MVPL- 9; AVNeo+CABG+MVPL-2; AVNeo+Asc.Ao-7; AVNeo+ Congenital-2;

Intraoperative Data: Cross clump time (min)- 114 ± 15.2; ECC (min)- 141 ± 20; Re Cross clump-3;

Postoperative Data: EF (%)-56.8 ± 2.5; Mean grad.(mm hg)- 5.3 ± 2.6; EROA-0.04 ± 0.04; NYHA-1.1; P/o. Blood loss (ml)- 410; REDO-2 (in 13months); Mean Follow-up (month)- 28.0 (63-2); Hospital mortality-2.15 % (2).

Results: Therefore AVNeo is good choice especially for:Patients with narrow annulus;Female patients with child-bearing age.Younger patients who cannot or don't want to take anticoagulation, Infective Endocarditis,also Patients who are indicated for Ross procedure and Patients who don't want prosthesis.

You are not dependent on valve manufacturing companies and distributors (price, quality, size); No antico-agulation; No gradient;No regurgitation, it's Reproducible procedure;Optimized cross clamp time;Cost efficient – only sizers and glutaraldehyde solution are needed.Lack of immune response.Method of choice in patients with bacterial endocarditis.The best in patients with small aortic root,No clicking noise, as mechanical valve and Easy to redo.

Necessity to have decellularised pericardium in case of: (Redo;Adhesive Pericarditis;Median pericardiotomy is already done).Longer ECC and cross clamp time than AVR;Preferably for experienced surgeons;For non-tricuspid AV relatively complicated;When planning AVNeo surgery it is obligate to pay more attention to the age and multi-cardiac disease patients;

Conclusions: Our cases are the first reported experience for our country of homograft use to treat aortic valve disease after Ozaki procedure in the Georgia.We hope these results and cases will initiate many clinic to use that procedure and establish it,because based on much researches,clinical experiences, even in our country we can truly say, that Ozaki's Procedure is the golden standart treatment method in younger patients with narrow aortic ring. AVNeo is a safe and effective method for an infective aortic valve replacement with good short and midterm results.AVNeo also could be considered for aortic root abscesses as an alternative to allograft; low gradient is a positive point in the recovery of stressed myocardium.No necessity to use warfarin makes patient's postoperative life safer and better and cuts off the hospital days.

An autologous pericardium fixed in glutaraldehyde can be infected as easily as a bioprosthetic valve, but the risk is less than a synthetic sewing cuff.Infective endocarditis has a poor prognosis when the prosthetic valve is infected. Considering prosthetic valve infection and redo operation, AVNeo may be considered among young patients.The advantage of AVNeo is no sewing cuff, which makes redo operation easier.

Keywords: Avneo, Aortic Valve, Ozaki procedure, Anticoagualtion, Ascending aorta, replacement.

ARTISTIC GYMNASTICS AND SCOLIOSIS

[1]Ketevan Gotsiridze, [2]Maia Kakauridze, [1]Iamze Taboridze
[1]MD, PhD student, David Aghmashenebeli University of Georgia, Georgia.
Email: k.gotsiridze1989@gmail.com
[2]MD, PhD,Gudushauri Clinic, Georgia
[1]PhD, Professor, David Aghmashenebeli University of Georgia, Georgia.

ABSTRACT

The impact of physical and sport activity (PSA) on idiopathic scoliosis (IS) is still unclear. In addition to genetic factors, environmental and lifestyle factors are thought to play an important role in the onset of adult idiopathic scoliosis (AIS).
The aim of our study was to determine the impact of artistic gymnastics in the development of scoliosis
Methods: We studied 25 fit girls with scoliosis.
Research methods: anamnesis, physical examination, genealogical analysis, radiography.
Since gymnastics is not considered as IS therapy or a prognostic factor, the observed frequency may be related to a common factor that increases the likelihood of IS and promotes gymnastics. Joint hypermobility may be such a common factor.
Hypermobility of the joints was determined by the Carter-Wilkinson test. Most people engaged in artistic gymnastics were diagnosed with one or more orthopedic diseases, including the prevalence of tandem disorders.
Results: The average age of onset of exercise in the adolescent gymnasts we studied is 6.32 + 2.06. Among the orthopedic diseases we have identified is scoliosis, the age of manifestation of which varies from 5 to 15 years (9.31 + 4.05).
Scoliosis was observed in 13 (52%) gymnasts, of which 12 (48%) were idiopathic and 1 (4%) was dysplastic.
8 (32%) unstable, 5 (20%) stable. With 3 (12%) non-progressive and 10 (40%) progressive currents.
According to the shape of the curvature - C-like (with one curve) - 4 (16%), S-like (with two curves) - 8 - 32%, □-like (with three curves) - 1 (4%).
Risk factors include genetic factors such as scoliosis (52%) and other orthopedic diseases (up to 60%) in first-degree relatives.
Joint hypermobility was diagnosed in 36% of the patients examined.
Conclusions: Among girls who go to artistic gymnastics, a high incidence of scoliosis is noted.
Risk factors include genetic predisposition and joint hypermobility.
Keywords: Artistic Gymnastics, Joint hypermobility, scoliosis.

MULTIMODAL ANESTHESIA IS THE PREVENTION OF POSTOPERATIVE CHRONIC PAIN

[1]Ketevan Arabidze, [2]Irakli Gogokhia, [3]Nodar Lebanidze
[1]MD, PhD Student, David Aghmashenebeli University of Georgia,
Email: keti_arabidze@yahoo.com
[2]Irakli Gogokhia, MD, American Hospital Tbilisi
[3]Nodar Lebanidze MD, PhD, Professor, Ivane Javakhishvili Tbilisi State University.

Postoperative pain according to ICD 10 belongs to the category of unspecified pain. It arises directly at the site of injury (wound for surgical approach. I.e., tissue damage from the skin to the operative organ and surgical intervention performed on this organ). Tissue damage results in pain.The most cost-effective surgical intervention is related to the damage of both nerve fibers and other tissues. Damage to non-nervous tissues causes nociceptive, while damage to nerve fibers causes neuropathic pain. Any surgical intervention causes severe nociceptive and neuropathic pain.Data on the prevalence of chronic pain vary from 10% to 30%. [1] is 31% in abdominal surgery. [2] If we imagine the severity of this complication and the level of quality of life associated with it, its biological and social significance becomes clear.

The criteria for diagnosing chronic postoperative pain were first provided by Macrae and Davies in 1999 [3] and adjusted in 2014 by Werner and Kongsgaard to improve the diagnosis. They were considered to be the main diagnostic signs of chronic postoperative pain 1. Development or intensification of pain after surgery; 2. Pain affects quality of life and lasts for at least 3-6 months 3. Chronic postoperative pain is a continuation of acute postoperative pain or develops after an asymptomatic period 4. Pain is localized in the area of operation, is projected in the area of innervation of the nerve in the area of operation or is irradiated 5. Other causes of pain must be ruled out All patients were examined by us according to these criteria.

Prevention of chronic postoperative pain requires analysis of existing risk factors and their impact. Severe pain within 24 hours after surgery is considered a risk factor for developing postoperative chronic pain. The duration and intensity of postoperative pain contribute to its chronicity. [5] We use non-opioid analgesics in the postoperative period to maximally block perioperative pain.

Any surgical intervention related to tissue damage. Non-neural tissue damage causes nociceptive, while nerve fiber damage causes neuropathic pain. Minimal surgical intervention leads to nociceptive and neuropathic pain. The magnitude of the resulting pathological impulses is proportional to the intensity of the pain. [6] To block such a strong irritant we use a medicated reduction in impulse flow.

The patient's psych emotional condition is a risk factor for pain. Preoperative depression and post-traumatic stress are prerequisites for the onset and intensification of postoperative pain [7] Preoperative use of opioids increases the chronicity of pain by 25%, [8]. We provide appropriate premedication with non-opioid medications. while their postoperative use leads to mood swings and fear.

Our multimodal analgesic technique according to the mechanism of development of chronic postoperative pain provides prevention of acute pain chronicity at all levels. We examined 112 patients after surgery.All cases, more than 3 months had elapsed since the operation. Of these, 74 were partial opioids, where the amount of fentanyl was reduced by 10-fold, while other opioids were not used (opioids were reduced by more than 90%). 38 patients underwent multimodal opioid-free pain relief.

No pain was observed from the examined patients 101; None had constant or recurrent pain; 11 patients had a single pain that was not related to the surgery performed. The pain passed without interference to 7; 3 even needed to take painkillers.

The maximum duration of pain was 48 hours. None of the patients referred to the medical facility. None of the 112 patients we surveyed thus had chronic postoperative pain. Multimodal analgesia is the most reliable prevention of postoperative pain chronicity.

Keywords: non-nervous tissues, chronic postoperative pain.

The Sixth International Scientific – Practical Virtual Conference in Modern Medicine and Health: Prognosis, Achievement and Challenges

RELATIONSHIP BETWEEN SOCIO-ECONOMIC FACTORS AND STUDENT MORBIDITY

[1]Tamar Sultanishvili, [2]Ramaz Khetsuriani, [3]Ilona Sakvarelidze, [2]Manana Arabuli, [3]Nino Abaishvili, [4]Shalva Petriashvili

[1]MD, PhD student, David Aghmashenebeli University of Georgia, Email: tsultanishvili@yahoo.com
[2]MD. PhD, professor, Tbilisi State Medical University.
[3]MD, PhD, professor, [3]Tbilisi Humanitarian Teaching University.
[2]Associate professor, Tbilisi State Medical University.
[3]MD. PhD, Associate professor, Tbilisi Humanitarian Teaching University.
[4]MD. PhD, Professor, East-West Teaching University.

ABSTRACT

University students are the future social-economic, intellectual, creative potential of the country. Their frequent illness leads to a decrease in the effectiveness of learning and subsequent interference with professional activities. The problem of student health is particularly acute in the current difficult social and economic conditions.

Students' social-demographic characteristics, stressors experience, psychological symptoms, and mental and general health ratings are related to their academic achievement. Thus it is important to establish morbidity predictions among students, of which the socio-economic status and education of the family play an important role.

The aim of the study is to establish a link between socio-economic status and morbidity.

Methods: 766 Georgian students, aged 15 to 35 (20.7±2.4) have been interviewed from Universities of Georgia, among them 347 men and 419 women. The cross-sectional study was performed, using the questionnaire form, created by us.

Universities and students were randomly selected.

Inclusion criteria: A student of Georgian universities, a citizen of Georgia, Consent on participation in the trial. Exclusion criteria: pregnant women, Refusal to participate in the study.

Statistical analysis: Qualitative data are shown in the form of quantity and percentage. Correlation analysis – by means of Spearman's ranking correlation.

The statistical analysis was performed using software package SPSS 23

Results: Among the respodents Female are unreliably predominant, 56% of students are employed, the majority of them - for paid work.

Almost half of the students live with their families and parents, most of them - 48% are from Tbilisi, the frequency in other regions varies from 2% to 4%.

Diseases identified during student life correlate with the following socio-economic characteristics of the family:

Shows a positive correlation with pathologies of the gastrointestinal tract: socially vulnerable - r=0.050, p=0.164; Single mother - r=0 .075 *, p=0.038; Divorced parents - r=0.154 **, p<0.001; Negative - higher education of parents: r=-0.107 **, p=0.003;

Shows a positive positive correlation with cardiovascular diseases: socially vulnerable family - r=0.103 **, p=0.004; Single mother - r=0.100 **, p=0.006; Negative - higher education of parents - r=-0. 113 **, p=0.002;

Abrupt weight loss correlates with socially vulnerable status - r=0.078 *; p=0.031.

Nervous system disorders are negatively correlated with parents's higher education r=-0.080 * p=0.028.
Shows a positive positive correlation with sexually transmitted diseases: high-income family - r=0.076 *; p=0.035, single mother - r=0.098 **; p=0.006, divorced parents - r=0.100 **; p=0.006; Negative - parents with higher education - r=-0.179 **, p<0.001.
Conclusion: Student illness is related to the social-economic characteristics of the family and the education of the parents.
Keywords: students' morbidity, social-economic factors.

THE USE ADIPOSE-DERIVED STEM CELLS (ADSCS) IN DISEASES OF THE SKIN AND IT'S MORPHO-PYSIOLOGICAL ASPECTS

M. Matoshvili, D. Tophuria, N. Adamia
Tbilisi State Medical University, Georgia.

Introduction: The Adipose-derived stem cells ADSCs are heterogeneous, no specific marker for them has been identified, and the location of stem cells in adipose tissue is difficult to determine. However, most of them occur in the perivascular regions. The morphology of ADSCs resemble fibroblasts, consisting of a large endoplasmic reticulum and nuclei. ADSCs do not have a specific marker and the expression of antigens is similar to bone marrow MSCs: CD10, CD13, CD29, CD34, CD44, CD54, CD71, CD49b, CD90, CD105, CD117, and STRO-1. However, they do not express the hematopoietic markers, such as CD14, CD16, CD31, CD45, CD56, CD61, CD62E, CD104, CD106, CD144, the endothelial cell markers CD31, CD144, and von Willebrand factor. Moreover, they are privileged cells with reduced immunogenicity; therefore, there is no expression of HLA-DR [1]. ADSCs may also be a precursor of chondrocytes, osteocytes, muscle cells, neurons, and fibroblasts as well as keratinocytes under proper conditions. However, their most important function is the stimulation of surrounding cells to differentiate into specialized cells under the influence of certain growth factors [2]. It has been shown that the ADSCs are even necessary for the activation of epidermal stem cells in the skin. Their exogenous administration mobilizes other stem cells, including the stem cells of the epidermis from the "bulge" region of the hair follicle. This action is based on the production of growth factors, including epidermal growth factor (EGF), fibroblast growth factor (FGF-β), hepatocyte growth factor (HGF), transforming growth factor (TGF-β), vascular endothelial growth factor (VEGF), keratinocyte growth factor (KGF), granulocyte-macrophage colony-stimulating factor (GM-CSF), stromal factor 1-alpha, and cytokines, such as IL-6, 8, 11, 12, and TGF-α. This paracrine secretion of cytokines explains their high concentrations in obese patients [3]. ADSCs also inhibit the production of proinflammatory cytokines, enhance the production of anti-inflammatory IL-10, and stimulate the regulatory T cells. They also stimulate angiogenesis by differentiation in endothelial cells. ADSCs can protect against apoptosis, which offers great opportunities for their use in regenerative medicine [4]. Expression of the receptor for PDGF and CD10 is constant, regardless of the number of passages. Traktuev et al. showed that cells with the CD34+/CD31 phenotype have the ability to stabilize the endothelial network in vitro and stabilize neovascularization in vivo. In addition, perivascular ADSCs (CD146+) also function as a niche for hematopoietic stem cells in vitro [5].
Methodology: Out of the particular interest is platelet-derived growth factor-D (PDGF-D), which is secreted by the ADSCs. It is a mitogen for mesenchymal cells, which induces the transformation of

cells and also accelerates tumor growth, but its role is not quite understood. Kim et al. showed that PDGF-D and PDGF receptor β are expressed in ADSCs, but PDGF-B is not. PDGF-D can increase the proliferation and migration of ADSCs for the generation of mitochondrial reactive oxygen species (MTRose) and by controlling mRNA expression of various growth factors (VEGF, FGF-1, FGF5, EGF, leukemia inhibitory factor, inhibin, and IL-11) [6]. ADSCs from this niche have ultrastructural features similar to primitive MSCs (large nucleus, immature cytoplasmic organelles). Although Rubio et al. reported that human ADSCs can undergo malignant transformation during long passages of more than four months, five years later, the authors were not able to reproduce the phenomenon of transformation, most likely due to contamination artifacts [7]. The ADSCs have an antioxidant effect. They can capture free radicals and heat shock protein in ischemia status. Research has revealed that during the aging processes and in diabetes, the function of ADSCs is impaired.

Vitamins can affect the proliferation of ADSCs. The addition of folic acid and vitamin B12 slightly increases their activity in cell culture, while vitamin C significantly stimulates ADSCs in a dose-dependent manner. Vitamin C increases the expression of the mRNA of HGF, VEGF, bFGF, and KGF. There are some differences in the physiological and biological features of ADSCs derived from different anatomical sites. Siciliano et al. compared the characteristics of stem cells from mediastinal fat and skin. Subcutaneous ADSCs demonstrated greater proliferation and differentiation capacity, an increased IL-6 secretion, and a smaller VEGF-C than ADSCs isolated from the mediastinum. ADSCs from the mediastinum showed a higher proangiogenic potential. On the other hand, ADSCs from the visceral fat have a reduced susceptibility to apoptosis, and ADSCs from the pericardium, omentum, and groin have a different phenotype. Excessive weight has an influence on the differentiation potential and immunogenicity of ADSCs. The study by Perez et al. demonstrated that stem cells derived from murine and human nonobese sources had increased sensitivity to insulin and can inhibit lipolysis during differentiation into mature adipocytes. In contrast, cells isolated from obese patients showed an impaired uptake of glucose, insulin resistance, and less antilipolytic effect of insulin. Moreover, they released a greater amount of proinflammatory cytokines (mainly TNF-α) and showed disturbances in the production of adiponectin [8].

Interestingly, the preferred factor for proliferation, migration, and differentiation of the ADSCs is hypoxia (an oxygen concentration of 1–5%). Hypoxia induces the expression of HIF-1α (hypoxia-inducible factor 1-α) and increases the production of growth factors, particularly VEGF, bFGF, and HGF which are involved in neovascularization . This phenomenon is observed in obesity. Local hypoxia in the adipose tissue induces the formation of free radicals (ROS) and leads to the secretion of growth factors which stimulate the formation of new blood vessels [9].

Pachon-Pena et al. have also found that obese-derived hADSCs demonstrate increased proliferation and migration capacity, but decreased lipid droplet accumulation, which is correlated with a higher expression of human leukocyte antigen- (HLA-) II, a cluster of CD106 differentiation, and a lower expression of CD29. Of interest, adipogenic differentiation modified CD106, CD49b, and HLA-ABC surface protein expression, which was dependent on the donor's BMI. Moreover, low oxygen tension increased proliferation and migration of lean but not obese hASCs, which was correlated with an altered CD36 and CD49b immunophenotypic profile [29]. Moreover, in obesity, ADSCs indicate changes in their transcriptomic profile (set of mRNA molecules present in a particular point of a cell) with a loss of plasticity, simultaneously showing an increasing similarity to the adipocyte phenotype [10].

Conclusions: Nowadays, ADSCs are used in aesthetic dermatology for skin rejuvenation, to correct wrinkles, to correct facial lipoatrophy, and even to improve erections. They are described in the

treatment of perianal fistulas in Crohn's disease, bone grafts, and type 1 diabetes. However, the therapeutic use of ADSCs is still experimental.

Keywords: ADSCs, CD10, CD13, CD29, CD34, CD44, CD54, CD71, CD49b, CD90, CD105, CD117, and STRO-1.

TREATMENT OF NON-HEALING SKIN WOUNDS WITH USAGE OF ADIPOSE-DERIVED STEM CELLS

M. Matoshvili, D. Tophuria
Tbilisi State Medical University, Georgia.

ABSTRACT

The promising results derived from the use of adipose-derived stem cells (ADSCs) in many diseases are a subject of observation in preclinical studies. ADSCs seem to be the ideal cell population for the use in regenerative medicine due to their easy isolation, nonimmunogenic properties, multipotential nature, possibilities for differentiation into various cell lines, and potential for angiogenesis. This article reviews the current data on the use of ADSCs in the treatment of non-healing of chronic wounds.

Introduction: Brown and white adipose tissue is a source of mesenchymal stem cells, specifically adipose-derived stem cells (ADSCs). It is an inexpensive, unlimited reservoir of stem cells. From 300 ml of adipose tissue, 2-3 × 108 ADSCs can be obtained. This is between 100 and 1000 times more than the mesenchymal stem cells from the bone marrow. In addition, they can be easily obtained with no ethical dilemmas pertaining to their use [1,2].

Methodology: Skin damage leads to debilitating effects forming wounds. A wound is defined as a disruption of the normal anatomic structure and functional integrity of the skin. Chronic or nonhealing wounds are wounds that do not progress through the normal wound healing process, resulting in an open laceration of varying degrees of severity [3]. Impaired healing is often associated with ischemia, diabetes mellitus, tumor, venous and pressure ulcers, and severe infections, and it can be the cause of reduced quality of life, disability, and even death. Therefore, wound healing remains a major challenge, and there is a need to develop treatments for improved therapy. Among the various strategies, the most promising seems to be the use of stem cells. This process remains a challenge to date and causes debilitating effects with tremendous suffering. Recent advances in tissue engineering approaches in the area of cell therapy have provided promising treatment options to meet the challenges of impaired skin wound healing [4].

The healing of the wound is a complex process, covering four mutually overlapping phases: hemostasis, inflammation, proliferation, and remodeling [5]. For the proper process to proceed, all steps must occur in the correct order and time. In many chronic wounds, the elongation inflammatory phase leads to the damage of normal tissues, the production of an excessive amount of proinflammatory cytokines, and the prolonged presence of neutrophils, which causes the degradation of the extracellular matrix (ECM) due to an increase in the secretion of matrix metalloproteinases (MMPs) [6]. The restoring the integrity of the skin involves several cell types, extracellular matrix components, and cytokines [7]. It is believed that what is physiologically responsible for the renewal of epidermal stem cells is located only in the basal layer of the epidermis. However, after damage to the skin, stem cells "bulge" in the region of the hair follicle and take additional responsibility for

skin regeneration, particularly in the initial stage [8]. Cell cultures enriched with stem and progenitor cells can be administered to patients via various methods: a direct application on the wound (e.g., as a suspension), injectable (arteriography), intravenous administration, or application of the culture on the appropriate biological scaffold. The most populous cells are the autologous progenitor cells of the epidermis. Current research is focused on bone marrow and adipose-derived stem cells being used in wound healing [9]. ADSCs are involved in the process of healing indirectly by secreting a number of growth factors (IGF, TGF-β1, VEGF, HGF, and FGF2) with a paracrine action that activates keratinocytes and fibroblasts of the skin by stimulating the processes of neovascularization through the generation of anti-inflammatory cytokines, as well as having antioxidant and antiapoptotic effects. ADSCs release wound healing factors and can stimulate recruitment, migration, and proliferation of endogenous cells in the wound environment. The studies suggest that ASCs can affect other cell types specifically in skin tissue via the paracrine method. They may also be directly transformed into fibroblasts and keratinocytes. The first attempts at healing chronic wounds were performed using ADSCs from lipoaspirate, even without culturing in vitro. This technique is commonly used in aesthetic medicine, avoiding the manipulation that might influence their biological functioning. The simplest method is the application of a component of the adipose tissue-derived multicellular stromal vascular fraction (SVF), after enzymatic digestion and centrifugation of lipoaspirate. SVF is a heterogeneous population of MNCs that include ADSCs of the mesenchymal phenotypes (analogous to MSCs), endothelial progenitor cells (EPCs), hemopoietic progenitors, monocytes, leukocytes, and pericytes. Pericytes are the most important for angiogenesis, and they stabilize nascent blood vessels [10]. Researchers nowadays are focused on the three-dimensional (3D) culture systems of ADSCs to build multicellular constructs with an extracellular matrix (ECM) and to demonstrate better therapeutic efficacy. The study by Cerqueira et al. used human ADSCs with an extracellular matrix (ECM) as a natural tissue glue that was applied to three layers to form a 3D structure (these are known as “technique sheets”). The next step in the current research is looking for additional materials that may resemble a physiological niche for stem cells to enhance cell retention. Conditioned media for ADSCs have been reported to enhance angiogenesis, enhance epithelialization, and affect recruitment or proliferation of macrophages and endothelial progenitor cells during the healing process.

Conclusion: Based of various studies, the best wound healing is achieved by using ADSCs with platelet-rich plasma (PRP). On the other hand, higher concentrations of PRP in vitro culture can slow down the rate of regeneration due to proteolytic enzymes (PRP-collagenase, elastase, and cathepsin) which inhibit cell growth. The best results have been achieved after using a maximum 10% PRP. Healing of chronic cutaneous wounds and ulcers is troublesome and may require the use of skin substitutes. Adipose-derived stem cells have immense potential as an autologous cell source for treating wounds and regenerating skin,

Keywords: IGF, TGF-β1, VEGF, HGF, and FGF2.

TREATMENT OF VITILIGO AND ALOPECIA WITH USAGE OF ADIPOSE-DERIVED STEM CELLS

M. Matoshvili, D. Tophuria
Tbilisi State Medical University, Georgia.

There are promising research outcomes of the use of adipose-derived stem cells (ADSCs) in many diseases are a subject of observation in preclinical studies. ADSCs seem to be the ideal cell population for the use in regenerative medicine due to their easy isolation, nonimmunogenic properties, multipotential nature, possibilities for differentiation into various cell lines, and potential for angiogenesis. This article reviews the current data on the use of ADSCs in the treatment of vitiligo and various types of hair loss.

Introduction: Bone marrow adipose tissue is a source of mesenchymal stem cells, specifically adipose-derived stem cells (ADSCs). It is an inexpensive, unlimited reservoir of stem cells. From 300 ml of adipose tissue, $2\text{-}3 \times 10^8$ ADSCs can be obtained. This is between 100 and 1000 times more than the mesenchymal stem cells from the bone marrow [1–3]. ADSCs are heterogeneous, no specific marker for them has been identified, and the location of stem cells in adipose tissue is difficult to determine. However, most of them occur in the perivascular regions. The morphology of ADSCs resemble fibroblasts, consisting of a large endoplasmic reticulum and nuclei [4-5].

Methodology: The Skin Depigmentation-Vitiligo is a disorder caused by the loss of melanocytes. Repigmentation of vitiligo depends on available melanocytes from three possible sources: from the hair follicle unit which is the main provider of pigment cells, from the border of vitiligo lesions, and from unaffected melanocytes within depigmented areas. Melanocytes rarely undergo mitosis without growth factors; therefore, mitogenic factors are used in transplantation treatments [6].

ADSCs can be a source of growth factors for melanocytes cultured in the presence of keratinocytes. Lim et al. showed efficacy in mice and Sprague-Dawley rats after administration of human melanocytes alone or enriched with human ADSCs. Better results have been shown with a coadministration of melanocytes and ADSCs, which were grown separately and then mixed in a ratio of 1 : 1, 1 : 2, or 1 : 3, as compared to the administration of pure melanocytes alone [7].

Although the interaction between ADSCs and melanocytes are well known, in the study of Kim et al., an increase in the secretion of HGF by ADSCs after prior exposure to bFGF or EGF was demonstrated. They showed that the proliferation and migration of melanocytes were significantly stimulated by coculturing the ADSCs in comparison with monoculture melanocytes. This may be related to the presence of bFGF and melanocyte growth factor (MGF) produced by ADSCs. The ratio of melanocytes with positive expression of TRP-2, E-cadherin, and N-cadherin were significantly increased in the cocultures with ADSCs compared to keratinocyte and melanocyte monocultures. Melanocytes with a positive expression of TRP-2 (tautomerase dopachrome) are considered to be melanocyte precursors, but TRP-1 positive is considered to be diverse and mature. This is an important result, because the greater the number of immature melanocytes, the better clinical outcomes. In addition, cadherin-calcium-dependent cell adhesion receptors take part in cell-cell interactions. E-cadherin determines the adhesion between keratinocytes and melanocytes, and N-cadherin facilitates the contact between fibroblasts and melanocytes. They also play a role in the differentiation of melanocytes. These studies have confirmed that cultures with ADSCs increase the proliferation and migration of melanocytes, while reducing their differentiation.

Skin depigmentation-Alopecia Multipotent stem cells can regenerate hair follicles and sebaceous glands in the skin. The stem cells can be used to regenerate hair growth in a number of therapeutic methods:(i)the reversal of pathological mechanisms that contributes to hair loss (androgenetic alopecia);(ii)complete regeneration of hair follicles with “bulge”;(iii)neogenesis of hair follicles with a stem cell culture.

Hair follicles are surrounded by subcutaneous fat cells and skin, which make up the interfollicular dermal macroenvironment, important in maintaining normal cell growth in the region bulges and hair follicles. ADSCs are necessary for the activation of epidermal stem cells. Their action is based primarily on the secretion of growth factors, such as VEGF which regulates hair growth and the size of the hair follicle by stimulating angiogenesis, HGF which is engaged in the length of the phases of the hair cycle, PDGF which induces and maintains the anagen phase, and IGF-1 which controls the cycle of hair growth and hair cell differentiation. ADSCs stimulate angiogenesis and enhance blood supply to the hair papilla cells. They also have immunomodulatory and immunosuppressive effects through direct interactions between the cells and secrete prostaglandin E2 (PGE2), leukemia inhibitory factor (LIF), and kynurenine. Huang et al. studied the effect of ADSCs on papilla cells of the hair. During the cell culture, the hair retained its own markers. After adding ADSCs (isolated from rats), characteristics common to coculture were observed. There were mixed papilla and medulla cells with ADSCs. The core and the inner shell of the outer coat also contained ADSCs. The best results were achieved in the second cocultures [8]. It was also shown that subcutaneous adipose tissue played an important role in the extension of the anagen phase. There was a proliferation of progenitor cells, which were adipocytes in the transition from the telogen phase to the anagen phase of the hair follicle. The layer thickness of subcutaneous adipocytes during active hair growth (anagen) increased significantly compared to their amount in the resting phase (telogen). ADSCs stimulated hair follicle cells via peroxisome proliferator-activated receptor, which has been detected in three isoforms (PPARα, PPARγ, and PPARδ). In contrast, mature adipocytes have a negative effect on the proliferation of hair follicles, as well as the proliferation of fibroblasts surrounding the follicle in the cocultures. Changing the properties of the adipocyte cell lines may cause skin and hair disorders. Lipid metabolism may lead to defects in the structure of the skin and its functions. Overexpression of human apolipoprotein C1 (APOC1) with hyperlipidemia in transgenic mice results in abnormal hair growth correlated with the expression of the human APOC1 gene in the skin. Musina et al. assessed the influence of hypoxia as a stimulating factor for ADSCs to secrete growth factors. Subcutaneous injection induces the anagen phase in mice, as well as increases the proliferation of human follicular cells, keratinocytes, and hair papillae. Under the influence of hypoxia, there is an increased secretion of insulin-like growth factor binding protein- (IGFBP-) 1 and 2, M-CSF, M-CSF receptor, PDGF-β, VEGF, and decreased EGF secretion.Unfortunately, the studies proved that the two-dimensional (2D) culture of the papilla cells lose their ability to form the hair (trichogenicity) and require a spheroidal form (3D) in culture [9,10].

Conclusions: ADSCs appear as the ideal cell population for the use in regenerative medicine:they are unlimited in supply and easily obtainable from adipose tissue; they are autologous, nonimmunogenic cells;they have a multipotential nature and easily differentiable into various cell lines;they have a significant potential of angiogenesis;they can be easily cultured and have high affinity for 3D scaffolds.

CO-AGGREGATION OF S100A9 WITH L- DOPA AND CYCLEN-BASED COMPOUNDS

L. Arabuli[1,2], I. A. Iashchishyn[1], N. V. Romanova[1], G. Musteikyte[3], V. Smirnovas[3], H. Chaudhary[1], Ž. M. Svedruži´c[4], L. A. Morozova-Roche[1]

[1]Department of Medical Biochemistry and Biophysics, Umeå University, SE-90781 Umeå, Sweden
[2]Department of Natural Sciences, School of Science and Technology, UG, Georgia
[3]Institute of Biotechnology, Life Sciences Center, Vilnius University, Lithuania
[4]Department of Biotechnology, University of Rijeka, Croatia
E-mail: [1]l.arabuli@ug.edu.ge

ABSTRACT

We consider the effect of cyclic compounds and their conjugates on the amyloid formation of pro-inflammatory S100A9 protein, which was found to be a common denominator in Alzheimer's and Parkinson's disease as well as in traumatic brain injury, which is considered as a pre-cursor state for neurodegenerative ailments [11,12]. Indeed, amyloid formation is commonly associated with neuroinflammation, and pro-inflammatory S100A9 protein acts both as an alarmin, inducing the production of pro-inflammatory cytokines, and as a highly amyloidogenic protein, which self-assembles into amyloids under physiological conditions.

The amyloid cascade is central for the neurodegeneration disease pathology, including Alzheimer's and Parkinson's, and remains the focus of much current research. S100A9 protein drives the amyloid-neuroinflammatory cascade in these diseases. DOPA and cyclen-based compounds were used as amyloid modifiers and inhibitors previously, and DOPA is also used as a precursor of dopamine in Parkinson's treatment. Here, by using fluorescence titration experiments we showed that five selected ligands: DOPA-D-H-DOPA, DOPA-H-H-DOPA, DOPA-D-H, DOPA-cyclen, and H-E-cyclen, bind to S100A9 with apparent Kd in the sub-micromolar range. Ligand docking and molecular dynamic simulation showed that all compounds bind to S100A9 in more than one binding site and with different ligand mobility and H-bonds involved in each site, which all together is consistent with the apparent binding determined in fluorescence experiments. By using amyloid kinetic analysis, monitored by thioflavin-T fluorescence, and AFM imaging, we found that S100A9 co-aggregation with these compounds does not hinder amyloid formation but leads to morphological changes in the amyloid fibrils, manifested in fibril thickening. Thicker fibrils were not observed upon fibrillation of S100A9 alone and may influence the amyloid tissue propagation and modulate S100A9 amyloid assembly as part of the amyloid-neuroinflammatory cascade in neurodegenerative diseases.

Keywords: DOPA-D-H-DOPA, DOPA-H-H-DOPA, DOPA-D-H, DOPA-cyclen,H-E-cyclen, S100A9.

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