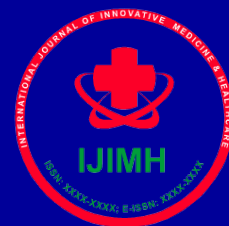


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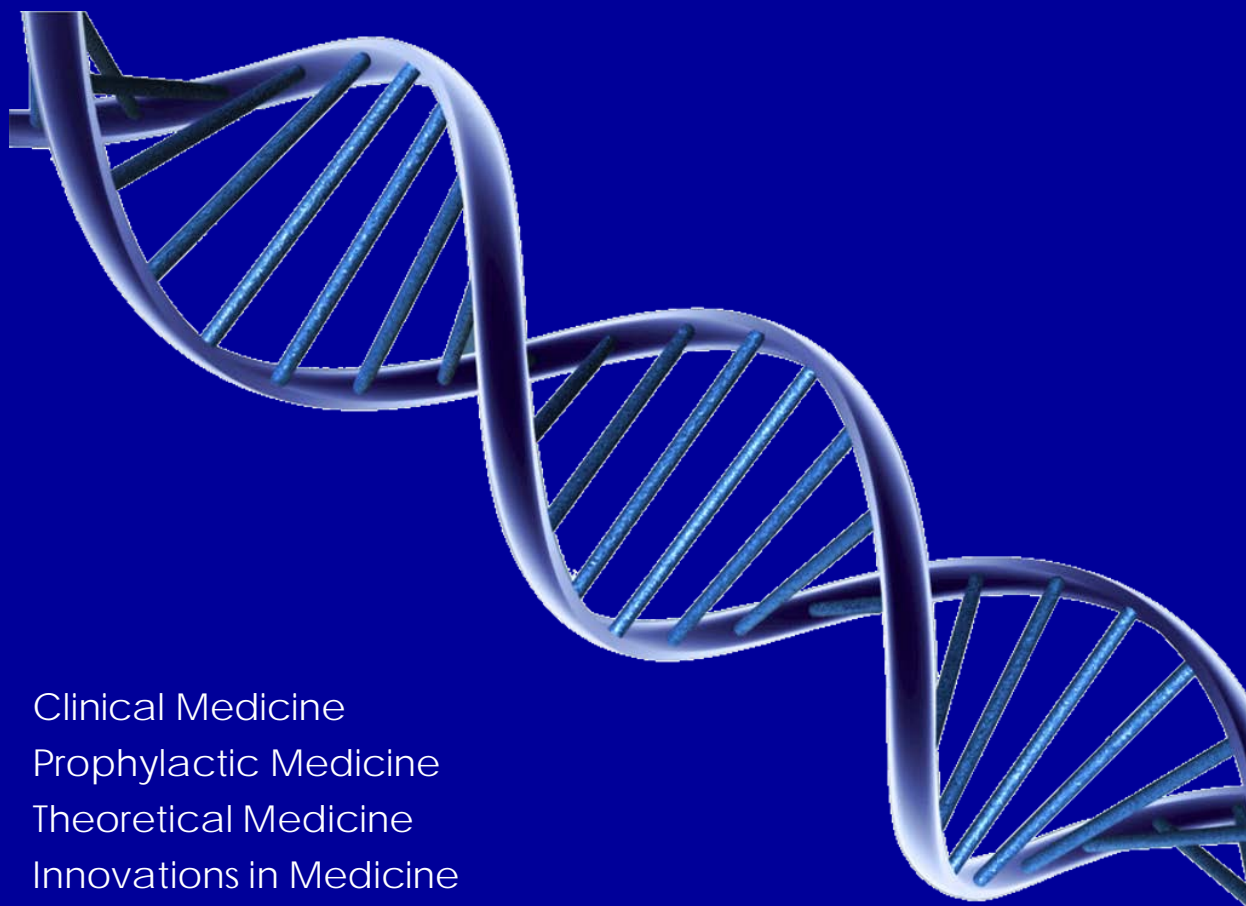
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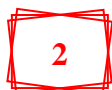
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HIV/AIDS WITHIN THE SCOPE OF SAFE MOTHERHOOD AND THE NURSE'S ROLE

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ABSTRACT

Safe motherhood is the provision of safe and healthy care needs of all women during pregnancy, childbirth and postnatal period. In the case of non-intervention, the rate of HIV transmission to her child during pregnancy, childbirth and breastfeeding of a mother living with HIV is between 15% and 45%. To reduce maternal and infant mortality, prenatal, natal and postnatal care for HIV-infected women offers the opportunity to protect the lives of mothers and their babies by optimizing HIV/AIDS management. Preventing the vertical transmission of the HIV infection to the infant during pregnancy can be achieved by employing HIV/AIDS care and management in accordance with the guidelines during the antenatal, prenatal and postnatal periods. Pregnancy may increase the susceptibility to AIDS in women with symptomatic HIV findings. Therefore, providing maternal and fetal health protection and consultancy services fully, diagnosis and treatment during early periods will bring primary responsibility to nurses who play a key role in the timely initiation of antiretroviral drug administrations. Timely and effective approaches will facilitate the process management of the HIV/AIDS infection for pregnant women who are fragile and need support.

Keywords: Pregnancy, childbirth, HIV, AIDS, nurse

Introduction

One of today's greatest pandemics, Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS) is a global public health concern with a high rate of morbidity and mortality, which has caused the death of 36.3 million people so far (1,2). AIDS is a chronic contagious disease whose etiological agent is HIV and which progresses with opportunistic infections as a result of the suppression of the immune system. Of all AIDS cases worldwide, 98% comprise of HIV-1 (3).

In HIV-1 which is more contagious, the development time of the disease is shorter and the emergence of clinical findings is earlier (3). As HIV-2 has a longer prognosis than HIV-1, its impact on the immune system and AIDS development occur later. Transmission from mother to infant occurs at the rate of 10-40% in HIV-1 and at the rate of 2-7% in HIV-2 (4). In developing countries, the primary reason of transmission for the HIV infection continues to be transmission from mother to infant (1). Transmission of HIV-1 from mother to infant may occur during pregnancy, birth or breastfeeding. The nonintervened HIV infection is transmitted to approximately 35% of infants born from HIV-infected women. The transmission occurs during pregnancy in 10%, during birth in 15% and during breastfeeding in 10% (1).

The World Health Organization (WHO) reported in 2020 that 37.7 million people lived with HIV and 1.5 million cases had recently been infected with HIV. Although the pediatric HIV rates worldwide have been reduced by 50%, the newborn HIV rates are still too high. The number of HIV-infected children under the age of 15 is 1.7 million. Among children under the age of five, nearly 160,000 new HIV infection cases occurred in 2020 (2,5).

According to the numbers explained worldwide, most individuals diagnosed with HIV are women (2). Higher rates of diagnosis among the adult female population increases the estimations of increase in neonatal transmission. Therefore, taking protective measures to prevent the HIV/AIDS transmission during the prenatal, pregnancy, birth and postnatal period will help to decrease issues related to HIV/AIDS (5). One of the subjects discussed within the scope of the safe motherhood program, which has been prepared by WHO and begun to be used in most countries is HIV/AIDS. This compilation sought to discuss the HIV/AIDS management during pregnancy, birth and postnatal period within the scope of safe motherhood and the nurse's role.

HIV/AIDS During Pregnancy

As most women are diagnosed with HIV for the first time during pregnancy, it is of paramount importance to investigate HIV during pregnancy. Similarly, situations in which one couple or both couples are HIV-positive and intend pregnancy are equally significant (6). Due to the risk of fetal transmission and decrease in the cellular immunity, predisposition to the HIV infection is higher during pregnancy and early postnatal period. Therefore, it is crucial that the HIV infection is identified prenatal (7,8). Most women find out that they are HIV-positive with the tests performed during pregnancy. The period when the transmission is the most frequent is the perinatal period. However, there are many women who desire to continue their pregnancy despite positive test result (9,10). In recent years, the prenatal HIV test, antiretroviral therapy (ART), planned c-section for HIV-positive women with a higher viral load, appropriate ART for infants and avoidance of breastfeeding have yielded encouraging results (6). In the perinatal transmission, viral load rate, clinical features and immunological condition of a mother's infant are significant. Maternal viral load rate is the most important factor affecting perinatal transmission (11). Present evidences demonstrate that the HIV fetus transmission occurs at a probability of 15% to 40% at the end of the second trimester and at the beginning of the third trimester during the uterine period (7). Receiving antiretroviral therapy and if possible, starting the therapy during the prenatal period and decreasing the HIV RNA load down to undetectable levels will prevent the perinatal HIV transmission (2, 5).

HIV/ AIDS During Birth

The HIV infection may be transmitted to the infant during birth. HIV has been detected in the vaginal and cervical fluids in pregnant women diagnosed with HIV and in the gastric secretions in newborns (12,13). Transmission from mother to infant during birth occurs when the infant sucks and aspires the mother's blood and cervical secretions and the blood of the mother and the infant leaves the placenta and gets mixed. Acute chorioamnionitis, rupture of membrane and assistive devices used during birth increase the risk of transmission (11). In addition to these, premature birth action increases the risk of intrapartum transmission 3.7 times. When the early rupture of membrane takes longer than four hours, the risk increases from 15% to 25% (14). In order to prevent the risk of HIV/AIDS transmission, it is recommended that elective c-section be performed during the 38th gestational week. Interventional tearing of membranes, use of routine



fetal heart electrodes for fetal monitor and application of vacuum, forceps and episiotomy are to be avoided. The infant's umbilical cord should be clamped as early as possible. It has been reported that having elective c-section decreases the risk by 50% (15).

HIV/AIDS During the Postnatal Period

In order to decrease the maternal and neonatal mortality, postnatal care for women diagnosed with HIV optimizes the HIV management and provides an opportunity for protecting the lives of both mothers and infants. During the postnatal period, nurses face a variety of situations related to HIV. While some women diagnosed with HIV already use ART, there is a lack of ART use especially among unregistered cases (16). ART is recommended for all individuals with HIV in order to decrease the progression risk of the disease and prevent HIV from being sexually transmitted. ART should continue after birth. If the HIV infection is confirmed during birth, ART is to be recommended. ART should be given prior to discharge in order to prevent the therapy from being interrupted (8). As long as the United States of America has safe infant feeding alternatives, breastfeeding is not encouraged for people who confirm HIV or estimate the presence of HIV. It is recommended for people who intend to breastfeed to receive evidence-based counseling in terms of infant feeding options (8). The Canadian guidelines do not recommend breastfeeding no matter what the plasma HIV viral load and antiretroviral therapy use are (17). However, in the light of recent evidences and proven advantages of breastfeeding, it has once again been recommended for women living with HIV to completely avoid breastfeeding (18). Recent guidelines of the English HIV Association have suggested that the safest way of feeding infants from mothers with HIV is formula milk, however, it is possible to encourage breastfeeding in women who are virologically suppressed with combination antiretroviral therapy (Cart) and adhere to a good therapy with commitment (19). The risk of transmission via breastfeeding is 0.064% per litre received and 0.028% with breastfeeding in a day (20). Unless an intervention is performed to prevent transmission, the risk of transmission via breastfeeding will vary from 13% to 48% (21, 22). An infant receiving breast milk will receive HIV from the intestinal mucosa at the rate of 25% to 44% (23). WHO recommends breastfeeding for infants receiving formula due to polluted water resources in low income countries, because morbidity and mortality arising from infection progress more severely via breast milk than the risk of HIV transmission (24). HIV-infected infants are to receive breast milk only within the first six months and continue breastfeeding with complementary feeding until at least two years of age (25). WHO and the United Nations International Children's Emergency Fund (UNICEF) guidelines related to infant feeding and HIV recommend that mothers who are diagnosed regularly receive ART to decrease the risk of HIV transmission and protect their infants and that mothers who regularly take antiretroviral medicine breastfeed their infants. ART which continues during breastfeeding is effective on decreasing the HIV transmission and neonatal mortality (2,5).

Approach to a Newborn Diagnosed with HIV/AIDS

In order to prevent HIV exposure in newborns, standard measures are to be taken in the early postnatal care. As is performed in all newborns, the infant should be warmed up immediately after birth. The mother's secretions and blood on the newborn should be washed with warm water and a soap. Infants of mothers who have recently been diagnosed with HIV during the intrapartum period should start presumptive HIV treatment and the ART resource for the infants should be procured prior to discharge. All newborns who are perinatally exposed to HIV should take



antiretroviral medicine after birth in order to decrease the risk of perinatal HIV transmission (8). Neonatal ART regimes which are administered in appropriate doses for the infant's gestational age are to be started as close to the hour of birth as possible, preferably within the six hours after birth. The newborn's ART regime should be determined according to the maternal and neonatal factors which affect the risk of perinatal HIV transmission. If the patient's HIV condition is not known and its accelerated HIV test comes out to be positive during or shortly after birth, the possible HIV treatment for the infant should be started. If the mother tests negative, the infant's ART regime should be ceased. In premature newborns (<37 weeks), the use of antiretroviral medicine outside ZDV, lamivudine and nevirapine is not recommended for any indication due to a lack of dose and safety data (8). For infants who are exposed to the HIV infection and for those who are breastfed during the postnatal period, WHO recommends ART for extra six weeks (2). As long as an HIV-infected infant continues ART within the first twelve weeks, it will have 75% less possibility of death from a disease related to AIDS (26). For early diagnosis, WHO recommends the HIV test for newborns of HIV-infected mothers within the first four to six weeks (27). It will be possible to exclude HIV after attaining two or more negative tests. Of these tests, the first one is performed 14 days later and the other one is performed after the first month (1). The final test for the infant is recommended at 18 months or when the breastfeeding is ceased (28). HIV virological diagnosis tests are to be developed during postnatal 14-21 days, 1-2 months and 4-6 months (29). Exact exclusion of HIV in infants not receiving breast milk will only be possible through two or more negative virological tests performed after the first and fourth month (1).

Nursing Approach

How nurses give care to HIV-positive mothers and infants is of paramount importance in terms of managing these women effectively and decreasing the mortality rate of infants who are exposed to HIV. It is significant to convince a mother who is diagnosed with HIV during pregnancy to come to prenatal care regularly and manage the process collaboratively. In women with HIV, it is recommended that maximum viral load be reduced to minimize the infant's risk of perinatal HIV transmission without trying to conceive for the sake of their own health (8).

During birth, HIV is transmitted to the infant as a result of aspirating the mother's cervical secretions. A pregnant woman should be informed of the possible risks of vaginal delivery and c-section when deciding on the mode of delivery (15). In pregnant women who plan to have c-section, the delivery is recommended during the 38. gestational week. When a pregnant woman who receives ART gives birth, she should also continue the treatment during the postnatal period. IV ART application is to be started for a pregnant woman who does not receive ART or has a higher viral load (more than 1000 copies / mL) or an unknown viral load during birth. Intravenous ART is easily transmitted from a pregnant woman to the unborn child throughout the placenta. When it enters the child's system, it prevents HIV from infecting the child during birth. A nurse is responsible for performing and maintaining the right treatment method for the mother and the infant. Antiretroviral prophylaxis is recommended for mothers diagnosed with HIV after birth. The mother and the newborn should be protected from other possible contagious diseases and the family should be given counseling in terms of vaccine program, breastfeeding, family planning and continuation of ART (30).

It should not be forgotten that the privacy of patients diagnosed with HIV/AIDS is to be protected carefully and this is a right above all things. Situations in which privacy is violated may have a



higher possibility of causing negative results in the lives of individuals with HIV. In order to prevent this, sensitivity of the medical staff should be enhanced. All pregnant women, mothers and infants diagnosed with HIV/AIDS should be reported to the Ministry of Health with their codes and followed (31).

Conclusion and Recommendation

It is of vital importance to follow women and infants diagnosed with HIV. Nurses play a major role in the care, follow-up and treatment of pregnant women, mothers who have given birth and newborns. Nurses are to support the process by defining the risk factors for all kinds of negative maternal or fetal outcomes for pregnant women or newborns, adapting training and counseling according to personal needs of patients and optimizing maternal and fetal outcomes. Identifying the HIV infection preconception more frequently and maintaining the care of more women will provide more opportunity for optimizing the health of HIV-infected women preconception and between pregnancies, especially with new guidelines recommending early ART. Therefore, in order to learn appropriate approaches for pregnant women and newborns with HIV/AIDS during the care process and put these approaches into practice in clinic, it is recommended to give detailed information about this matter via in-service trainings. Active participation of nurses with their primary role and their contribution to the process management with integrated awareness by providing effective and conscious counseling will be the most important step in enhancing the individual, family and community health and maximizing the mother-child health.

Contribution to the Field

Within the scope of safe motherhood, knowing and using the right approaches during the care and treatment process of pregnant women and newborns with HIV/AIDS during the pregnancy, birth and postnatal period will increase the quality of nursing care and contribute to decelerating the global pandemic by protecting and maintaining the mother-child health. Identification of the HIV/AIDS infection preconception will increase the confidence between the nurse and the woman and decrease the level of anxiety and fear of being exposed to stigma. Nurses taking an active role in the diagnosis and treatment stages will contribute to the right management of the process, removal of wrongs that are known to be right and protection of the mother-child health.

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THE PECULIARITIES OF REMDESIVIR AND ITS OUTLOOKS FOR THE TREATMENT OF COVID-19 DISEASE

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ABSTRACT

The aim of the study was to investigate and analyze the properties of remdesivir and its outlook in the treatment of COVID-19 disease. The antiviral remdesivir, a nucleotide analog prodrug, has a broad spectrum of activity against viruses of several families. After showing its strong antiviral activity against coronaviruses in preclinical studies, remdesivir has emerged as a drug candidate for the treatment of 2019's novel coronavirus disease (COVID-19) caused by the acute respiratory syndrome 2 (SARS-CoV-2) coronavirus infection now a worldwide pandemic. The use of remdesivir to treat COVID-19 began in early 2020 and has shown promising results so far. In 2020, many countries have conditionally approved the use of remdesivir in patients with severe COVID-19. This was followed by a rapid series of conditional approvals across countries / regions. Briefly, remdesivir has been shown to inhibit the coronavirus and improve lung function for prophylactic and therapeutic purposes (early infection) based on in vitro and in vivo data. However, data on COVID-19 patients remained limited.

The global pandemic of the 2019 novel coronavirus disease (COVID-19) caused by the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has created an urgent need for effective antiviral drugs. Remdesivir (formerly GS-5734) is a prodrug of a nucleoside analogue that is currently being investigated in clinical trials for COVID-19. Its unique structural features enable the intracellular delivery of high concentrations of the active triphosphate metabolite and avoid re-inhibiting efficiently viral RNA synthesis. In preclinical models, remdesivir has shown strong antiviral activity against a variety of human and zoonotic β -coronaviruses, including SARS-CoV-2. This article critically evaluates the available data on remdesivir, focusing on microbiology, biochemistry, pharmacology, pharmacokinetics and in vitro anticoronaviral activity, as well as on clinical experience and ongoing advances in COVID-19 clinical trials.

Keywords: Remdesivir, coronavirus, pharmacology, COVID-19, disease, treatment, outlooks.

Aim of the research

The aim of the research was to study and analyze the peculiarities of remdesivir and its outlooks for the treatment of COVID-19 disease.



Material and methods

The material of the article was data from the scientific literature, processed and analyzed by generalization and systematization. The scientific research ensues the fundamentals of assessment development of significant reviews. Were used the ensuing databases (for searching considerable literature for the peculiarities of remdesivir and its outlooks for the treatment of covid-19 disease: PubMed, Web of Science, Clinical key, Thomson Reuters, Google Scholar, Cochrane Library, and Elsevier bases. Additionally studied national and international policy and guidelines and also grey literature.

Results and discussion

Remdesivir's potential mechanism of action against coronavirus remains unclear. Several reasons have been suggested for interpreting the effects of remdesivir. First, remdesivir can disrupt the function of the nsp12 polymerase even when the corrective activity of the exonuclease is intact. Furthermore, remdesivir can efficiently generate the pharmacologically active nucleoside triphosphate (NTP), which serves as an alternative substrate and terminator of the RNA chain. NTP can then inhibit the coronavirus by incorporating active triphosphates into the viral RNA. Additionally, there is a high genetic barrier to coronavirus resistance to remdesivir, suggesting that remdesivir may maintain the efficacy of coronavirus therapy [1].

Remdesivir is a phosphoramidized prodrug of the 1'-cyano-substituted nucleoside analog (GS-441524). It inhibits viral replication by competing with endogenous nucleotides for integration into viral RNA replication by RNA-dependent RNA polymerase (RdRp). The non-structural protein RdRp (nsp12) is highly conserved in coronaviruses, making it an attractive target for broad-spectrum antiviral drugs. Upon entering cells, remdesivir is rapidly metabolised by intracellular kinases to nucleoside triphosphate, the active metabolite (GS443902). The rate-limiting step in the activation of nucleoside analogs is usually the formation of nucleoside monophosphate. Phosphoramidate nucleosides such as remdesivir (and GS-441524) are monophosphate bioisoters and can therefore bypass this limiting step. However, phosphoramidate nucleosides must be administered as prodrugs to sequester the charged phosphonate group and allow for faster entry into the cell. In the case of remdesivir, the negative charge is masked by the 2-ethylbutyl and L-alanine groups, which are rapidly removed by the intracellular esterases. Furthermore, the 1'-CN group of remdesivir and its metabolites offers a high selectivity for RdRp with respect to human polymerases[2].

Remdesivir has demonstrated broad spectrum activity in several in vitro systems against a heterogeneous group of zoonotic and clinically significant human coronaviruses including SARS-CoV-1, SARS-CoV-2 and MERS-CoV with micromolar EC₅₀ or IC₅₀ values. For example, in cultures of human respiratory epithelial cells, remdesivir inhibited the replication of SARS-CoV-1 and MERS-CoV. New evidence suggests that remdesivir also shows potent activity against SARS-CoV-2. Remdesivir has been proposed as a promising treatment option for COVID-19 based on laboratory experiments and charity use reports. Its safety and efficacy in humans require high-quality evidence from well-designed and well-designed clinical trials. Launched for more details. Similar to the inconclusive effect on SARS-CoV and MERS-CoV, the impact of remdesivir on the SARS-CoV-2 outbreak in current clinical practice should not be overestimated. More research is urgently needed to cure COVID-19 and control SARS-CoV-2 [3-4].

The evolution of coronavirus resistance to remdesivir was assessed using cell culture in MHV with EC₅₀ values comparable to those of SARS-CoV-1, SARS-CoV-2 and MERS-CoV.11. The



side effects of remdesivir should be taken into account. Remdesivir's safety profile information is changing rapidly. Until recently, most clinical experience has been in patients infected with Ebola virus, whose clinical manifestations are very different from those of COVID-19, making it difficult to extrapolate drug safety to populations. During the study, patients treated with remdesivir for an Ebola virus infection experienced serious side effects that the researchers believe could be related to remdesivir. The most serious of these was hypotension after taking the full dose, followed by rapid cardiac arrest and death. Of those who survived Ebola virus infection and were enrolled in the unique phase II PREVAIL IV study, patients required a dose reduction of remdesivir due to increased transaminase activity. Safety data from four phase 1 pharmacokinetic studies in healthy volunteers were also partially presented. In these studies, subjects received single doses of up to 225 mg of remdesivir or multiple doses of 150 mg once daily for 7 or 14 days, or 200 mg once followed by 100 mg daily for a total of 5 or 10 days. The most common side effects were phlebitis, constipation, headache, bruising, nausea, and body aches. Asymptomatic transient increase in the level of alanine aminotransferase (ALT) of 1 or 2 degrees [5-6].

Remdesivir has caused drug interactions. At the time of writing, no in vivo interaction studies with remdesivir have been published, but remdesivir's ability to inhibit or induce cytochrome P450 enzymes and transporters (CYP450) has been tested in vitro. However, it is important to note that as a prodrug, remdesivir is rapidly cleared in vivo, limiting the potential for clinically significant drug-drug interactions. Data on the ability of remdesivir metabolites to react with drugs is even less. In in vitro studies, remdesivir was a weak inhibitor of CYP1A2, CYP2C9, CYP2C19 and CYP2D6. The IC₅₀ of remdesivir for CYP3A was 1.6 M, suggesting that short-term inhibition may occur at normal human exposure. Inhibition of remdesivir by the metabolites of the CYP450 enzyme has not been studied.¹⁴ Tests on the induction of CYP450 with remdesivir have been conflicting; can induce CYP1A2 and CYP2B6.¹⁴ Here, too, the clinical relevance is questionable. GS-441524 and GS-704277 did not demonstrate CYP450 induction in these studies. Remdesivir has been found to be a substrate (OATP1B, P-glycoprotein) or inhibitor (OAT1B1, OAT1B3) of several drug transporters. In current clinical studies with remdesivir there are no exclusion criteria for drug interactions [7-8].

There are currently no scientifically proven treatments that reduce mortality from COVID-19. Current treatment focuses heavily on supportive care and prevention of complications. Therefore, effective and safe antiviral drugs are urgently needed to relieve the burden on healthcare systems. As described in this review, remdesivir is a nucleoside analogue prodrug with unique structural features that allow intracellular delivery of high concentrations of the active metabolite triphosphate. Coronaviruses, including SARS-CoV-2, in both in vitro and animal models. These data, combined with early safety data from clinical experience with Ebola virus infections, provide strong rationale for prioritizing remdesivir testing in COVID-19 clinical trials. However, the unpredictability of the pandemic poses many challenges for researchers attempting to conduct clinical trials. The first randomized controlled trial evaluating remdesivir for COVID-19 was conducted at multiple sites in the epicenter of the first epidemic, but failed to reach the targeted sample size due to slow recruitment after the peak levels subsided, and did not produce conclusive results [9-10].

Remdesivir, a nucleotide analog prodrug, is metabolized in host cells to the pharmacologically active nucleoside triphosphate. As an analogue of adenosine triphosphate (ATP), remdesivir triphosphate competes with the natural substrate ATP for integration into new viral RNA filaments using RNA-dependent RNA polymerase. When the triphosphate from the strip is



accidentally inserted into the chain and a small number of extra nuclei are added (usually three for corona virus), RNA production stops. Remdesivir has a broad spectrum of antiviral activity against various viruses, including Ebola, Nipah and respiratory virus, as well as endemic and coronary heart disease in animals. In primary cultures of human respiratory epithelial cells, remdesivir inhibited severe acute respiratory distress syndrome (SARS-CoV) and Middle East coronavirus (MERS-CoV) with an inhibitory half microstructure value (IC 50). These results suggest that remdesivir is an antiviral agent with potential activity against novel coronaviruses [11-12].

In vitro, remdesivir demonstrated antiviral activity against SARS-CoV-2 in primary cultures of human respiratory epithelium and inhibited highly dose-dependent SARS-CoV-2 replication at a half maximum active concentration (EC50) of 0.01 μM . This antiviral activity appears to be specific to the virus; Remdesivir is non-cytotoxic in this culture system at a dose of $\leq 10 \mu\text{g}$. In Vero-E6 cells, EC50 levels of remdesivir and its anti-SARS-CoV-2 metabolite GS-441524 were 1.65 μM and 0.47 μM , respectively, reflecting the reduced capacity of Vero-E6 cells. E6 for remdesivir metabolism. When co-cultured at clinically important concentrations of remdesivir and chloroquine phosphate in respiratory virus-infected HEp-2 cells, chloroquine phosphate inhibited the antiviral activity of remdesivir in a dose-dependent manner. Higher remdesivir EC50 levels and lower remdesivir triphosphate levels in normal human bronchial epithelial cells have been observed with elevated levels of chloroquine phosphate. Therefore, co-administration of remdesivir with chloroquine phosphate or hydroxychloroquine sulfate is not recommended [13-15].

In mice infected with a chimeric SARS-CoV virus that encodes the SARS-CoV-2 RNA-dependent RNA polymerase, treatment with remdesivir significantly reduced viral load in the lungs and improved it in vehicle-treated subjects. loss of lung function. A similar therapeutic effect was observed in a model of SARS-CoV-2 infection in rhesus monkeys. Although the possibility of QT interval prolongation in humans has not been fully evaluated, current preclinical and clinical data do not indicate a risk of QT interval prolongation with remdesivir.

Conclusions

Limited data are available to evaluate the side effects of remdesivir. Hypersensitivity reactions, including infusion-related and anaphylactic reactions, have been reported relatively rarely during and after administration of remdesivir. A transient increase in aminotransferase activity was observed with the use of remdesivir in phase 1 studies in healthy volunteers. A serious adverse event, fatal hypotension, likely related to the use of remdesivir, was reported in the phase 3 of study.

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THE SPECIFICITIES AND PHARMACOLOGICAL ACTION OF GEOMIN FORTE FOR THE COVID-PANDEMIC THERAPY

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ABSTRACT

The aim of the research was to study and analyze the specificities and pharmacological action of geomin forte for the covid-pandemic therapy. Antioxidants are substances that the human body constantly needs in order to maintain it in a normal state, which means maintaining the necessary balance between free oxidative radicals and antioxidant forces, the role of which is played by antioxidants. Vitamin E increases the body's nonspecific resistance, and by activating the synthesis of cytokines, tocopherol stimulates its own anti-inflammatory activity. The effect of vitamin E is to stimulate the reproduction of immune cells, systems that need to quickly multiply when they meet the source of a possible disease. In the body, this process is called mitogenesis. The pharmacodynamic effects of tocopherol are synergistic when combined with vitamins C and A. Retinol provides formation of immune (protective) cells, lining respiratory tract and gastrointestinal tract, serving as a natural barrier to infection. Medicine will enhance possibilities of adaptation of the organism to the changed environment, because, in many cases, it is very difficult to protect the population from the impact of the negative factor (including ionizing radiation, natural disasters, etc.) According the study results we think that Geomin Forte will help to consider the diversity of symptoms of postcoid syndrome, and it will be quite flexible and creative to use it in the period of postcovid rehabilitation.

Keywords: Specificities, pharmacological, Geomin Forte, covid-pandemic, therapy.

Introduction

Human immune system is the main opponent of the coronavirus and has protective function, which uses various mechanisms against the invading virus. However, it has been known that the mechanisms of subtle regulation of the immune system under the influence of viruses can be disrupted and develops autoimmune processes. In such a case, the immune system may become the main threat and the autoantibodies (or so-called Cytokines, interleukins, interferons, etc.) produced by them can damage the human body [1-3].

The biologically active substances that increase immunity and have an antioxidant effect are, first of all, all vitamins, especially the antioxidant series (vitamin C, carotene, vitamin E), B vitamins, as well as phenolic compounds with P-vitamin and antioxidant activity (catechins, flavanols, anthocyanins, hydroxycinnamic acids, etc.), polyphenolic substances (tannins), minerals (especially selenium, zinc, iron, iodine, potassium, calcium, etc.), chlorophyll (a and b), terpenoids, essential oils, resins, glycosides with an adaptogen effect, polyunsaturated fatty acids,



essential amino acids (especially sulfur-containing ones), complete proteins, ballast substances (dietary fiber, pectin, inulin), fermented foods, etc. The carriers of these substances are mainly products of plant origin (fruits, berries, vegetables), wild berries, medicinal and technical plant materials, natural spices, algae, flower pollen. In this section, we will consider in sufficient detail almost all groups of these substances and their content in plant materials and food products, their therapeutic and prophylactic effect and role in a healthy diet [4-5].

Aim and objectives of the research

The aim of the research was to study and analyze peculiarities and prospects for the use of zeolite containing Geomin Forte in the treatment of COVID-19 and post COVID-19 condition.

Material and methods

The material of the article was data from the scientific literature, processed and analyzed by generalization and systematization. The scientific research ensures the fundamentals of assessment development of significant reviews. Were used the ensuing databases (for searching considerable literature for prospects of the using of zeolite containing Geomin Forte in the treatment of COVID-19 and post COVID-19 condition): PubMed, Web of Science, Clinical key, Thomson Reuters, Google Scholar, Cochrane Library, and Elsevier bases. Additionally studied national and international policy and guidelines and also grey literature.

Results and discussion

Biologically active food supplements ("Geomin", "Phytomin", "Geomin Forte") can be used in combination with traditional medications for the treatment, rehabilitation and prevention of diseases caused by various factors. According the pharmacotherapeutic outcomes, here we note that a series of drugs based on clinoptilolite ("Geomin", "Phytomin", "Geomin Forte") are used in combination antioxidant therapy and the positive effect is based on the strong sorbent properties of these drugs [6-7].

Structural zeolites (clinoptilolites) are from the family of aluminosilicates and cations that are grouped together to form macro aggregates in separate cavities. In the medical field they are involved in the detoxification mechanisms of ions and molecules through their holes. In fact, we make about 140 types of natural and 150 synthetic zeolites for specific and selective use. Clinoptilolite is a natural zeolite most commonly found in the pharmaceutical market and used in medicine to compensate for pathological oxygen starvation in the tissues of the human body [8-9]. Natural zeolites are crystalline aluminosilicates with unique adsorption, cation exchange, and catalytic properties that have several uses. Clinoptilolite of natural zeolite, with enhanced physicochemical properties, is the basis of megamine and lycopenomine in food supplements, which have been shown to have antioxidant activity in humans. Investigation of the effect of TMAZ supplementation on the immune system in patients treated for immunodeficiency disorder. A total of 61 patients received daily TMAZ doses of 1.2 g (lycopenomine) and 3.6 g (megamine) for 6 to 8 weeks, during which time the patients' primary medical therapy remained unchanged. Megamine intake significantly increased the number of CD4 +, CD19 + and HLA-DR + lymphocytes and significantly decreased the number of CD56 + cells. Lycopenomine is associated with increased CD3 + cell count and CD56 + lymphocyte count. No negative reactions were observed [10-11].



It is known that Zeolites are porous minerals that have a high absorption and ion exchange capacity. Their molecular structure is a dense network of AlO_4 and SiO_4 , forming cavities in which water and other polar molecules or ions can enter / exchange. Although there are several synthetic or naturally occurring types of zeolite, the most common and studied is natural zeolite clinoptilolite (ZC). ZC is an excellent detoxifying, antioxidant and anti-inflammatory agent [12-13].

We thought we had defeated the bacterial world. Less than 100 years have passed and we have encountered a problem - this strong bacterial resistance Towards preparations. It became necessary to create new vaccines and treatments. Also in focus is the post-Covid period, as the medical community and science have faced many undesirable syndromes.

Considering the above-mentioned properties of the mineral zeolite (clinoptilolite), the 500 mg activated clinoptilolite "Geomin Forte" developed by us is characterized by antioxidant action. Unlike the conventional antioxidants, it stimulates the body's endogenous antioxidant system and is a direct-acting oxidoreductive agent. Its activated natural mineral zeolite (clinoptilolite) acts directly on the cell membrane as a surface-active donor of electrons. With its oxidizing effect, "Geomin Forte" is 200 times more than vitamins C and E [14].

Therefore, it can be used during intoxications (used as the best sorbent for food, infectious, occupational intoxications, chronic metals and chronic exposure to radiation). As well as when the functional state of the immune system is impaired and fatigue; And as an adjunct for allergic diseases; In case of impaired gastrointestinal tract and liver function, hepatitis (improves general condition); In women and men with pre-and menopausal nervous disorders and impaired ability to work; "Geomin Forte" Recommended as an additional source of minerals (calcium, magnesium); "Geomin Forte" Recommended as adjunctive therapy in oncology patients - for elimination of side effects of chemical and radiation therapy. (Reduction and disappearance of hair loss, intoxication events, nausea, vomiting, toxic polyneuropathy; stimulation of bone marrow function); Skin diseases (it is recommended to apply the powder externally on wounds or damaged parts of the skin several times a day); "Geomin Forte" Used in combination with antioxidant therapy in the context of standard treatment for the following diseases: Diabetes mellitus; Accelerated aging process; Alzheimer's disease; Parkinson's disease; Endocrine pathologies; Atherosclerosis and ischemic heart disease; Hypertensive disease; Stroke; Rheumatism;

We have mentioned that it is 200 times more than vitamins C and E, and here we also mention that vitamin E is an antioxidant -and also vitamin C has an antioxidant features. It has the ability to protect various substances from oxidative changes, inhibits the metabolism of proteins, nucleic acids and steroids: To maintain muscle function, for the vascular and endocrine systems; Protects against heart and nervous diseases, the harmful effects of smoking and polluted air; To maintain a youthful appearance, to slow down the aging process of cells; Dilates blood vessels; Protects the lungs from air pollution; Prevents the appearance of blood clots; Accelerates burn healing; Acts as a diuretic and can lower blood pressure; Protects the fetus from miscarriage.

Ascorbic acid or vitamin C is known to be a powerful antioxidant. It regulates blood clotting, regulates capillary permeability, participates in blood formation, acts against inflammation and allergies, regulates the problems caused by stress, strengthens reparative (recovery) processes, increases resistance to infections. Among the positive properties of vitamin C, our attention was drawn to the characteristics that are most pronounced in patients with COVID-19 and for the post-



Covid period: Reduces blood cholesterol levels; Protects against many viral and bacterial infections; Reduces the chance of blood clots;

Our attention was drawn to the features that are most evident in COVID-19 disease and today, when postcoid syndrome, also known as Long Covid, is often observed: Fatigue; Difficulty breathing, cough or shortness of breath; Smell / taste loss (anosmia); Headache; muscle and joint pain; Problems of concentration and memory; Nerve disorders (neuropathies); Depression and anxiety disorders and sleep disorders.

Also known as critically severe current COVID-19: need for controlled breathing (non-invasive or invasive ventilation) during the following conditions: Severe pneumonia; Acute respiratory distress syndrome (ARDS); Sepsis/septicemia; Septic shock; Poly organ failure [15-16].

Conclusions

Based on study results, we hope that "Geomin Forte" developed by us, which has all the characteristics of vitamin C and vitamin E, and exceeds these properties by 200 times. We think that Geomin Forte will help to consider the diversity of symptoms of postcoid syndrome, and it will be quite flexible and creative to use it in the period of postcoid rehabilitation.

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TETHERED CORD SYNDROME-CASE PRESENTATION

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ABSTRACT

Introduction

Tethered cord is a term for several different conditions. Common to all conditions of the tethered cord is that the movement of the spinal cord is limited at its base. During daily activities, the spinal cord can not move up and down inside the spinal canal, retreating against the restriction. Withdrawal of the spinal cord if minimal is unlikely to cause damage. In severe cases, the pressure can permanently injure the spinal cord.

This functional disorder can be congenital (present at birth, the result of developmental malformations) or it can be acquired (arise later in life). Congenital attachment is usually detected in childhood, but not always. In some cases, congenital malformation is not detected, or properly diagnosed, until adulthood. Tethered Cord Syndrome is relatively rare in adults.

Methods and materials

We present a 2-year-old child, who has frequent urinary tract infections since infancy. Examined by a neurologist from our Clinic at 2 years of age with the presence of spasticity of the lower extremities and pes equinovarus on the right leg.

Results

Contrast-enhanced magnetic resonance imaging (MRI) diagnosis and consultation with a neurosurgeon are recommended.

Conclusion

The most common symptoms of this disease in children are lesions of the lower back, fatty tumors of the lower back, skin discoloration of the lower back, back pain, worsened by activity and relieved with rest, leg pain, especially in the back of legs, leg numbness, difficulty walking, deformities of the legs, scoliosis of the spine. If tethered cord sy is later diagnosed it can lead to loss of bladder and colon control. MRI is used for diagnosis. Early surgery is recommended in children to prevent further neurological deterioration.

Keywords: Thetered cord, spinal cord, medulla spinalis

Introduction

Tethered spinal cord Sy is a functional disorder of the spinal cord that occurs due to abnormal stretching of the caudal part of the spinal cord, anchored with an inelastic structure. The causes may be congenital (primary) or secondary (acquired). Most cases are associated with spinal dysraphism (1). Symptoms most often appear in childhood. The most common symptoms are back and leg pain, orthopedic deformities, deterioration of gait, foot deformities, muscle weakness, progressive scoliosis, skin signs, urinary dysfunction, sphincter incontinence. Children

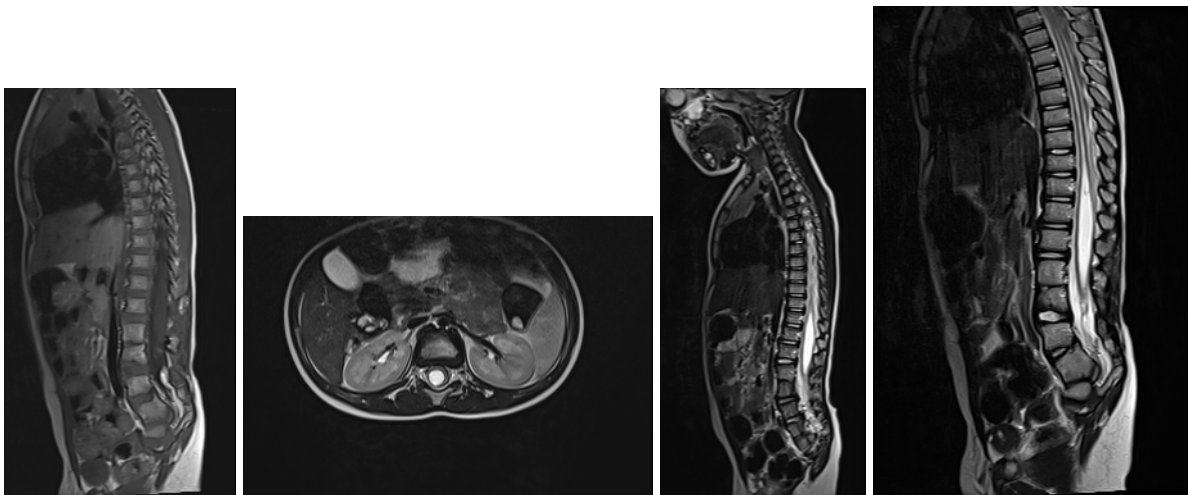
in early childhood have skeletal growth disorders and asymmetry of the lower extremities, ie different lengths of the lower extremities .Adolescents and adults often suffer from back pain that lasts for a long time.(2.3.4) Echo in newborns and magnetic resonance imaging in older children are used for diagnosis. Radiological abnormalities such as low lying medullary cone, lumbosacral lipoma, or thick film (5).

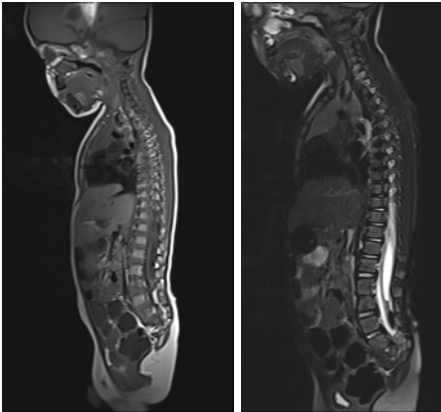
As a diagnostic method, radiographic imaging cannot be the basis for making a diagnosis.(6) If the patient has a normal radiological finding, this should not rule out the existence of the Tethered Cord Syndrome .(4,7) In some patients there is a high chance of restoration of neurological functions. In such patients, in order to avoid irreversible loss of neurological functions, it is very important to make an early diagnosis and perform surgical untethering Once the diagnosis has been confirmed or when there is an established probability that the syndrome is progressing the neurosurgeon should choose between treatment alternatives (1) . .

Case report

We present a two-year-old child with orderly perinatal and postnatal development who came to our clinic due to spasticity of the lower extremities. On clinical examination, a parieto-occipital region and a right leg with pes eqvinovarus were found, which may be part of a tethered cord sy or vascular changes. The child first came to our clinic at the age of 2 months and since then he has had more hospitalizations at our clinic due to recurrent urinary tract infections. Computed tomography and magnetic resonance imaging were performed due to suspicion of tethered cord Sy. The diagnosis is confirmed and surgery is suggested.

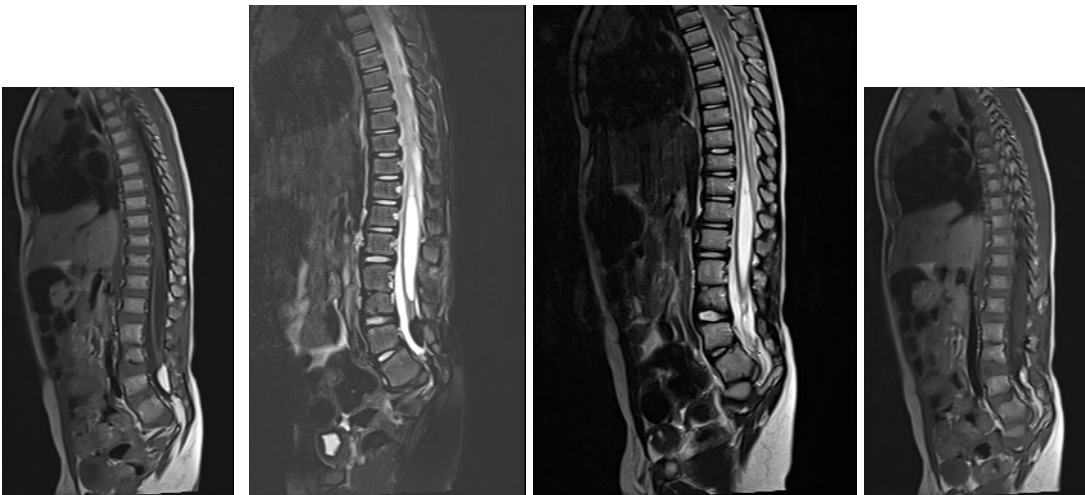
MR (before surgery)

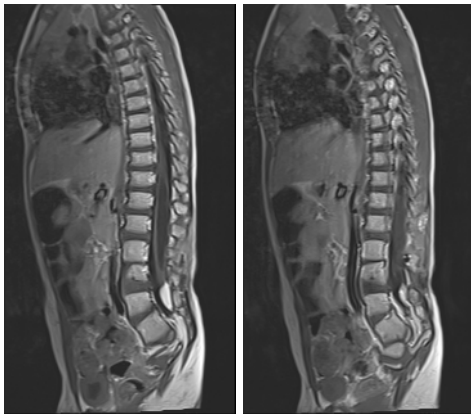




Persistent central spinal canal with cystic dilatation of the medullary cone and Tethered spinal cord Sy with conical medulla to some extent are followed. L4 / L5 level with partial block of L3 / L4 vertebral bodies and filum terminale is attacked with lipomatous lesion posteriorly at L5 level, about 15mm x 6mm long. No transverse incisions have been made in this segment, an adequate assessment is not possible but spina bifida is probably present, followed by dysraphism or dysplasia, agenesis of the sacrococcygeum. The cerebellum, cerebellum, and brainstem without age-appropriate focal lesions, with as yet unfinished myelination in the parietal periventricular zones being somewhat normal. The ventricular system and subarachnoid spaces are neatly wide, free. Pansinusitis.

MR (after surgery)





Persistent central spinal canal with cystic dilatation of conical medullary and tethered spinal cord Sy with conical medullary to some extent l4 / 15 level with partial block of l3 / l4 vertebral bodies, filum terminale is attached with lipomatous lesions posterior length5 of about 15mm x 6mm. No transverse incisions have been made in this segment, an adequate assessment is not possible, but spina bifida is likely to occur and dysraphism is observed at the level of the sacrococcygeal region. Finding identical to the previous MR examination of 28.09.2021

Discussion

TCS can be present at any age group, but our study is focused on effect of TCS in children. Analyzing the findings in for TCS treatment in the literature surgery showed to be best treatment for pediatric patients, which also the therapy proposed by our clinic. Studies had also showed very little morbidity rate the surgical filum sectioning intervention (8). The fundamental goals of surgical intervention in TCS are as follows: 1) to improve or stabilize deficits in the symptomatic patient and 2) to prevent future deficits in the asymptomatic patient (8). Surgical untying is indicated in patients with progressive or emerging symptoms. surgical treatment achieves pain relief, stabilization of neurological function. reduces chronic cable tension. early surgery gives better results (9). The results showed that one of the symptoms that TCS patients suffer most pain, showed to have serious positive impact. At children many report indicate that sometime almost 100% of children undertaking surgery had pain relief (9). Also there have been other serious positive impacts on the stabilization of neurological decline at children even though this is not significant as in pain relief, improvement of neurological functions had 80-90% of pediatric patients and their motor functions at 20-80% of the cases. Scoliosis with long term stabilization ranged between 43 to 63% of the cases and and bladder function improved in 50% of the cases (8;9)

But in order the results of the surgery of TCS to have higher positive effect timing is very important. Many studies have proved that an early intervention will result in more positive results after the surgery (10;9) Timing is very important and it is related not only with the time of healing of the patients but also in the quality of the surgery. Patients suspected of having TCS must be referred and treated by the age of 2 years, or soon after diagnosis, as they are likely to develop progressive neurological deficits if untreated (11). Thus research have pointed that the percentage of invalidity at patient is depends from right time of undertaking the surgery, if the surgery is taken sooner that the chances for invalidity decline. It is important to mention that diagnosis can be difficult due to the subtleness of the signs and symptoms, which may be easily



overlooked (12). Thus it is important to have proper education of the relevant health care personnel in order to have early diagnosis and prompt referral (11).

Also there are some surgical complications that need to be addressed, such is cerebrospinal fluid (CSF) leak and retethering, and in some cases wound infection, meningitis, bladder dysfunction, and neurological injury (13;8). The most common is CSF leak, this is a complication during the surgery in children who have a tethered cord because the dural anatomy may be abnormal before surgery and may be compromised further by the operative procedure (13). Retethering of the released spinal cord which may occur over time in certain subgroups of patients. Thus it is important for pediatric patients to be followed regularly in order to monitor their neurologic, orthopedic, and urologic stability (13).

Conclusion

This syndrome occurs equally in men and women, and its incidence is still unknown. It may be present at birth as a congenital disease and then is most often associated with spina bifida or appear later in life as an acquired disease. If this disease is congenital it is not always detected immediately after birth but can be detected and diagnosed during early childhood or sometimes after adulthood. Treatment can be surgical and in children it is recommended to have surgery as early as possible to prevent further neurological deterioration. In asymptomatic adults only careful monitoring is recommended. Regarding the prognosis, all patients who are timely diagnosed and treated appropriately have a normal life expectancy. However, in some patients certain motor and neurological disorders can not be completely corrected. Patients with this syndrome who have clinical signs and symptoms, but have a regular radiological finding should be referred to specialized centers where the diagnosis will be confirmed or rejected. Of great importance is the good education of the appropriate medical staff for timely referral of patients to appropriate centers and early diagnosis, and thus early treatment of patients and better prognosis and quality of life.

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AGE-RELATED CHANGES OF HORMONAL HOMEOSTASIS IN POLYCYSTOSIS OF OVIANS

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ABSTRACT

Violation of hormonal homeostasis in polycystic ovary syndrome (PCOS) causes a number of changes in the body of a woman in the postmenopausal period. One of the clinical features of the climacteric syndrome in PCOS is the presence of rare and weak hot flashes, a decrease in the menopausal peak of gonadotropins, and a distinct appearance of local urogenital symptoms. With age, in women with PCOS, a history of insulin resistance and dyslipidaemia predisposes them to early onset of cardiovascular disease and type 2 diabetes. Pathogenetic treatment of women with a history of PCOS in the postmenopausal period should be carried out in order to prevent atherosclerotic and metabolic complications.

Keywords: postmenopause, polycystic ovary syndrome, insulin resistance

Introduction

A modern woman spends about a third of her life in postmenopause [6]. Menopause has a certain effect on impaired insulin secretion, estrogen deficiency, thereby affecting hormonal homeostasis [4,7]. Insulin resistance (IR) is an important pathophysiological feature of polycystic ovary syndrome (PCOS) contributing to the occurrence of cardiovascular disease and diabetes mellitus type 2 [2]. In the pathological course of the menopause, the combination with PCOS can become a mutually aggravating factor.

PCOS is a serious disease of women of reproductive age, but what happens to a woman entering the menopause period, whether the existing disturbances in hormonal homeostasis affect the further state of the body.

Aim

The study of clinical and hormonal characteristics in patients over 50 years of age with PCOS and insulin resistance.

Materials & Methods

We examined 25 patients aged 50 to 60 years (54 ± 2.5 years) with an intact uterus in postmenopause (48.5 ± 2.7) with PCOS and visceral obesity. The control group consisted of 43 clinically healthy women. Postmenopause is a term to describe the time after someone has gone through menopause [1]. Exclusion criteria: treatment of osteoporosis; other endocrine, hepatorenal disorders in history; long-term use of glucocorticoids and use of hormonal contraception or metformin within 3 months prior to enrollment in the study.

All women were examined according to the generally accepted scheme: anamnesis, gynecological examination, anthropometric measurements with the calculation of body mass index (BMI), waist hip ratio (WHR) and waist circumference (WC). The menopausal status of the examined women was assessed using the Kupperman index. General clinical, ultrasound, hormonal examinations were used (determination of the level of insulin, fasting glucose, insulin, vitamin D (25(OH)D),

prolactin (PRL), free testosterone (FT), dehydroepiandrosterone (DHEA), follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid stimulating hormone (TSH), thyroxine (T4), determined by ELISA), blood lipid spectrum study (total cholesterol (CS), high density lipoproteins (HDL-C), low density lipoprotein (LDL-C), triglycerides (TG)). Insulin resistance (IR) was defined as HOMA-IR > 2.5. Metabolic syndrome (MS) was assessed according to the IDF-AHA [3,5].

The data were processed by methods of mathematical statistics using the BioStat Pro 6.2.2.0 program (AnalystSoft Inc., Walnut, USA) with the calculation of the arithmetic mean and mean error ($M \pm m$). The significance of differences was assessed by Student's t-test.

Results

Among the observed patients, the average age of menopause was 48.5 ± 2.7 years, which is 1.5-2 years earlier than in the general population. The duration of the climacteric syndrome at the time of the study was 4.8 ± 2.1 g. The prevalence of severe and moderate forms of climacteric syndrome (67%) over the lungs was revealed, which is not typical for this age. Symptoms of neurovegetative dysfunction were detected in 93%. Sweating, a tendency to edema, hot flashes, and palpitations were more common. Urinary incontinence during physical exertion, dryness in the vagina bothered $62.86 \pm 9.52\%$ of the examined women.

In 56%, memory and mood disorders were noted, including anxiety, apathy, a tendency to depression, and psychosomatic disorders. Metabolic and endocrine disorders accounted for 63%. An increase in insulin levels was found in 15 patients.

Ultrasound revealed an increase in the ovaries with multiple cystic formations. In 18 patients, a significantly elevated level of free testosterone was found. In 33% of patients, the LH/FSH index was 3. DHEAS levels were higher in the 12 postmenopausal PCOS women studied than in the control group with the same age but not matched with BMI, which indicates a mixed form of PCOS and an erased form of adrenogenital syndrome. In the examined women BMI was 29.7 ± 1.4 kg, waist hip ratio (WHR) 0.96 ± 0.08 , waist circumference (WC) 98.2 ± 5.4 cm. The dynamics of insulinemia was characterized by a decrease in the insulin response (HOMA_{secr} - 16.5 ± 7.4 ; integral insulin response index - 5.4 ± 1.5).

Patients with PCOS have a history of severe hyperlipidemia and a high degree of atherosclerosis (type II, b). The study of the relationship between the presence of PCOS in history and indicators of the blood lipid spectrum determined that patients with PCOS had a history of significantly high levels of cholesterol ($p < 0.005$), triglycerides ($p < 0.01$); a trend towards an increase in the content of LDL-C and a decrease in HDL-C (45.2 ± 14.7 mg/dL). However, neither BMI nor WC correlated significantly with LDL-C levels.

Discussion

It was found that in women with overweight in postmenopause and PCOS, the accumulation of abdominal fat is higher than in women in the control group of the same age and BMI. Because BMI does not take into account fat distribution of the body, obesity defined by WC has a higher sensitivity and specificity for identifying the presence of resistance to insulin [5]. PCOS is often characterized by abdominal obesity, regardless of BMI, in postmenopausal women there is an increase in the volume of fat mass and a redistribution of fat in the abdomen [3]. This suggests that the presence of PCOS in history further exacerbates the impaired lipid metabolism in menopause, thereby contributing to the development of cardiovascular diseases in the late



postmenopausal period. In women with PCOS, elevated androgen levels do not decrease in postmenopausal women, which is confirmed by the data of a number of studies [7].

Conclusions

The clinical feature of the climacteric syndrome in the presence of PCOS in history is the rare occurrence and low intensity of hot flashes, suppression of the menopausal peak of gonadotropins, and the severity of local urogenital symptoms. With age, in women with a history of PCOS, insulin resistance and dyslipidemia can contribute to the early onset of cardiovascular disease and type 2 diabetes. Pathogenetic treatment of women with a history of PCOS in the postmenopausal period should be carried out in order to prevent atherosclerotic and metabolic complications.

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MULTIMODAL FUSION ANALYSIS OF MEDICAL IMAGES BY DISCRETE WAVELET TRANSFORMATION

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ABSTRACT

Medical image fusion is the development of registry and fusion of different pots of one or more imaging modalities in order to improve image value and reduce uncertainty and concern, to improve the applicability of the medical image for clinical opinion or the evaluation of medical care. difficulties. Multimodal medical image fusion algorithms and devices have achieved a remarkable result in improving the veracity of clinical decision support in medical images. The main objective is to improve the understanding of medical images using Discrete Wavelet Transform technology. DWT mainly uses blending rules involving the average pixel. Discrete wavelet transform has been implemented using fusion technology for medical image fusion.

Fusion Power is calculated based on PSNR, MSE, and Total Progression Moment. The result demonstrates the success of the fusion scheme on wavelet transform imaging (MRI) and positron production tomography (PET). Other variants of MRI (magnetic resonance imaging) and PET (positron emission tomography) performed for medical diagnosis.

Keywords: Multimodal fusion of medical images, fusion rules, magnetic signs, PET.

Introduction

The image combination implies that the progress of matching the associated data of a large amount of image information with the final new image is reasonable and meets the ultimate goals of human visual recognition and computer processing. The merged image should gradually contain complete data, becoming increasingly valuable for human or mechanical observation. The advantages of image fusion [1, 2] are improved reliability and reliability. In medical imaging, CT scan, attractive reverberation imaging, MRI, PET, SPECT and many more fields. Image processing method that reflects human data in different positions. In this article we will present and discuss the purpose of merging computed tomography images and magnetic resonance images. So far, several processes have been planned to merge the written images. Some techniques are identified through the merging of multimodal images. Image blending mainly controls three types such as pixels, features and decision-making techniques.

Due to its simplicity of execution and computational competence, the pixel-level image synthesis system is often used for merging medical images. That is why he is involved in the proposed work.

There are several essential requirements for the image fusion process [5]. The merged image must retain all significant sequence in the combination of input images, it must not be an initial object that could lead to misdiagnosis. First, incredibly important steps need to be taken. Procedure, Chronicle in pictures. Multimodal recording means the coincidence of the same scene received from different antennas. Corresponding characteristics, image listing methods can be divided into



three categories: point-based, exterior-based or size-based methods [6, 5, 9]. In point-based verification, the coordinates of the associated position are determined in special images, and these corresponding points are used to estimate the geometric transformation. Verification of the external medium consists of determining surfaces of images that fit together and minimizing the measurement of the space in the middle of this resulting plane. Volume based registration requires data optimization that takes into account some predefined characteristics that measure the agreement of all geometrically resulting voxel connections. Some image fusion methods have been introduced in the literature, with effortless point-to-point averaging using SNR (signal to noise ratio) [11].

Related Work

Image processing technology plays an important role in medicine. The automation of computer processing is the most real and well-known method. Brain diseases can be detected by magnetic signs (MRI) and (PET). Additional variants of MRI and PET scan have been used for medical diagnosis. Medical experts need a solid computer review and associated analysis. In various imaging procedures, i. H (CT), (PET) and MRT), accurate information is obtained for disease assessment and effects. In image output, image merging is a method of merging two images into a single image.

Compared to the original single scan image, the single fusion image obtained using multiple multimodal medical images is an improved anatomy with ideal spectral information [14]. This multimodal fusion framework is positive for experimental analysis by healthcare professionals. In doing research work; the facility is adapted to provide magnetic resonance or PET imaging. Preprocessing techniques improve the quality of inserting photos, making them unreadable. For the preprocessing method, we apply a Gaussian filter with spatial filter technology. The upper image is transferred through the (DWT) to the blending of dissimilar areas of the main image. This structure achieves approximately 90-95% of perfect results due to changes in color tone. Fusion images were obtained solely behind ethereal or anatomical records. The experiment checked for image data of Alzheimer's disease, mean affiliation, or regular coronary syndrome. Measuring and Charting Inbound (DWT) can greatly enhance rendered merged images.

Medical Image Fusion

Multimodal medical imaging algorithms and devices have shown that the accuracy of medical image-based decision making has been clearly recognized in evolution. The choice of the imaging model for the objective clinical study requires medical knowledge specific to the research structure. It is nearly impossible to lock in the factor of an imaging modality to ensure medical accuracy and robustness in analysis and analysis of results. (a) Identification, improvement and development of imaging techniques useful for medical image fusion (b) Development of different medical image fusion technologies (c) Applications of medical image fusion to study human concentration organs in the assessment of medical conditions.

Image fusion methods

There are many methods for image fusion applications [13], but image fusion technologies are basically divided into two categories, namely spatial domain fusion methods and transformation

domain merging methods. These explanations are as follows: (I) Spatial Domain Fusion Technology. In spatial domain technology, we process image pixels directly. Manipulate the pixel values to achieve the desired result. These techniques are based on grayscale mapping, and the type of mapping used depends on the criteria selected for improvement. The disadvantage of spatial domain methods is that they create spatial distortions in the merged image.

(II) Transformation-based fusion technology or frequency domain technology is based on the orthogonal transformation operation of the image, not the image itself. The domain transformation technology is suitable for image processing based on frequency content.

Recommended Approach

Image fusion based on the wavelet transform. The original concept and theory of wavelet based multi-resolution analysis comes from Mallat.

The Wavelet transform is a numerical instrument capable of detecting local characteristics in the signal procedure. It can also be used to analyze two-dimensional (2D) signals (such as 2D grayscale image signals) at different resolution levels for multi-resolution analysis. Wavelet transformation has been used extensively in numerous fields such as texture analysis, data compression, feature detection, and image blending. In this section, we briefly analyze and evaluate wavelet-based image fusion techniques. $I(x, y) = W^{-1}(\emptyset(W(I_1(x, y)), W(I_2(x, y)))$

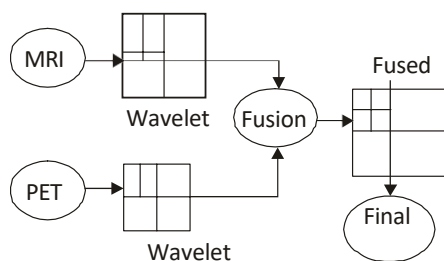


Figure 1. Image Fusion using discrete wavelet transform.

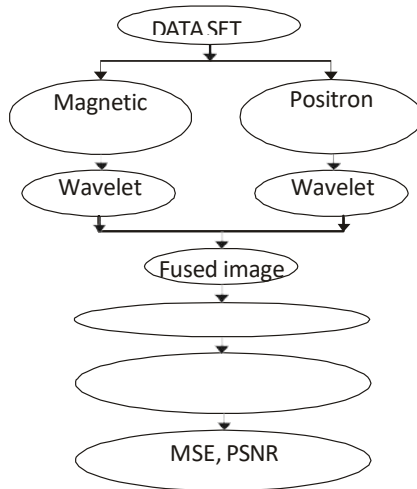
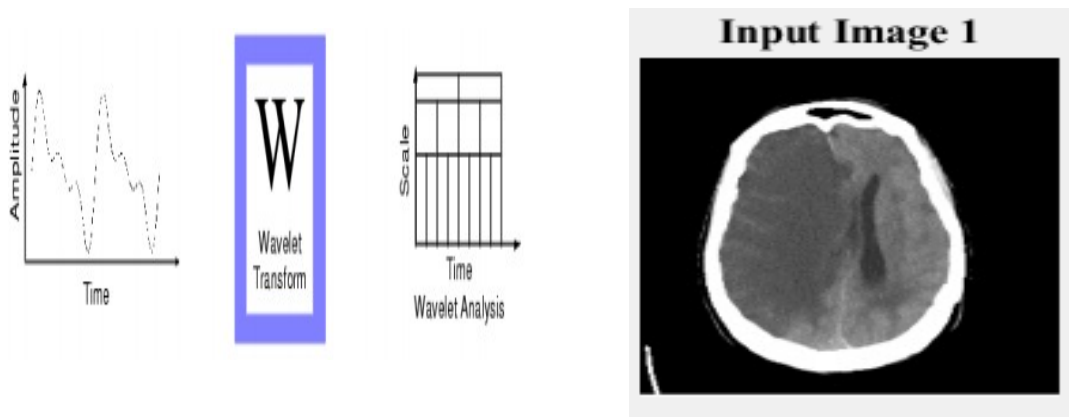


Figure. 2. Proposed flow chart [12].

Wavelet Transformation. Wavelet search corresponds to the next logical step: windowing techniques with regions of different sizes. Wavelet analysis allows you to use longer time intervals where a more accurate sequential low rate is required and shorter time intervals that can be used in areas where a high sequential rate is required. In a (1D) measurement, the basic idea of DWT is to represent a signal as a superimposed wave.



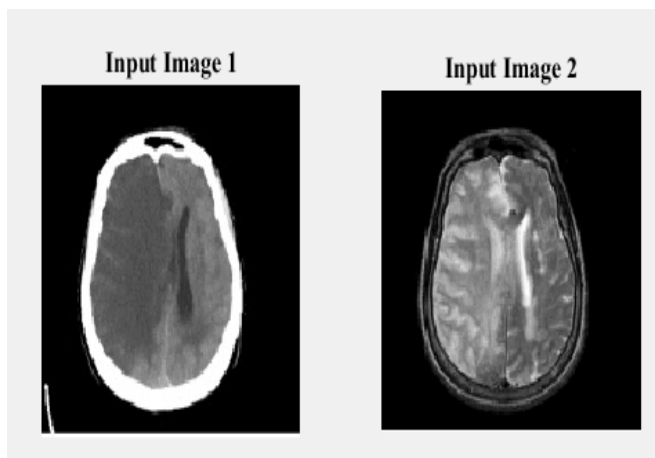
Algorithm. The following algorithm was developed and implemented in MATLAB software.
 Not:

1. Read figure I1 and find its size.
2. Read the second image I2 and find the dimension.
3. Calculate and match the size, if it is not the same, make it the same.
4. Convert both grayscale images to indexed images to perform various wavelet functions. If the color map is horizontal, the wavelet transform can be overtly applied to the indexed representation, otherwise the indexed image must be converted to a grayscale format.

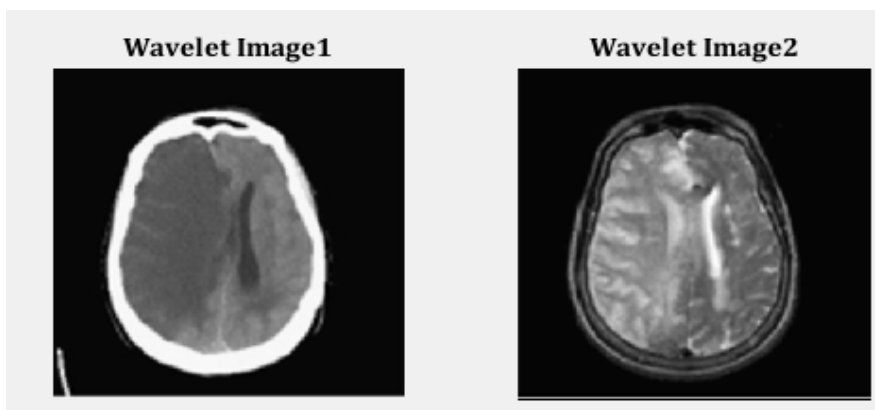
5. Perform a multi-level wavelet decomposition using an arbitrary wavelet (Haar).
6. Generate the level three approximation coefficient matrices and the horizontal, vertical and diagonal details.
7. Construct and visualize approximations and details of the coefficients.
8. Generate an image using multilevel inverse wavelet transform.
9. Repeat the same with the second image.
10. Now join the wavelet coefficients using an average, maximum or minimum technique.
11. Generate a final array of fused wavelet coefficients.
12. Calculate the inverse wavelet transforms to obtain the fused image.
13. Finally it calculates PSNR and MSE and displays the results.

Results

We considered wavelets, especially hair, to merge PET and MRI images. With the merger, rules were put in place. Since the Haar wavelet associated with the maximum rule gave better results in terms of PSNR and MSE, they were used for further analysis. The two input images are read first and converted to indexed images. After that, wavelet decomposition is performed to find approximate, horizontal, vertical and diagonal details. The level of decomposition and the type of wavelet used are specified.



DWT is then performed on the input images. The coefficients found are then fused using a specific fusion rule and then the images are restored back using inverse discrete wavelet transform.



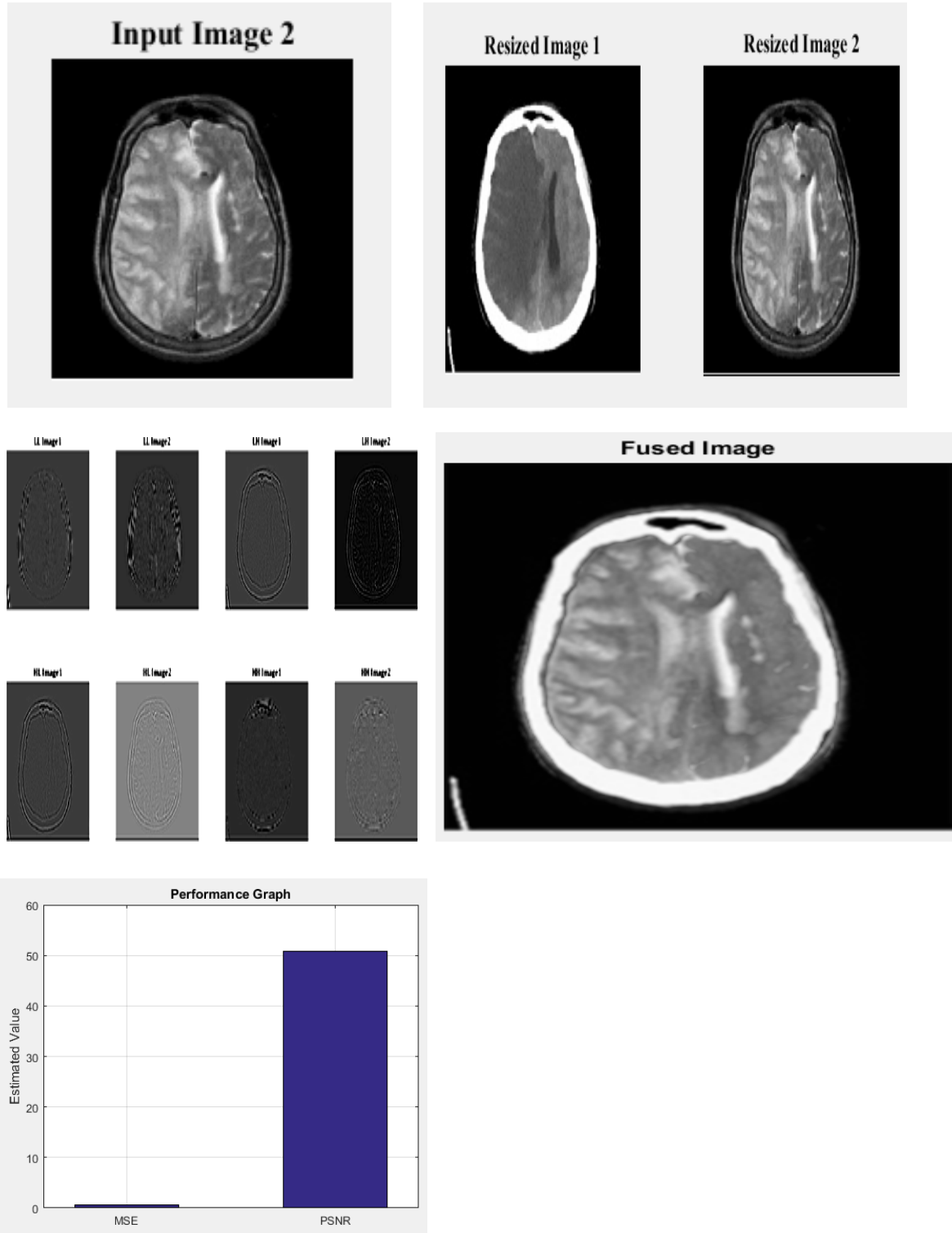


Table 1: Performance measure based on PSNR, MSE of the output Fused Image.

Data set	Previous work	Proposed work
PSNR	43.12	50.10
MSE	0.012	0.012

Conclusion

This article proposes a wavelet-based fusion method for MRI and PET images. The wavelet decomposition of the data set will be divided into four levels, with active areas low and high, respectively. This experiment will test the haar wavelet method. Haar's wavelet is used to merge the database of multiple 3D medical models. The preprocessing method will apply a Gaussian filter of spatial filtering technology, using MSE and PSNR to test the quality of the merged image.

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POLYPEPTIDE THERAPY FOR EPILEPSY

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ABSTRACT

Goal: Investigate the role of cortexin in stopping and achieving remission of seizures in epilepsy.

Material and methods: 47 patients with various forms of epilepsy were examined at the reception of a neurologist of the polyclinic department of the United City Hospital No. 7 during 2020-2021. To assess the psycho-emotional status, the Ziqmond scale was used. As a means of increasing stress resistance, cortexin was used. Statistical calculations of qualitative parameters were carried out using the Fisher criterion. The results are presented at the level of reliable significance $p < 0.05$.

Results and discussion: Psycho-emotional status, determined by the Ziqmond scale before treatment with cortexin, was rated low in all patients (6.91 ± 0.13 ; $m = 4$, $M = 11$), and in female patients statistically significantly lower (8.05 ± 0.32 ; $m = 6$, $M = 13$) than in male (8.83 ± 0.21 ; $m = 5$, $M = 12$), ($p = 0.046$). During the study period (1 year), in 36 patients (31 cases from the group taking cortexin and 5 cases from the placebo group), seizures did not recur. The study proved a fairly high (83.78%) effectiveness of cortexin in improving the mental and emotional states of patients with epilepsy didn't repeat themselves.

Conclusions: The inclusion of cortexin in the interictal period in the treatment regimen allows you to achieve a thymoleptic effect and prolong the remission of epileptic seizures.

Keywords: polypeptide therapy, psycho-emotional status, cortexin, neuropeptides, epilepsy.

Introduction

Polypeptide therapy is the parenteral administration of medicines based on analogues of natural regulatory peptides of human and animal embryos (bovine, pig) into the body. The priority use of polypeptide therapy methods in the healthcare system may lead to the activation of treatment regimens for existing key nosologies, effectiveness in therapy, recovery and rehabilitation of patients. The role of polypeptide therapy in stopping and achieving remission of seizures in epilepsy is very important. [1, 2]

Epilepsy is one of the most common neurological disorders affecting about 70 million people worldwide. In some cases, epilepsy has a genetic etiology, while in others, triggering events such as head trauma, inflammation, stroke, tumors, or long-term febrile seizures in childhood lead to the development of epilepsy. [4] The main characteristic of epilepsy is the occurrence of recurrent unprovoked seizures. These seizures are the result of excessive electrical discharges in a group of neurons. Antiepileptic drugs suppress seizure activity and thus significantly improve the quality of life of patients with epilepsy. Unfortunately, currently only two-thirds of patients achieve good seizure control with pharmacological treatment. Therefore, new drugs are needed to improve the effectiveness of epilepsy pharmacotherapy. [3]

Scientists have found that seizures are caused by an imbalance in the delicate balance between inhibition and excitation in the brain. This imbalance is facilitated by two main "players" at the level of neurotransmitters: the inhibitory transmitter GABA and the excitatory transmitter glutamate. Neuropeptides are potent modulators of these classic neurotransmitters. They either alter their release or regulate their effects at the receptor level, and therefore may influence the balance between inhibition and excitation. In recent years, scientists have discovered numerous neuropeptides in the plasma, cerebrospinal fluid, and resected tissues of patients with epilepsy and in various animal models of seizures. Therefore, these neuropeptides and their receptors are attractive targets for the development of new antiepileptic drugs. [1]

Table №1. Neuropeptides affecting seizures in epilepsy.

NP with proconvulsive effect	NP with anticonvulsant effect	NP with pro- and anticonvulsant effect
arginine vasopressin	ACTH	oxytocin
enkephalin	angiotensin	melanin-concentrating hormone
endorphin	cholecystokinin	nesfatin-1
pituitary adenylate cyclase activator	cortistatin	vasoactive intestinal peptide
tachykinins	dynorphin	
arginine vasopressin	galanin	
enkephalin	ghrelin	
endorphin	neuropeptide Y	
pituitary adenylate cyclase activator	neurotensin	
tachykinins	somatostatin	
arginine vasopressin	Thyrotropin-releasing hormone	

To this end, it is very important to provide information about new opportunities in medicine not only to scientists, researchers, but also to practicing doctors, introducing them to discoveries in the field of biomedical technologies (Table № 1). Currently, one of the few neuropeptide drugs available for use in therapy is Cortexin. The main tissue-specific property of the drug is manifested by neuroprotective, neuromodulatory, nootropic and anticonvulsant effects. The cerebroprotective effect of Cortexin is associated with a decrease in cytotoxic cerebral edema in acute and chronic neuronal damage and a decrease in the possible toxic effects of neurotropic substances.

Objective

To study the role of cortexin in the relief and achievement of remission of seizures in epilepsy.

Material and methods

In the period from 2020 to 2021, 47 patients with various forms of epilepsy were examined at a neurologist's appointment at the outpatient department of the United City Hospital No. 7. The study included male and female patients in the age range from 15 to 45 years. The study was conducted in the interictal period during drug remission for more than 6 months. The Ziqmond scale was used to assess the psychoemotional status. Cortexin at a dose of 10 mg (37 patients) was used as a means of increasing stress resistance, and a solution of sodium chloride 0.9% - 2 ml was used as a placebo (10 patients). Cortexin was administered intramuscularly according to the scheme: daily for 10 days, then every other day (5 ampoules in total) and 2 days later (5 ampoules in total). Statistical calculations of qualitative parameters were carried out using the Fisher

criterion. Correlation analysis was carried out using Pearson's rank correlation coefficient. The results are presented at a significance level of $p < 0.05$.

Results and discussion

The psychoemotional status, determined by the Ziqmond scale before treatment with Cortexin, was assessed low in all patients (6.91 ± 0.13 ; $m=4$, $M=11$), and in female patients it was statistically significantly lower (8.05 ± 0.32 ; $m=6$, $M=13$) than in the male (8.83 ± 0.21 ; $m=5$, $M=12$), ($p=0.046$) (Table № 2).

Table №2. The psychoemotional status before treatment with Cortexin

Patients	Psychoemotional Status	p
Male	8.83 ± 0.21 ; $m=5$, $M=12$	
Female	8.05 ± 0.32 ; $m=6$, $M=13$	
All	6.91 ± 0.13 ; $m=4$, $M=11$	0.046

In most patients, subclinical (8-10 points) (22 (59.4%) cases) and clinical (>10 points) depression and anxiety (11 (29.7%) cases) prevailed. An acceptable level of anxiety and depression (0-7 points) was observed in 4 (10.8%) male patients.

Table №3. The psychoemotional status after treatment with Cortexin

Ziqmond scales points	Result, according to the Ziqmond scale before Cortexin	Result, according to the Ziqmond scale after Cortexin	All result	p
0-7	4 (10.8%)	27 (72.9%)	31 (83.78%)	0.021
8-10	22 (59.4%)	18 (48.6%)	4 (10.8%)	
10>	11 (29.7%)	9 (24.3%)	2 (5.4%)	
Placebo result	5 (50%) – 0-7 points			0.034

After applying Cortexin on day 25, the number of patients in the group with subclinically and clinically significant levels of anxiety and depression decreased. 18 (48.6%) patients with 8-10 points of anxiety and depression and 9 (24.3%) -> 10 points could calmly overcome the feeling of fear of a possible convulsive seizure, a dull and dreary state, more often associated with constant taking an antiepileptic drug. As a result, according to the Ziqmond scale, in 27 (72.9%) patients with epilepsy on the 25th day after the application of cortexin, the psycho-emotional level was assessed in acceptable units - 0-7 points ($p = 0.021$). During the study period (1 year), 36 patients (31 cases in the Cortexin group and 5 cases in the placebo group) did not relapse. In the placebo group, only 5 (50%) ($p = 0.034$) patients had an acceptable level of anxiety and depression by this day. These were patients with comparatively less frequent epileptic seizures. The conducted study proved a rather high (83,78%) effectiveness of cortexin in improving the mental and emotional state of patients with epilepsy (Table № 2).

Conclusions

Thus, the inclusion of cortexin in the interictal period in the treatment regimen allows achieving a thymoleptic effect and prolonging the remission of epileptic seizures.



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INVESTIGATION OF ALLERGEN SENSITIVITY OF SYRIAN REFUGEE CHILDREN WITH ALLERGIC DISEASES

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ABSTRACT

Background: The aim of this study was identification of the allergic sensitivities of Syrian refugee children residing in Western Turkey and diagnosed with various allergic diseases.

Materials and methods: Syrian refugee children younger than 18 constituted the target population of this study. A group of patients were assigned to the control group. The levels of total immunoglobulin E, A, G, M, eosinophil counts and percentages, and the results of inhalant and food allergy tests of patients and controls were all recorded.

Results: The entire study cohort consisted of 34 patients (23 boys, 11 girls) in the study group and 30 patients (20 boys, 10 girls) in the control group. There were statistically significant relationships between patients and controls about eosinophil counts and percentages ($p=0.005$, $p<0.0001$, respectively).

Conclusion: Our study is the first report investigating the allergic sensitivities of Syrian children to the best of our knowledge. We believe that our findings will enlighten the approach of the clinicians taking care of Syrian children in different countries hosting Syrian refugees.

Keywords: inhalant allergen sensitivity, food allergen sensitivity, Syrian refugee, allergic disease

Introduction

The incidence of allergic diseases increased significantly in developing countries during the last decades (1). Therefore, the demand for allergy tests also increased. Since specific allergy diagnosis is required to determine the optimal anti-allergic treatment, the performance of the appropriate allergy tests is mandatory (1,2). It is known that most allergic responses are mediated by immunoglobulin E (IgE), and specific, and total IgE tests are useful in both diagnostic management and treatment of childhood allergic diseases (3). It was reported in population-based studies that the prevalence of asthma was 7-10%, while the prevalence of atopic dermatitis, allergic rhinitis, and conjunctivitis were 15-20% (1-2).

Due to the civil war started in Syria in 2010, four million refugees have taken refuge in our country so far, 1.74 million of them are children (4). The aim of this study was identification of the allergic sensitivities of Syrian children refugees residing in Western Turkey and diagnosed with various allergic diseases in our department. In this way, we believe that Turkish doctors can increase their knowledge on allergen sensitivities and allergic diseases of Syrian children.

Materials and Methods

This study was approved by the Ethical Review Committee of İzmir Tepecik Training and Research Hospital (approval date and no: 2019/12-13). Syrian refugee children younger than 18

who were referred to the same institution's pediatric allergy or dermatology outpatient clinics with suspicion of allergic disease between September 2019 and March 2020 constituted the target population of this study. Among these patients, those diagnosed with an allergic disease were included in the study group, while patients with a positive stool parasite test, systemic disease, or diffuse skin eruptions were excluded. A group of patients with similar age and gender distribution were assigned to the control group. These patients, who were also Syrian refugees, did not have an allergic disease, atopy, a history of atopy, systemic disease, or diffuse skin eruption. They all had negative stool parasite tests, inhalant allergies, and food allergies. The levels of total IgE, immunoglobulin A (IgA), immunoglobulin G (IgG), immunoglobulin M (IgM), eosinophil counts and percentages, the results of inhalant and food allergy tests were all recorded. The inhalant allergy test was performed as a skin prick test (ALK-Abello, Prick-test diagnostic, Madrid) in children older than two years, while food allergy tests were performed in all children by the prick-to-prick technique.

Statistical analysis

The power analysis was performed by G-Power 3.1.9.4 software, while Statistical Package for Social Sciences (SPSS v17.0, IBM Corp. Armonk, NY, US) software was used for all other statistical analyses. Data were analyzed using the independent t-test and Spearman's test. The p value was considered significant when it was lower than 0,05.

Results

The entire study cohort consisted of 34 patients in the study group and 30 patients in the control group. There were 23 (75%) boys and 11 (25%) girls in the study group, while there were 20 (66.6%) boys and 10 (33.3%) girls in the control group. Mean patient ages were 4.89 ± 4.17 and 5.83 ± 3.46 in the study and control groups, respectively. There was no significant difference between the groups in this regard ($p=0.28$). Among the 34 patients in the study group, 29 were diagnosed with asthma, 2 with atopic dermatitis, 2 with allergic rhinitis, while one patient had allergic and dietetic gastroenteritis and colitis. There were 11 patients with only inhalant allergy, four patients with only food allergy, and one patient was diagnosed with food and inhalant allergies. All other data are displayed in the tables 1 and 2.

Discussion

The rates of IgE-mediated allergies were reported to be as high as 25% in industrialized countries (5). It is known that the frequency of exposure to allergens is critical in the pathogenesis of allergic disorders; the risk of allergic disease increases by increased exposure frequency. During this process, the secretion of interleukin (IL) 4, IL5, and IL13 is induced from Th2 cells (5,6). These cytokines stimulate IgE production and eosinophil activation, which lead to clinical symptoms. Our study detected significantly higher total IgE levels in the study group than the control group (table 1). Since eosinophil counts and percentages were significantly higher in the former group than the latter, we suggest that assessment of eosinophil counts and percentages is as essential as evaluating total and specific IgE level measurements in the management of patients with allergic disorders (table 1).

Table 1. Laboratory findings of patients and controls.

Parameters (normal range)	Patient	Control	P
Count of eosinophil (0 – 0.7 x10 ³ /uL)	0.46 ± 0.41	0.23 ± 0.22	0.005*
Percent of eosinophil (0 – 7 %)	4.95 ± 3.53	2.47 ± 1.92	< 0.0001*
Total IGE (0 – 90 IU/ml)	316.59 ± 485.52	97.34 ± 170.56	0.007*
IGA (0.7 – 4 g/L)	0.98 ± 0.8	3.29 ± 10.73	0.21
IGG (7 – 16 g/L)	8 ± 3.34	23.6 ± 80.84	0.26
IGM (0.4 – 2.3 g/L)	1.46 ± 1.55	3.01 ± 12.3	0.41

Table 2. The results of inhalant and food allergy tests of the patients

Allergy tests	Patients (n/%)
Inhalant allergy	12 / 35.29
Alternaria	1 / 2.94
Olea europeae	1 / 2.94
Chenopodium	1 / 2.94
Polens	2 / 5.88
D. pteronyssinus	6 / 17.64
D. farinae	6 / 17.64
Cat	7 / 20.58
Dog	2 / 5.88
Parietaria	1 / 2.94
Food allergy	5 / 14.7
Egg yolk	2 / 5.88
Egg white	3 / 8.82
Cow milk	2 / 5.88
Peanut	2 / 5.88

Values are presented as mean ± standard deviation. IGE: immunoglobulin E, IGA: immunoglobulin A, IGG: immunoglobulin G, IGM: immunoglobulin M. * $p \leq 0.05$

On the other hand, we did not determine an association between total IgA, IgG, and IgM levels and allergic diseases in our study. It is important to note that these immunoglobulins' levels were lower in the study group than the control group without any statistical significance. Further studies conducted with more extensive patient series may reveal more significant findings in this regard. Wang et al. worked on 930 children, and they found a significant relationship between the rate of bronchial asthma and relatively high IgE levels (7). Similarly, Chauveau et al. included 529 patients in their study and concluded that allergic disorders were significantly related to increased serum IgE levels (8). Eng and DeFelice investigated the relationship between allergic diseases and eosinophil counts, and they found a significant association (9). In Jenkins et al.'s study, researchers found that allergic stimuli led to eosinophilia and increased total IgE levels (10).

Food allergy can be part of the clinical picture in some allergic disorders. Types of food allergy can be divided into two as IgE-mediated and non-IgE mediated. While cow milk, chicken egg, hazelnut, wheat, soy, fish, shellfish, sesame and kiwi can cause IgE-mediated allergic reactions, non IgE mediated food allergens are cow milk, soy, wheat and chicken egg mostly (11). The most frequent food allergens were chicken egg, cow milk and peanut in our series (table 2). Peters et al.

reported in a study including 2800 patients that the rate of food allergy was 10% in children aged 1 year (12). However, some other studies reported its prevalence as 1-6% (13, 14). This study revealed that there were significant relationships between food allergy and eczema in children at 1 year or 4 year of age ($p=0,001$ and $p=0,03$). It also showed that there was a significant association between food allergy and asthma diagnosed in children at the age of 4 ($p=0.04$). In the study of Peters et al (12), the most frequent allergens were cashew, hazelnut, cooked eggs, almond and cow milk. Among the children at the age of one, 23% were children with eczema and food allergy. On the other hand, among the children at the age of four, 3% were children with eczema, asthma and food allergy. Six percent of the children aged 4 had both asthma and food allergy (12). Senol and Koksall worked on 79 patients and reported that the most frequent allergens they encountered were cow milk (46,8%) and egg (27,8%) (15). Thirty-eight patients were diagnosed with atopic dermatitis, 15 with food protein-induced enteropathy, 7 with anaphylaxis, 5 with proctocolitis, 9 with urticaria/angioedema, 3 with food protein-induced enterocolitis, 1 with allergic rhinitis and 1 with wheezing child. Yardimci et al. reported that the rates of asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, urticaria, bronchial asthma and medication allergy were 10,9%, 10,2%, 3,9%, 4,3%, 2%, 6,4% and 1,7%, respectively (16). Additionally, the rates of combinations such as asthma-allergic rhinitis-allergic conjunctivitis and allergic rhinitis-allergic conjunctivitis was reported as 2,4% and 2%, respectively (%2,4). These authors also stated that bronchial asthma (47.8%), asthma (10%), allergic rhinitis (9.1%), atopic dermatitis (5.7%), allergic conjunctivitis (3.6%), urticaria (2.3%), medication allergy (2.3%), combination of allergic rhinitis+allergic conjunctivitis (2.5%) and combination of asthma-allergic rhinitis-allergic conjunctivitis (2%) were detected in children who were afflicted by food allergy for at least once during their past medical history. Thus, this study concluded that food allergy might be associated with other allergic disorders.

Sensitivity to inhalant allergens is usually detected in children after the age of one (17). De Jong et al. worked on 512 Dutch children aged up to 10 years and reported that children with eczema, asthma, or familial history of allergic disorders had a higher risk of sensitivity to inhalant allergy (18). These researchers stated that house dust mites (8%), cat hair (5%), and dog hair (3.5%) were the most frequent allergens. In this study, it was also detected that the risk of developing sensitivity to inhalant allergens was lower in girls than in boys. In line with De Jong et al., some other authors reported that house dust mites, cat hair, and dog hair were the most commonly encountered inhalant allergens in their series (18-22). Our study also detected a higher sensitivity to inhalant allergens in boys than girls, and our analysis revealed that *D. pteronysinus*, *D. Farinea*, cat hair, and dog hair were the most common culprits. In another study conducted with Polish children at the age of 7, it was reported that the rates of allergy to house dust mites and grass pollens were as high as 13,5% and 11,8% (23). The differences in these studies' results were ascribed to ethnicity's impact on the risk of developing sensitivity to inhalant and food allergies (24).

In a Turkish study, Kilic and Taskin included 786 children with asthma, and they detected that mixed grass pollens (44.5%), grain pollens (42.7%), *D. pteronysinus* (38.5%), *D. farinea* (37%), and mushroom extract (20,6%) were the most common inhalant allergens (25). In another Turkish report presented by Elmas and Ozdemir, 623 children diagnosed with allergic rhinitis were investigated (26). These authors noted that grass (66.4%), house dust (51.2%), tree pollens (20.8%), and mold allergy (7.6%) were detected as the main inhalant allergens in their series. Altogether, it can be suggested that different inhalant allergen sensitivity rates were detected in



different patient groups. This finding supports the hypothesis that ethnicity has a significant impact on the development of inhalant and food allergy in children. The fact that different results were obtained in the allergic sensitivity tests performed in children with different allergic disorders from different parts of the world also supports this hypothesis.

Our study is the first report investigating the allergic sensitivities of Syrian children to the best of our knowledge. We believe that our findings will enlighten the approach of the clinicians taking care of Syrian children in different countries hosting Syrian refugees.

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$$f(x) = a_0 + \sum_{n=1}^{\infty} \left(a_n \cos \frac{n\pi x}{L} + b_n \sin \frac{n\pi x}{L} \right) \quad (1)$$

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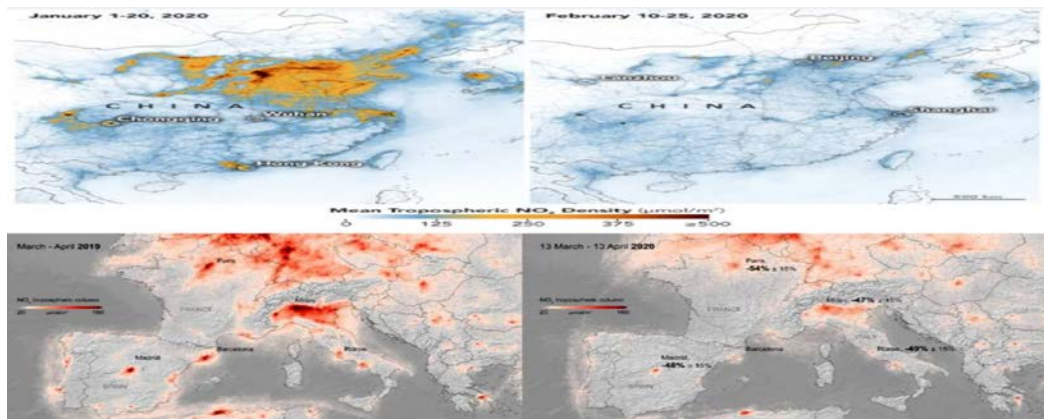


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6. M. Ahmad, “Importance of Modeling and Simulation of Materials in Research”, J. Mod. Sim. Mater., vol. 1, no. 1, pp. 1-2, Jan. 2018. DOI: <https://doi.org/10.21467/jmsm.1.1.1-2>

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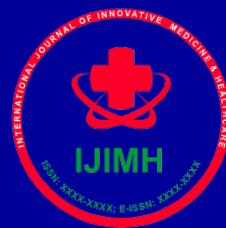
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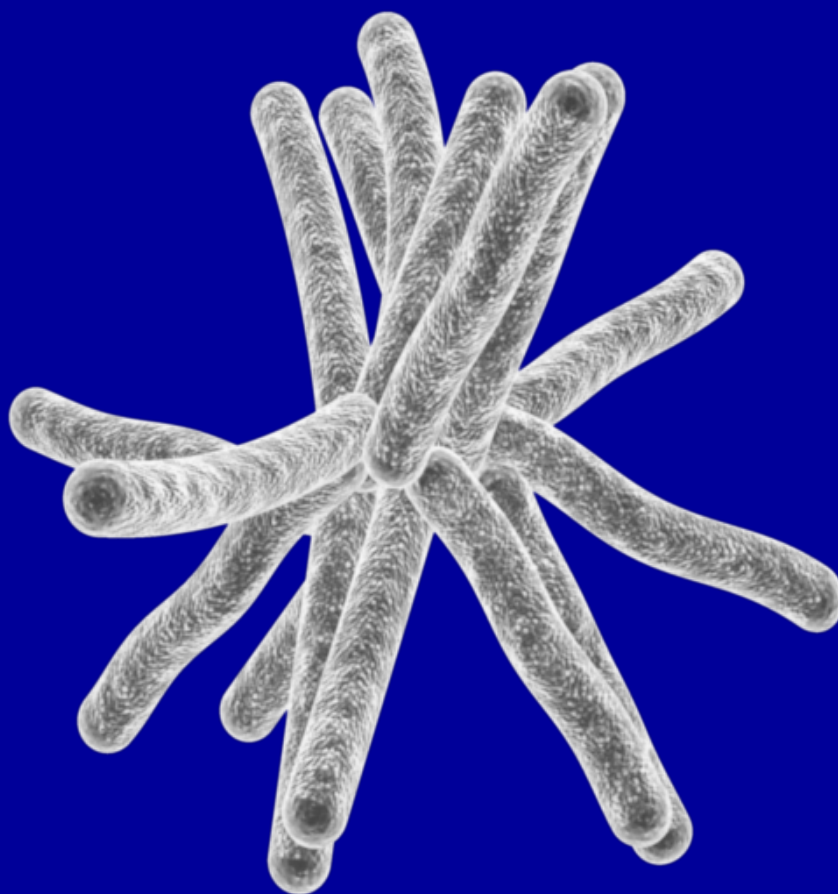
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