Aging Research Institute Newsletter

Tabriz University of Medical Sciences (TUOMS)

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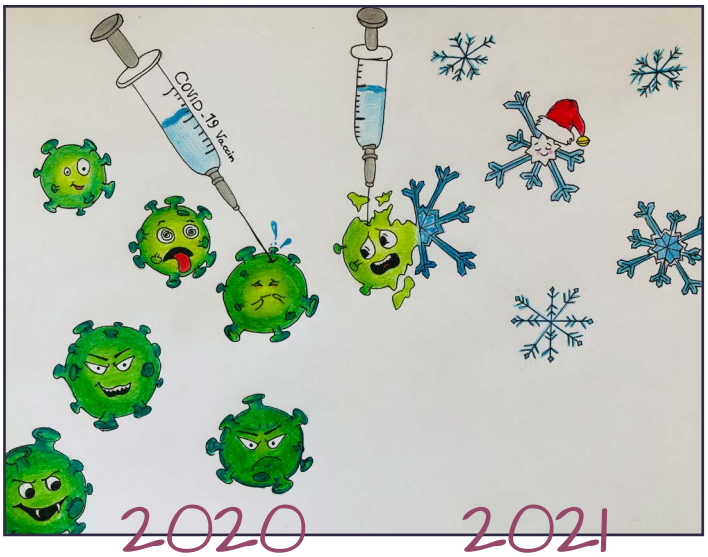
Happy 2021
New Year



Sketch: Negar Bonyadi, Medical Student at Tabriz University of Medical Sciences.

Supreme Leader Representation Message

Position of the Elderly in Islam

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While aging is a stage of life that refers to a certain age in different countries; it still relates to the gradual decay in the body's structures and function due to finite time of life which causes changes in various organs' structure and function. Its symptoms are different in multiple humans. The elderly have an impressive dignity and status in religious culture, and respecting their rights have been strongly recommended.

In the Holy Qur'an, God says about Prophet Moses (PBUH) and the daughters of Shu'ayb (PBUH) and the esteeming of their elderly father: "And next to them, he found two women who prevented their sheep from entering the water. He said to them: What are you doing? They said: Our manner is not to water the sheep so that the shepherd come out of the fountain and take their sheep out of it. Our father is an old man, and he can not bring our sheep here by himself (surah Al-Qasas, verse 23) " .

Elsewhere, the Holy Qur'an describes the actions of the sons of Ya'qub (PBUH) to rescue their brother Benjamin from the Potiphar's jail. They said to Potiphar: “he has an aged father. Please pick one of us instead” (Surah Yusuf, verse 78). They wanted to use elders' respect to free their brother or replace him with another.

The position of the elderly in Islam is very high. The Holy Prophet, Mohammad (PBUH),said: “The elderly among their families are like the Prophet among his nation”. Imam Zayn al-Abidin (AS) said: “Your confreres' right is that in your point of view, their elders are as same as your fathers, their youth are considered as your brothers and their aged ladies are also considered as your mother and their children are like your kids”.

Imam Ali (AS) emphasized the sanctity of elders and in his will to Imam Hassan (AS) mentioned : “Be kind to the young people of your family and respect the elderly”. Respecting the elderly is an accepted human endeavor among all humanity and an important religious issue in religions. Society has duty to reverence the elderly and commemorate them. Healthcare systems should not only respect our lovely elders, but also ensure to do their best to provide their health and their convenience as their health issues are one of the most critical concerns. Health means providing complete physical, mental, and social well-being, since the World Health Organization in 1997 added the spiritual dimensions in the definition of health. Health is approved as a dynamic state of providing complete physical, mental, social, and spiritual well-being and not just the absence of disease and disability.

In Islamic beliefs, health is a multifaceted topic and its different aspects are dependent on human existence. Therefore, it includes all physical, psychological, social and spiritual aspects, and if we consider health as a comprehensive concept that can effect all the people around the world, this could be an approach to lead the people toward perfection.

For the dear elderly, all aspects of health, especially its spiritual and psychological aspects are the most important of all because having a belief in what the life is, the world's beautiful discipline governing the whole systems in the world, and the superior power will give a profound concept to one's life. This belief is an essential component of mental health; having a faith in all these beliefs, the human soul transcends the individual, forgives and deals with others' needs more than its requirements. Nurturing the soul results in reducuction of human suffering. Communication with the Supreme Creator through worships, rituals, and relidiouse ceremonies give a new meaning to one's life. Spiritually healthy people have fundamental goals in their lives. They have learned how to feel love, happiness, peace, and spiritual richness and help themselves and others achieve their capacities.

Spirituality can help promote mental health and improve quality of life. Alexis Carrel belives that the need for praise and worship is one of the foundamental requirements rooted in human nature, and not responding these needs can cause tension in an individual. The elderly who do not have spiritual life suffer from anxiety, depression and God refers us to this fact in verse 124 of Surah Taha: "Whoever turns away from the remembrance of Me, will live in stricture".

It should be noted that sometimes poor livelihood is not necessarily because of low income, since people may have a lot of money and income, but if they are stingy and greedy for life, they would not want to be merciful to others, not only themselves. The stricture of life is more due to spiritual deficiencies and lack of spiritual richness and also due to uncertainty about the future and fear of the destruction of available facilities, and excessive dependence on the material world. Who believes in God and trusts him is prevented from all these concerns. It is hoped that the elderly will experience a calm and relaxed life by following the spiritual and mental health instruction.

Keywords: Elderly; Aging; Islam.
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COVID-19

A glance on the published articles about aging

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Globally as December 2020, there have been over 65,870,000 confirmed cases of COVID-19, including over 1,520,000 deaths, reported to WHO. Populations are generally susceptible to new coronavirus, but elderly people with underlying diseases are more susceptible. Different studies on patients with confirmed new type of coronavirus pneumonia found that almost a quarter of the infected people age over 60. Also In terms of mortality, the mortality rate of patients aged 60 years and over are significantly higher than that of patients under 60 years.

In this respect, Liu et al. intended to compare the clinical features of elderly and non-elderly patients with COVID-19. They conducted an extended descriptive study of the clinical characteristics of a total of 56 patients, 18 elderly patients and 38 young patients, with severe referrals from other hospitals to the Hainan General Hospital of China. The differences between elderly COVID-19 patients and young and middle-aged patients were analyzed, and information on in-hospital deaths was added.

During the study period, the most common symptoms in both groups were fever, followed by cough and sputum. The Pneumonia Severity Index (PSI) score of the elderly group was higher than that of the young and middle-aged group (P < 0.001). The proportion of patients with PSI grade IV and V was significantly higher in the elderly group than in the young and middle-aged group (P < 0.05).

The proportion of multiple lobe involvement in the elderly group was higher than that in the young and middle-aged group (P < 0.001), and there was no difference in single lobe lesions between the two groups. The proportion of lymphocytes in the elderly group was significantly lower than that in the young and middle-aged group (P < 0.001), and the C-reactive protein was significantly higher than in

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Review

Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients

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SUMMARY

Background: Due to the general susceptibility of new coronaviruses, the clinical characteristics and outcomes of elderly and young patients may be different.
Objective: To analyze the clinical characteristics of elderly patients with 2019 new-type coronavirus pneumonia (COVID-19).
Methods: This is a retrospective study of patients with new coronavirus pneumonia (COVID-19) who were hospitalized in Hainan Provincial People's Hospital from January 15, 2020 to February 18, 2020. Compare the clinical characteristics of elderly with Young and Middle-aged patients.
Results: A total of 56 patients were enrolled 18 elderly patients (32.14%), and 38 young and middle-aged patients (67.86%). The most common symptoms in both groups were fever, followed by cough and sputum. Four patients in the elderly group received negative pressure ICU for mechanical ventilation, and five patients in the young and middle-aged group. One patient died in the elderly groups (5.56%), and two patients died in the young and middle-aged group (5.26%). The PSI score of the elderly group was higher than that of the young and middle-aged group ($P < 0.001$). The proportion of patients with PSI grades IV and V was significantly higher in the elderly group than in the young and middle-aged group ($P < 0.05$). The proportion of multiple lobe involvement in the elderly group was higher than that in the young and middle-aged group ($P < 0.001$), and there was no difference in single lobe lesions between the two groups. The proportion of lymphocytes in the elderly group was significantly lower than that in the young and middle-aged group ($P < 0.001$), and the C-reactive protein was significantly higher in the young group ($P < 0.001$). The Lopinavir and Ritonavir Tablets, Chinese medicine, oxygen therapy, and mechanical ventilation were statistically different in the elderly group and the young and middle-aged group, and the P values were all <0.05.
Interpretation: The mortality of elderly patients with COVID-19 is higher than that of young and middle-aged patients, and the proportion of patients with PSI grade IV and V is significantly higher than that of young and middle-aged patients. Elderly patients with COVID-19 are more likely to progress to severe disease.

Since December 2019, some hospitals in Wuhan City, Hubei Province have successively found multiple cases of unexplained pneumonia with a history of South China seafood market exposure, which have now been confirmed as a new type of acute respiratory infection caused by a coronavirus infection. The coronavirus isolated from the lower respiratory tract of patients with unexplained pneumonia in Wuhan this time is a new type of coronavirus belonging to the genus β and named as a new type of coronavirus disease (COVID-19). As of March 2, COVID-19 has confirmed 80,175 cases in mainland China, and a total of 2915 deaths nationwide, with a case crude fatality rate of 3.63%. From the existing data, the mortality rate of new coronavirus pneumonia is lower than SARS-CoV (9.6%). And pneumonia caused by MERS-Cov (34%). New coronavirus populations are generally susceptible, but elderly people with underlying diseases are more susceptible. The underlying diseases are diabetes, hypertension, cardiovascular disease, and cerebro-vascular disease.[1] The elderly are more susceptible to severe illness and are admitted to the intensive care unit (ICU), and

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the young and middle-aged group (P < 0.001). There were no significant differences in white blood cell count, neutrophil ratio, procalcitonin, hemoglobin level, platelet, and serum creatinine in the two groups.

The ARDS in the elderly group was higher than that in the young and middle-aged group, and acute heart, liver,

and kidney function injuries were higher than those in the young and middle-aged group. The Lopinavir and Ritonavir Tablets, Chinese medicine, oxygen therapy, and mechanical ventilation were statistically different in the elderly group and the young and middle-aged group, and the P values were all < 0.05.

The new type of coronavirus mainly causes lung infections. Lung infections increase the burden on the heart. At the same time, it can lead to high blood sugar, which makes the infection control difficult. The characteristics of multi-system disease coexisting in the elderly lead to complicated and complex diseases. Multiple diseases affect each other. These factors make treatment in elderly, difficult.

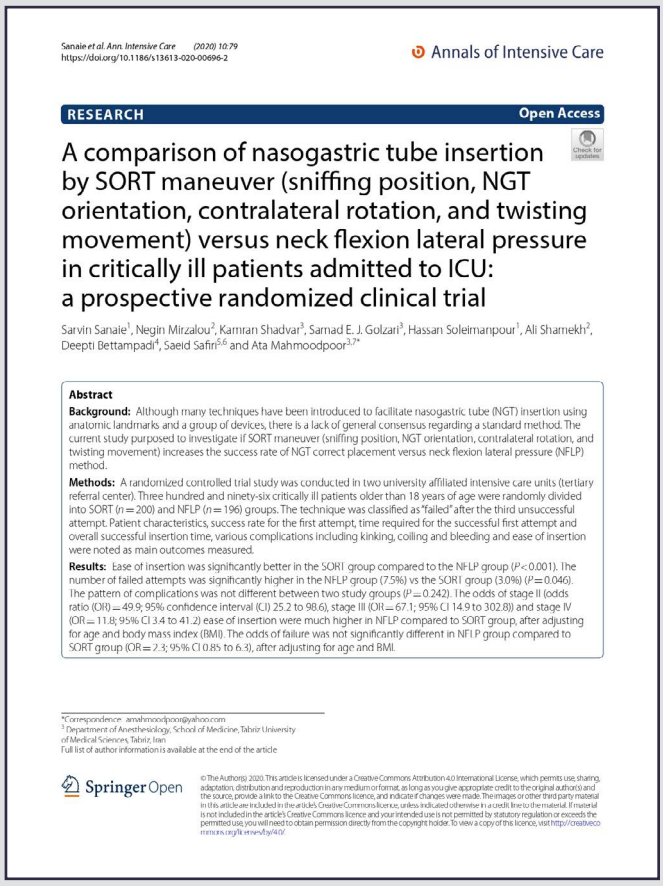
Because elderly patients are prone to multi-system organ dysfunction and even failure, other systemic complications should be prevented, including gastrointestinal bleeding, renal failure, disseminated intravascular coagulation (DIC) or deep vein thrombosis, delirium. For secondary infections, a multidisciplinary team approach is recommended.

However this study is limited by its small sample size and data selection from a single center which makes it susceptible to bias. It is recommended to conduct more studies with larger sample sizes and also more detailed information from patients to achieve better results.

Keywords: COVID-19; Aging; Pandemic.
Please cite this article as: Rahnemayan S. A glance on the published articles about aging. Aging research institute newsletter. 2021 January; 2 (4): 4-5.

Top Article

Congratulations to Dr. Sarvin Sanaie, Assistant Professor of Nutritional Sciences, TUOMS, on having her article entitled: "A comparison of nasogastric tube insertion by SORT maneuver (sniffing position, NGT orientation, contralateral rotation, and twisting movement) versus neck flexion lateral pressure in critically ill patients admitted to ICU: a prospective randomized clinical trial", published in Annals of Intensive Care (IF=4.124), which has been selected as the top article of this issue. Aging Research Institute expresses the warmest greeting to her.



Sanaie et al. Ann. Intensive Care (2020) 10:79
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Annals of Intensive Care

RESEARCH Open Access

A comparison of nasogastric tube insertion by SORT maneuver (sniffing position, NGT orientation, contralateral rotation, and twisting movement) versus neck flexion lateral pressure in critically ill patients admitted to ICU: a prospective randomized clinical trial

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Abstract

Background: Although many techniques have been introduced to facilitate nasogastric tube (NGT) insertion using anatomic landmarks and a group of devices, there is a lack of general consensus regarding a standard method. The current study purposed to investigate if SORT maneuver (sniffing position, NGT orientation, contralateral rotation, and twisting movement) increases the success rate of NGT correct placement versus neck flexion lateral pressure (NFLP) method.

Methods: A randomized controlled trial study was conducted in two university affiliated intensive care units (tertiary referral center). Three hundred and ninety-six critically ill patients older than 18 years of age were randomly divided into SORT ($n = 200$) and NFLP ($n = 196$) groups. The technique was classified as "failed" after the third unsuccessful attempt. Patient characteristics, success rate for the first attempt, time required for the successful first attempt and overall successful insertion time, various complications including kinking, coiling and bleeding and ease of insertion were noted as main outcomes measured.

Results: Ease of insertion was significantly better in the SORT group compared to the NFLP group ($P < 0.001$). The number of failed attempts was significantly higher in the NFLP group (7.5%) vs the SORT group (3.0%) ($P = 0.046$). The pattern of complications was not different between two study groups ($P = 0.242$). The odds of stage II (odds ratio (OR) = 49.9; 95% confidence interval (C.I) 25.2 to 98.6), stage III (OR = 67.1; 95% C.I 14.9 to 302.8)) and stage IV (OR = 11.8; 95% CI 3.4 to 41.2) ease of insertion were much higher in NFLP compared to SORT group, after adjusting for age and body mass index (BMI). The odds of failure was not significantly different in NFLP group compared to SORT group (OR = 2.3; 95% CI 0.85 to 6.3), after adjusting for age and BMI.

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Review Article

Biosensors for aging related disorders

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Abstract

Research and development of biosensors is becoming the most extensively studied discipline because the easy, rapid, low-cost, highly sensitive, and highly selective biosensors contribute to advances in next-generation medicines such as individualized medicine and ultrasensitive point-of-care detection of markers for diseases. Biomarkers are increasingly employed in empirical studies of human populations to understand physiological processes that change with age, diseases whose onset appears linked to age, and the aging process itself. Alzheimer's, Parkinson's and bone diseases are among the most important diseases related to aging. Each of these diseases has its own specific biomarkers. Identification of these biomarkers is one of the most important challenges in relation to geriatric diseases, so that their accurate and specific identification can play a very important role in the control and treatment of diseases. Major routine procedures include ELISA, Western blotting, calorimetry, and molecular-based tests such as PCR and real-time PCR. The need for advanced and expensive equipment, problem interpretation of the results, the need for specialized people as well as low accuracy and sensitivity are the main limitations of routine methods. Biosensors as inexpensive, simple and accessible tools with high sensitivity and specificity are among the modern and reliable methods for identifying biomarkers of various diseases. The main purpose of this article is to introduce these biosensors in diseases related to aging, including Alzheimer's, Parkinson's and bone diseases.

Introduction

Aging is an important period of life and today, due to rising life expectancy and declining birth rates in developed and developing countries, the phenomenon of aging has received more and more attention. Humans, for example, live longer than in the past[1]. As you know, increasing human life expectancy and increasing the elderly population is one of the achievements of the 21st century, and population aging is a phenomenon that some human societies have faced or will face. According to WHO theories, this phenomenon is due to the improvement of health conditions, which has led to the prevention of diseases and ultimately increased life expectancy[2]. Thus, population aging is actually a health success that will become a major challenge if not properly planned. Different diseases have their own markers, and diseases related to old age are no exception to this rule. Therefore, accurate identification of these markers will play an essential role in identifying the disease and further accurate identification can play a major role in the treatment, prevention and control of the disease[3]. Identification of these biomarkers is one of the most important challenges in relation to geriatric diseases, so that their accurate and specific identification can play a very important role in the control and treatment of diseases. Major routine procedures include ELISA, Western blotting, calorimetry, and molecular-based tests such as PCR and real-time PCR. The need for advanced and expensive equipment, problem interpretation of the results, the need for specialized people as well as low accuracy and sensitivity are the main limitations of routine meth-

ods. Biosensors as inexpensive, simple and accessible tools with high sensitivity and specificity are among the modern and reliable methods for identifying biomarkers of various diseases. The main purpose of this article is to introduce these biosensors in diseases related to aging, including Alzheimer's, Parkinson's and bone diseases[4].

Biosensors

Today, biosensors are used in various fields such as medicine, chemical industry, food industry, environmental monitoring and production of pharmaceutical and health products. These sensors are a powerful tool for detecting biological molecules. For example, the human olfactory and taste senses are an example of a natural biosensor that detects different odors and tastes[5]. The body's immune system is also a natural biosensor, which detects millions of different types of molecules. The most common use of biosensors is in medical diagnoses and laboratory sciences. Glucose biosensors are currently one of the most successful biosensors on the market that measure blood glucose concentrations. Insufficient insulin is produced in the pancreas of diabetic patients. In such cases, continuous blood glucose monitoring is necessary to regulate insulin intake. It helps patients with diabetes measure their blood glucose levels throughout the day and inject insulin at the required times[6]. Illustration of biosensor construction presented in fig.1.

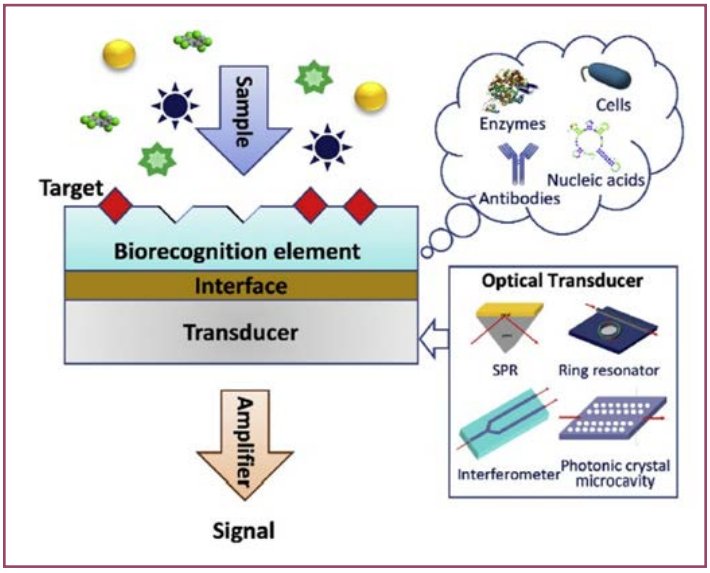

Fig.1. Schematic illustration of biosensor construction[7].

In fact, biosensors are analytical tools that can use the intelligence of biological materials to identify and react with a compound or compounds. The product of this reaction can be a chemical, optical or electrical message[7]. In a biosensor, the sensor element that responds to a biological substance has a biological nature. This element must be connected to a transducer to produce a response visible to the naked eye. They are related to certain chemicals that may also be physiological. These substances are usually called substrates, while the more general term is analyte. In general, each biosensor includes the following components: Analyte, Biological elements, Converter (4-processor) and display (monitor)[7]. The importance of these components is in their highly specific performance relative to the specific substrate, thereby preventing the interference of interfering substances that make many measurement methods inefficient. The biological component may catalyze the reaction of the substrate (enzyme) or optionally connect to the substrate. The use of enzymes as biological components is more common than other substances. Biological elements are the main selection factor in biosensors. These elements have such power that they only bind to certain substrates and do not react with other substrates[8].

Different kinds of biosensors being utilized based on two elements namely known as sensing element and transduction modes. Enzymes based biosensor, immunosensor which includes antibodies, DNA biosensor, Thermal and piezoelectric biosensor, biological tissues, organelles and microorganisms which can be detected with the help of whole cell biosensor comes under the category of sensing element[9]. Transduction mode relies upon the physiochemical change coming about because of detecting component. Subsequently on the premise of various transducers biosensors can be electrochemical (amperometric, conductometric and potentiometric), optical (absorbance, fluorescence and chemiluminense), piezoelectric (acoustic and ultrasonic) calorimetric[9].

Aging diseases and developed biosensors

Alzheimer's disease (AD) is the imperative progressive neurodegenerative disease that is considered by gradual synaptic integrity and loss of cognitive functions. In AD disorder core plaques and neurotic in the cerebral cortex was formed with selective neuronal death [10]. During AD, concentration of some components and biomarkers such as amyloid beta (Aβ), tau protein and micro RNA is altered significantly. Easy to obtain by safe techniques, measureable by simple and low cost methods in the primary stage of a disease and distinctive with other diseases biomarker are the most important aspects of ideal biomarkers[11]. Since Aβ can form complexes with some metal ions such as iron, so their existence is very important in pathogenesis [12]. Several studies indicated the relationship between AD progression and the amount of Aβ in body fluids. So, specific and sensitive detection of the level of Aβ is critical in AD clinical studies[12]. Tau protein is the second the most important biomarker of AD and belongs to (MAP) as a microtubule associated protein family. This protein expressed in the human central nervous system (CNS) and peripheral nervous system (PNS) as well as neurons, oligodend entrocytes, and astrocytes. In axons, tau protein interacts with tubulin and is revealed in four forms as well as the Proline-rich domain, N-terminal region, the C-terminal region and finally microtubule-binding domain. MicroRNAs (miRNAs) play a crucial role in a broad range of biological processes such as cell transcription and gene expression[13]. Hu and co-worker assembled novel immunosensor for sensitive detection of Aβ. They used colorimetric sandwich immunosensor technique based on twin antibody-modified gold nanoparticles. The result showed a good linearity in a range

from 7.5 nM to 350 nM and an ideal detection limit (LOD) of 2.3 nM along with simple structure and operation[14].

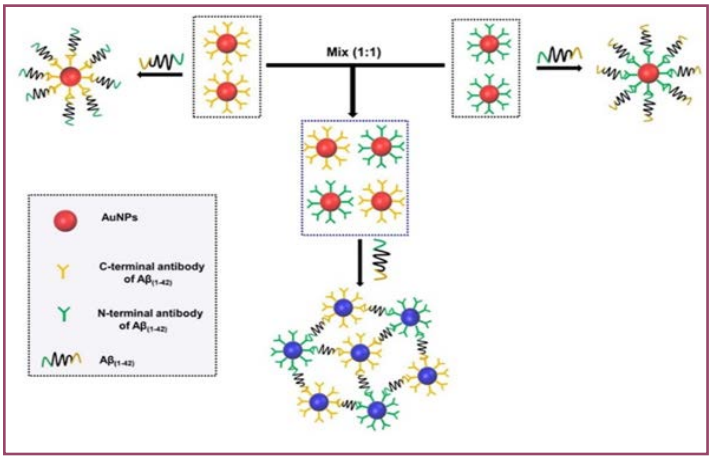

Fig.2. Schematic illustration of developed immunosensor[14].

The tau protein stabilizes microtubules in neuronal cells, but when hyperphosphorylated tau dissociates from microtubules and forms the neurofibrillary tangles (NFTs) and paired helical filaments (PHFs), which alongside amyloid-β plaques, are linked to neurodegeneration and Alzheimer's Disease.1-4 Tau's tendency to self-association is one of the triggers of its malfunction[15]. Tau pathology is associated with the existence of insoluble filaments of tau, but recent findings identified soluble tau oligomers as additional toxic species. The pathological tau is composed of phosphorylated tau protein, but nonphosphorylated tau protein may also aggregate. The mechanism of tau aggregation is still elusive[16]. The protein-based electrochemical sensing device was established for the detection of the tau protein by identifying the mis-folding proteins. This technique screens tau-taumisfolding structure and binding while the primary step of tau oligomerization. EIS was applied to detect binding occurrence between immobilized tau and solution tau protein and performed as a recognition element. Formation of tau-tau-Au complex not only increased selectivity and linear range significantly but also was recognized as an improved charge permeability of tau-tau-Au surface to a redox probe. Tau-tau binding induced conformational and electrostatic change and allowed for a rapid sample analysis.[17]

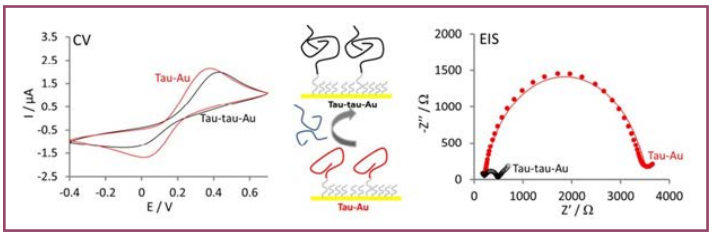

Fig.3. Schematic illustration of a developed biosensor for detection of tau protein[17].

In 2002, less than a decade after the discovery of miRNAs (Lee et al., 1993), the application of miRNAs as disease biomarkers was first explored. Calin et al. (2002) showed that miRNA expression patterns were altered in patients suffering from chronic lymphocytic leukemia. Shortly after this, miRNA expression was found to change during tumorigenesis (Michael et al., 2003), and could be successfully used to classify multiple human cancers (Lu et al., 2005). Since then, studies have examined the potential of miRNAs as biomarkers of diabetes (Farr et al., 2013, 2015a,b), Alzheimer's Disease (Lugli et al., 2015), and numerous other non-infectious conditions. Meta-analyses of multiple cancer studies strongly support the role for miRNAs as a diagnostic, providing the ability to identify a disease (Zhi et al., 2015) or a prognostic, identifying the likelihood of developing specific disease outcomes (Schmitz et al., 2016) biomarkers. Additionally, miRNAs may extend the clinical utility of current proteins or metabolite-based tests. For instance, a recent paper, demonstrated that miR-29a and miR-335 in combination with matrix metalloprotease protein-2 (MMP2), proved to be a superior diagnostic in breast cancer to the current carcinoembryonic antigen (CEA) and cancer antigen 15-3 (CA 15-3) tests that are widely used. Parkinson's disease (PD) is the second most common neurodegenerative disorder worldwide. Its main neuropathological hallmarks are the degeneration of dopaminergic neurons in the Substantia Nigra and alpha-synuclein containing protein inclusions, called Lewy Bodies. The diagnosis of idiopathic PD is still based on the assessment of clinical criteria, leading to insufficient diagnostic accuracy. Additionally, there is no biomarker available, allowing the prediction of the disease course or monitoring the response to therapeutic approaches. So far, protein biomarker candidates such as alpha-synuclein have failed to improve the diagnosis of PD[18]. Circulating microRNAs (miRNAs) in body fluids are promising biomarker candidates for PD, as they are easily accessible by non- or minimally-invasive procedures and changes in their expression are associated with pathophysiological processes relevant for PD. Advances in miRNA analysis methods resulted in numerous recent publications on miRNAs as putative biomarkers. Here, we discuss the applicability of different body fluids as sources for miRNA biomarkers, highlight technical aspects of miRNA analysis and give an overview on published studies investigating circulating miRNAs as biomarker candidates for diagnosis of PD and other Parkinsonian syndromes[18, 19].

A novel, sensitive and specific microRNA assay based on Colorimetric detection of gold nanoparticles and hybridization chain reaction amplification (HCR). The new strategy eliminates the need for enzymatic reactions, chemical changes, separation processes and, sophisticated equipment. The detection process is visible with the naked eyes and detection limit for this method is 0.25nM which is less than or at least comparable with the previous methods based on colorimetric of AuNPs. The important features of this method are high sensitivity and specificity to differentiate between perfectly matched, mismatched and non-complementary target microRNAs and also a decent response in the real sample analysis

with blood plasma. In conclusion, the simple and fast nanobiosensor can clinically be used for the early detection of Alzheimer's disease by direct detection of the plasma miR-137 in real clinical samples, without a need for sample preparation, RNA extraction, and/or amplification[20].

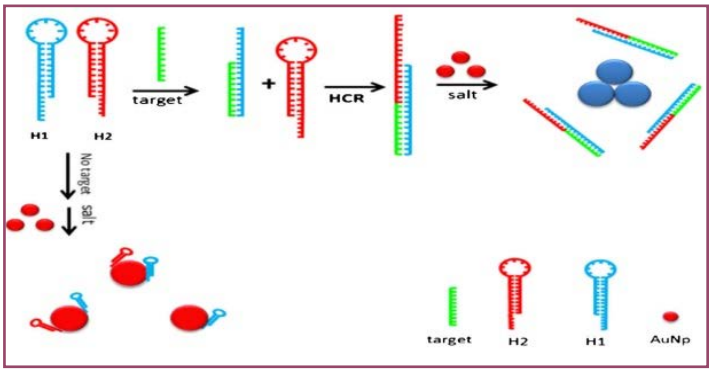

Fig.4. Schematic illustration of developed micRNA based biosensor[20].

Graphene was discovered in 2004 by Novoselov as two dimensional structured carbon nanomaterial. It has presented unique physical, chemical, and mechanical properties. In addition, graphene has a large surface area and a large delocalized electron system. Graphene oxide (GO) is one of the graphene derivative nanomaterial which contains carbonyl, epoxy, and carboxylic acid groups and shows better solubility in aqueous or organic solvents than graphene. The graphene oxide (GO) modified pencil graphite electrodes (PGEs) were utilized for electrochemical monitoring of microRNA-34a (miRNA-34a) in this study. The GO concentration was firstly optimized after its modification onto the surface of disposable PGE by passive adsorption. The electrochemical behaviour of GO–PGEs was investigated by cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS) as well as microscopic characterization by using scanning electron microscopy (SEM). The impedimetric detection of hybridization between the miRNA-34a target and its complementary DNA probe was recognized under the optimum conditions. The selectivity of the impedimetric genosensor was furtherly studied against other miRNA sequences; such as; miRNA-15a, miRNA-155 and miRNA-660 in PBS (pH 7.40) or fetal bovine serum (FBS): PBS (1:1) diluted solution[21].

In the last decade, the necessity to investigate alpha-synuclein (αS) conformational changes in vivo and the pathological consequences of its misfolding on cell function, gave rise to the development of fluorescent molecular tools, able to track the formation of αS high molecular weight (HMW) species. αS, the dominant component of Lewy bodies, proteinaceous inclusions found in Parkinson's disease (PD) patients, can aggregate in highly ordered protofibrils, according to a nucleation reaction, with different intermediate states of oligomer assembly. Specifically, at least two types of oligomer structures have been described in vitro, while for protofibrils a growing consensus based on cryo-electron microscopy (cryo-EM) data showed a Greek key type of conformation, rich

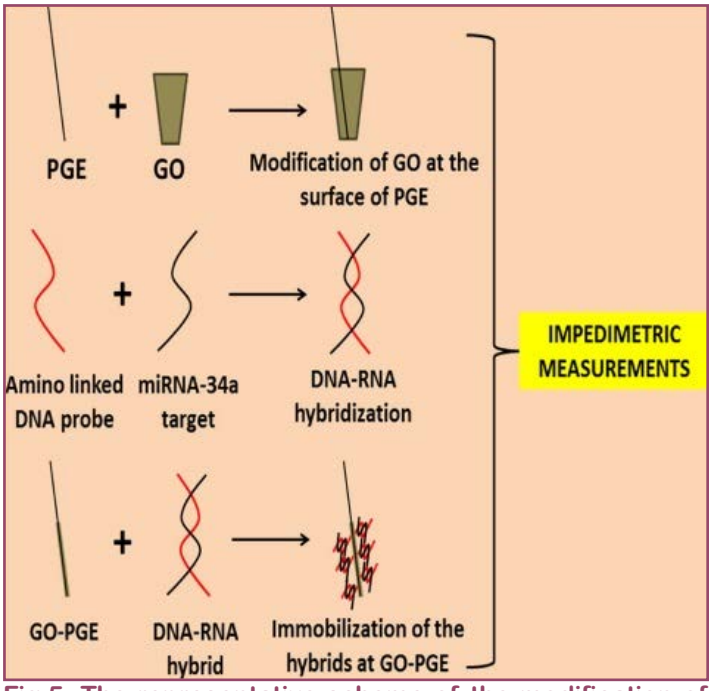

Fig.5. The representative scheme of the modification of PGE by using GO, the hybridization of miRNA-34a target and its complementary DNA probe, and the immobilization of the hybrids at the surface of GO–PGE[21].

in parallel β-sheets, orderly stacked to form a filament, although other arrangements have been described[22, 23].

Endoplasmic reticulum (ER) dysfunction is important for alpha-synuclein (αS) acquired toxicity. When targeted to the ER in SH-SY5Y cells, transient or stable expression of αS resulted in the formation of compact αS-positive structures in a small subpopulation of cells, resembling αS inclusions. Thus, because of the limitations of immunofluorescence, αS FRET biosensors (AFBs) able to track αS conformation in cells was developed. In native conditions, expression in i36, a stable cell line for ER αS, of intermolecular AFBs, reporters in which CFP or YFP has been fused with the C-terminal of αS (αS-CFP/αS-YFP), resulted in no Förster resonance energy transfer (FRET), whereas expression of the intramolecular AFB, a probe obtained by fusing YFP and CFP with αS N- or C- termini (YFP-αS-CFP), showed a positive FRET signal. These data confirmed that αS has a predominantly globular, monomeric conformation in native conditions. Differently, under pro-aggregating conditions, the intermolecular AFB was able to sense significantly the formation of αS oligomers, when AFB was expressed in the ER rather than ubiquitously, suggesting that the ER can favor changes in αS conformation when aggregation is stimulated. These results show the potential of AFBs as a new, valuable tool to track αS conformational changes in vivo[24, 25].

Conclusion

Additionally, in the last years, significant attentions have been focused to detect the biomarkers of biomarkers. In this regard, biosensors are very attractive and applicable tools for providing rapid, sensitive, specific, stable, cost-effective and non-invasive detections for disease

diagnosis. Thus, cancer biosensors consisting of specific biorecognition molecules such as antibodies, complementary nucleic acid probes or other immobilized biomolecules on a transducer surface. The biorecognition molecules interact specifically with the biomarkers (targets) and the generated biological responses are converted by the transducer into a measurable analytical signal. Depending on the type of biological response, various transducers are utilized in the fabrication of cancer biosensors such as electrochemical, optical and mass-based transducers. Recent developments in biological methods and instrumentation after using fluorescence tag to various nanocarriers such as nanoparticles, nanowires, nanotubes, etc. have improved the sensitivity of biosensors. Utilization of nucleotides/aptamers, affibodies, molecule imprinted polymers, and peptide arrays offer great tools to prepare advanced biosensors. Merging of nanotechnology with biosensor systems enhanced the diagnostic capability. This review gives an outline of the advances in biosensors technology relating to biomedical sciences.

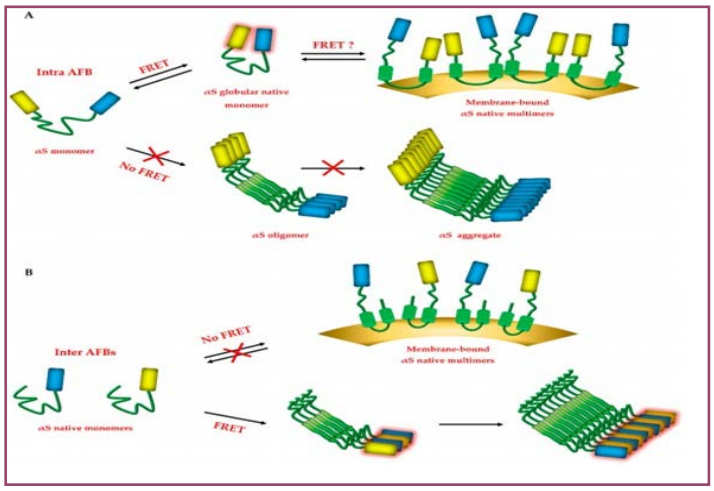

Fig.6. Schematic panels describing AFBs hypothetical behavior in detecting different αS species in the cellular environment. (A) Intra-AFB could, theoretically, sense the native state of αS (globular monomeric or the bidirectional conversion to a membrane-bound multimeric, as shown by the double arrows) as well as aggregated forms. In our system, though, Intra-AFB is sensitive only to the native state of αS, since when aggregation is stimulated no significant variation of FRET signal for the intra-AFB is recorded (crossed arrow). (B) Inter-AFB can sense only HMW species under pro-aggregating conditions, at a distance of 2–10 nm, according to FRET principles, but cannot detect native multimeric αS structures bound to membranes[26].

Keywords: Biosensors; Aging; Alzheimer; Parkinson.
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Vitamin D and Parkinson's disease

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Parkinson's is a neurodegenerative disease that affects people over the age of 60 (1,2). Environmental and genetic factors play a role in the development of the disease (3). The most important ones are genetic mutations (4), sex (5), exposure to pesticides (6), and calcium channel blockers (7). Nowadays, Vitamin D is not only considered as a vitamin, but also as a hormone. Indeed vitamin D plays its biological role by binding to vitamin D receptors (VDRs), which are receptors for steroid hormones. Therefore, vitamin D deficiency is associated with an increased risk of many chronic diseases such as cardiovascular disease, MS, and diabetes (8,9). Since vitamin D deficiency inhibits the expression of one of the most important genes that play a principal role in regulating dopamine biosynthesis and the expression of neurotrophic factors, it seems to cause Parkinson's disease. The results of these studies are inconsistent (10). To this regard, several systematic reviews and meta-analyses have been conducted in the field of vitamin D's role in the incidence of this disease and the effect of supplementation in controlling symptoms. Results indicate these:

Risk of Parkinson's disease

The results of several systematic reviews and meta-analyses showed that deficiency and insufficiency of vitamin D levels significantly increase the risk of Parkinson's disease (11-13). Less exposure to sunlight also increases the risk of Parkinson's disease (11).

The effect of vitamin D supplementation on the symptoms of Parkinson's disease

The clinical trial results in this field indicate the positive effect of adjuvant supplementation on symptom control and worsening prevention (14,15). In contrast, the results of the meta-analysis study showed that vitamin D supplementation does not affect symptoms (11).

Finally, according to the results of studies, it can be concluded that the use of rich sources of vitamin D, exposure to sunlight, and vitamin D supplementation is one of the economical ways to prevent Parkinson's disease. However, more clinical studies are needed to investigate the effect of vitamin D supplementation on Parkinson's disease's motor symptoms.

Keywords: Biosensors; Aging; Vitamin D; Parkinson.
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Student Letter

Polypharmacy in Elderly

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What is polypharmacy?

The consumption of drugs has increased over recent years, the elderly population in particular.

Not only the process of aging itself, but also its associated physiological and pathological change puts the elderly at a higher risk of multimorbidity and complications related to various treatments. Today, polypharmacy, a very common and critical problem related to drug use, occurs subsequent to this multimorbidity in the elderly in all populations. [1]

It is commonly defined as the concomitant consume of four or more medications, especially in the outpatient setting, but in the context of institutionalised or hospitalised patients, the minimum number of drugs varies and can include up to ten different medications.[2-4]

Polypharmacy in the elderly complicates therapy, increases cost, and is challenging for healthcare providers. [5]

Polypharmacy can arise from different phenomena and can therefore be divided into several various subgroups.

- Appropriate polypharmacy, when a patient takes several concomitant drugs, all of which are for specific indications. In this case, an estimation of the appropriateness of the treatment is often more convenient than simply attempting to cut down the number of medications.
- Inappropriate polypharmacy, when a patient takes much more drugs than is required.
- Redundant pseudopolypharmacy, when the recordings shows taking more drugs than the patient actually do.[6]

Causes of Polypharmacy

Inappropriate polypharmacy stems from two main sources:

Polypharmacy Due to Healthcare Providers

The number of drugs prescribed increases with the number of physicians seen and with the number of pharmacies used. Minimizing the number of physicians and pharmacies visited, can decrease the incidence of polypharmacy [4,7,8], Many doctors do not request the patient to compile a complete list of drugs taken (including all over-the-counter drugs) or do not review the patient's drug list to evaluate medications that could be stopped. [8] Similarly, symptoms that may be an adverse drug reaction are easily wrongly attributed to a new illness. Drug adverse effects are treated with another drug in 80% of visits to the physician.[9]

Polypharmacy Due to Patients

In any age category, 50% of patients also expect the physician to prescribe a new drug at each visit (and physicians often think that the patient wants a prescription) because prescription of a medication is seen as acknowledging the patient's ailment. It has been estimated that 75% of visits end in the patient receiving a prescription. [10]

Two other frequent thoughts in the elderly population are self-medication with over-the-counter drugs and borrowing medications from family members and friends. As the elderly often believe that they need a 'pill for every ill', over-the-counter drugs are actually used to cure an illness that the patient does not want to report to his prescribing physician.[11]

Other issues related to drug use include low literacy in general or low health literacy in particular. Additional contributing factors include miscommunication or misunderstanding physician orders as a result of cognitive

dysfunction, and mistaking drugs because of similarity in shape or colour, both of which can arise more often in older age groups.[12-15]

Consequences of Polypharmacy

The consequences of polypharmacy fall into six major categories

Nonadherence: complexity of the drug regimen,

Drug-drug interactions,

Adverse drug reactions (ADR),

Medication errors: more drugs a patient receives, the less accurately the medical chart reflects the patient's therapy,

Increased risk of hospitalization,

Increased cost, due directly to the medication and indirectly to the cost of treating adverse events. [16]

How to manage polypharmacy?

There are various approaches to manage polypharmacy, some of which are described below:

• Deprescribing and Prescribing Omitted Therapies: Look for medications that have no valid reason for being used; evaluate the overall risk of drug-induced harm; assess current or future benefit versus risk; prioritize discontinuation and consider removal of medications with lowest benefit to heightened harm risk first; and implement a plan to discontinue and monitor follow-up.

• Avoiding the Prescribing Cascade: The prescribing cascade happens when a medication is used to treat the side effect of another medication.

• Individualization of Medication Use: Individualization of care due to the heterogeneous health status of patients aged 65 and older is an important consideration in the therapy of older adults.

• Medication Reconciliation: Medication reconciliation is typically defined as getting the most accurate list of medications a patient is using. Appropriate medication reconciliation involves patient and caregiver interviews, lists from health records, pharmacy records, hospitalization records, controlled substance refill reporting, and accounting for over-the-counter medication, supplements, herbal products, and vitamins.

• The "brown bag medicine review", an assesment in which the patients bring everything they are taking at the current time in a bag to each apponitment, is the gold standard for medication reconciliation. The ideal is to go through the brown bag assessment at each office visit, although once per year at minimum is helpful. [17]

There are also algorithms and processes for monitoring appropriateness and need of medication use in older adults , which have been created and can be useful in development of a systematic approach to monitor the medication use. [18,19]

Keywords: Polypharmacy; Aging; Elderly.

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