The Effect of Amlodipine on Insulin Sensitivity in Prediabetic Hypertensive Patients

Hypertension is closely related to metabolic disorders such as insulin resistance and type 2 diabetes.

In Myanmar, prevalence of hypertension was 29.9%, prevalence of diabetes mellitus was 10.5% and prevalence of prediabetes was 19.7% in 2014. The effects of antihypertensive drugs in diabetic patients had been studied, and it was found that amlodipine can improve insulin sensitivity.

This study was aimed to investigate the improvement of insulin sensitivity in prediabetic hypertensive patients after 12 weeks treatment of amlodipine 5mg single dose.

The before and after drug treatment intervention study was done in 25 newly diagnosed prediabetic hypertensive patients with amlodipine 5mg and observed the insulin sensitivity after 12 weeks treatment. Systolic blood pressures, diastolic blood pressures, fasting blood glucose levels and fasting insulin levels were compared before and after amlodipine 5mg 12 weeks treatment. Data of systolic blood pressure and diastolic blood pressure were represented as the mean ±SD.

Data of fasting blood glucose level, fasting insulin level and HOMA-IR level were represented as the median. Mean systolic blood pressure was decreased from 143.6±5.69mmHg to 126±6.45mmHg (p<0.001) and mean diastolic blood pressure was decreased from 91.6±3.74mmHg to 81.6±3.74mmHg (p<0.001). Median fasting blood glucose level was decreased from 6.14 mmol/L to 5.02 mmol/L (p=0.001). Median fasting insulin level was decreased from 15.8μU/mL to 13.61μU/mL (p=0.861).

Improvement on insulin sensitivity was observed with HOMA-IR values which were calculated from fasting blood glucose levels and fasting serum insulin levels. After 12 weeks treatment with amlodipine, median HOMA-IR level decreased from 4.01 to 3.38 (p=0.005) which indicated that insulin sensitivity was improved.

These results suggested that amlodipine had beneficial effect on insulin sensitivity and fasting blood glucose level in hypertensive prediabetes. Therefore, this study may provide the additional benefits of antihypertensive drug regimens chosen for prediabetic patients although larger group interventions are needed.
Evaluation of LIPS (Luciferase Immunoprecipitation System) for Serodiagnosis of Toxoplasmosis

Development of reliable, quantitative technologies for serodiagnosis of *Toxoplasma gondii* infection remains desirable. The luciferase immunoprecipitation system (LIPS) is a relatively simple, highly sensitive, and rapid quantitative immunoassay. The major advantages of this assay over ELISA are a wider dynamic range, shorter overall assay time, and less sample volume. In this study, we aimed to use this method for the serodiagnosis of toxoplasmosis. Recombinant Toxoplasma antigens (dense granule antigens GRA6, GRA7, and GRA8 and bradyzoite antigen BAG1) fused with nanoluciferase (Nluc, a small luciferase enzyme) were expressed in *Escherichia coli*, purified, and tested in LIPS assays with sera from experimental mice infected with *T.gondii* and a WHO standard anti-*Toxoplasma* human immunoglobulin (TOXM). In the experimentally infected mice, LIPS assays detected antibodies against Nluc-GRA6, Nluc-GRA7, and Nluc-GRA8 as early as day 14, whereas antibodies against Nluc-BAG1 remained undetected until day 21 and then showed significant elevation on day 60. In TOXM sera, LIPS assays with each Nluc recombinant protein produced reliable standard curves with a coefficient of determination (R2) of 0.980–0.989 for GRA6, 0.986–0.990 for GRA7, 0.998–0.999 for GRA8, and 0.942–0.987 for BAG1. The detection limits were estimated to be 3.9, 2, 1, and 1 IU/ml for rGRA6, rGRA7, rGRA8, and rBAG1, respectively.

The LIPS assay for toxoplasmosis could detect antibodies against *T. gondii* in the mouse and human sera with a reasonably high sensitivity.

We consider the LIPS assay to be a promising alternative tool for screening, diagnosing, and monitoring toxoplasmosis. In particular, detection of antibodies against BAG1 may be useful for a longitudinal seroprevalence study in suspected high-risk areas on the basis of its elevated serum concentration in the chronic phase.


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News about Medicine & Health

Safer Sleeping Pills Keep Brain Alert to Danger

Most sleeping pills are so strong that the sound of a fire alarm is unlikely to wake those who take them. However, a new study, published in the journal *Frontiers in Behavioral Neuroscience*, proposes a safer alternative to these drugs.

One-third of adults in the United States do not get enough sleep on a regular basis, according to the Centers for Disease Control and Prevention (CDC). Between 50 and 70 million individuals in the country either have sleep disorders such as insomnia or live with sleep deprivation.

The CDC also report that about 4 percent of the U.S. population over the age of 20 take sleeping pills and that this figure tends to increase with age and education. According to the same source, 1 in 8 adults in the country who have sleeping problems take sleeping aids. But how safe are these drugs? Researchers have linked various adverse health effects with the prolonged use of sleeping aids, and the risk of addiction is well-known.

New research points to another safety hazard that sleeping pills may pose that the ability to wake from sleep in response to dangerous situations is an ideal characteristic of safe hypnotics. But most sleeping pills do not have this characteristic. In a trial of widely used hypnotics quoted by the researchers, half of the participants who took the drugs did not wake up at the sound of a fire alarm.

The researchers tested a novel hypnotic drug in mice and found that the rodents woke up as quickly as their drug-free counterparts when confronted with a danger signal. They were also able to fall back asleep just as quickly when the threat was gone.

*Studying a safer alternative to sleeping pills*

Benzodiazepines, the most widely used type of sleeping aid, suppress our brain's ability to respond to the sensory information it processes during sleep. These pills "stimulate the widespread brain receptor GABA-A," explains the researcher, "which makes us sleepy but also suppresses off-target brain areas — including the 'gatekeeper' that decides which sensory inputs to process."

A new class of hypnotics, called dual orexin receptor antagonists (DORAs), may enable the brain to stay alert to danger signals, providing a safer alternative to existing sleeping pills.

To test their hypothesis, the researchers administered DORAs to one group of mice, gave another group a benzodiazepine called triazolam, and administered a placebo to the third group. DORA-22 and triazolam had similar sleep-promoting effects, extending the duration of deep sleep by 30–40% compared to placebo.

Within 1–4 hours of giving the mice the sleeping pills, the researchers presented them with various danger signals: the smell of a fox, an alarming sound, or a trembling of their cages, which mimicked an earthquake.

*How DORAs affect sleep and wakefulness*

As expected, arousal in response to these threatening stimuli was delayed significantly in the triazolam treatment, but not in the DORA-22 treatment, compared to placebo. Importantly, the sleep-inducing effects of DORA-22 continued after the threat had passed. Even though the DORA-22-treated mice were quickly woken by a threat, they subsequently fell back asleep as quickly as with triazolam, and significantly faster than with placebo.

DORAs are also less likely to induce drowsiness the next day and affect one's ability to drive vehicles. Human clinical trials are needed to further test the benefits and safety of DORAs, but the researchers are hopeful that the benefits will translate to humans. Although it remains to be seen whether DORAs have the same properties when used in humans, our study provides important and promising insight into the safety of these hypnotics.

Source:https://www.medicalnewstoday.com/articles/324173.

Contributed by Virology Research Division
Silicone Breast Implants Linked to Increased Risk of Some Rare Harms

Women receiving silicone breast implants may be at increased risk of several rare adverse outcomes compared to the general population, reports a study in Annals of Surgery.

"We are reporting an analysis of the largest prospective study to date on silicone breast implant safety," comments Mark W. Clemens, MD, and colleagues of The University of Texas M.D. Anderson Cancer Center, Houston. "We are sharing critical information on complication rates and rare associations with systemic harms. This data gives women important safety information about silicone breast implants to have real expectations and to help them choose what is right for them." Based on an FDA-mandated "post approval" database, the analysis is the largest study of breast implant outcomes to date.

First analysis of data collected after re-approval of silicone breast implants

In the early 1990s, the FDA prohibited the use of silicone breast implants in response to public concerns about health risks including cancer, connective tissue diseases, and autoimmune diseases. Subsequent research found no link between breast implants and disease. In 2006, the FDA approved silicone gel-filled implants from two manufacturers (Allergan and Mentor Corp), stipulating that the manufacturers conduct large post approval studies (LPAS) to monitor long-term health and safety outcomes.

"Despite abundant data collection, and open public access, the LPAS database had not yet been analyzed and reported," according to Dr. Clemens. The researchers analyzed data on nearly 100,000 patients enrolled in the LPAS between 2007 and 2009-10. More than 80,000 patients received silicone implants; the rest received implants filled with sterile saline solution. Seventy-two percent of the patients underwent primary breast augmentation, 15 percent had revision augmentation, 10 percent had primary breast reconstruction, and three percent had revision reconstruction procedures. The large size of the database enabled researchers to assess the risk of rare adverse outcomes.

Women receiving silicone implants were at increased risk of several rare harms compared to the general population. The elevated risks included three conditions classified as autoimmune or rheumatologic disorders: Sjogren's syndrome, with a risk about eight times higher than in the general population; scleroderma, a seven-fold increase in risk; and rheumatoid arthritis, about a six-fold increase in risk.

"These findings are associations compared to the general population and determining why these associations are observed or any causation requires further study," says Dr. Clemens.

Silicone implants were also associated with a 4.5-fold increase in the risk of stillbirth, but no significant increase in the risk of miscarriage. Risk of melanoma, a serious type of skin cancer, was nearly four times higher in women with silicone implants.

There was no significant association with the risk of suicide, which had been suggested by a previous study. The database included just one case of breast implant-associated anaplastic large cell lymphoma -- a rare but serious type of cancer previously linked to breast implants.

Compared to saline-filled implants, silicone implants were also linked to a higher risk of some surgical complications. These included capsular contracture (scarring around the implant), which occurred at a rate of 5.0 percent with silicone implants versus 2.8 percent with saline-filled implants. Capsular contracture occurred in 7.2 percent of primary breast augmentation procedures, and was the most common reason for reoperation in this group.

While certain rare harms appeared to be more common in women with silicone implants, absolute rates of these adverse outcomes were low. The researchers emphasize that their results are inconclusive, due to limitations inherent in the use of post approval databases -- including the lack of complete patient information and individual follow-up data.

"To resolve the remaining uncertainty in the evidence base, it is important that this data be analyzed in an unbiased manner," Dr. Clemens and coauthors write. "It remains the plastic surgery community's duty to provide definitive evidence for the risks associated with breast implants."


Contributed by Quality Assurance Division

New Function of A Key Component in the Immune System Discovered

The complement proteins that circulate in our blood are an important part of our immune system. They help identify bacteria, viruses and other harmful organisms, making it easier for our white blood cells to find and neutralize dangerous microbes. Researchers at Lund University in Sweden have now discovered a previously unknown function of the central complement protein, C3, which describes how C3 regulates autophagy. Autophagy is the basic mechanism that controls cells' ability to break down their own material, i.e. dispose of cellular waste, and generate new energy by reusing their own components.
Disruption of the autophagy mechanism is thought to contribute to the development of several diseases. Therefore, this knowledge can play an important role in our understanding of the onset and treatment of type 2 diabetes and other diseases. A few years ago, the research teams led by immunologist Anna Blom and diabetes researcher Erik Renström at Lund University showed that the complement system, which consists of some 40 proteins in the blood, is also present within our beta cells in the pancreas.

One protein, CD59, was shown to be essential for enabling beta cells to secrete insulin. Another protein, C3, was produced in large amounts in the beta cells, but its exact role was unclear. In a new study, which has now been published in Cell Metabolism, the researchers discovered that the complement protein C3 can protect the beta cells from stress (e.g. long-term high blood sugar levels) when diabetes is in progress. When the researchers, using CRISPR/Cas 9, removed the gene that expresses the complement protein C3 from the beta cells, autophagy was disrupted and the cells died more easily from stress. They also found that C3 production in beta cells increases considerably in response to diabetes and inflammation, probably in an attempt to protect beta cells.

"C3 is a very old protein from an evolutionary perspective and we have now shown that it not only has a role in the relatively modern immune system in the blood, but also within cells, where it is needed for one of the most fundamental cellular functions, autophagy. In all likelihood, this applies to many cell types and opens the way for new principles in the treatment of diseases such as type 2 diabetes and certain neurodegenerative diseases for which there is a need to protect cells from stress," concludes Anna Blom.

Contributed by Immunology Research Division

Long-Term Renal Effects of Tenofovir Disoproxil Fumarate vs. Entecavir in Chronic HBV-Infected Patients

Tenofovir disoproxil fumarate should be avoided in patients with moderate renal impairment and in those over age 60. The majority of patients who receive oral antiviral therapy for chronic hepatitis B virus (HBV) infection will require long-term viral suppression, since complete eradication is unlikely. Safety data on the long-term use of some of those agents are conflicting, especially around nephrotoxicity.

This retrospective study was performed between 2000 and 2016 and involved HBV-infected patients receiving either tenofovir disoproxil fumarate (TDF) or entecavir (ETV) daily. Serial laboratory testing was performed to rigorously monitor renal function and collect detailed data regarding potential risk factors. Patients were propensity-score-matched for age, sex, baseline estimated glomerular filtration rate (eGFR), follow-up duration, and presence of hypertension, diabetes, and cirrhosis. The primary endpoint was renal outcome, based on eGFR.

A total of 239 TDF- and 171 ETV-treated, HBV-infected patients were identified during the study period. During a median follow-up of 43 to 46 months, of the patients with intact renal function at baseline (eGFR ≥60 mL/minute/1.73m²), there was no difference in renal function between the TDF and ETV groups. However, among patients with moderate renal impairment at baseline (eGFR<60 mL/minute), TDF patients had significantly lower eGFR than the ETV group (44.7 vs. 50.8 mL/minute). Also, in a subanalysis, patients older than age 60 years had worse renal outcomes with TDF compared with ETV. Although tenofovir alafenamide was recently approved by the FDA and has an excellent safety profile, TDF and ETV are still the most widely used agents for the treatment of HBV infection.

This study confirms previous findings that overall renal function is preserved with longer-term use of both TDF and ETV; however, it shows that in those with moderate renal impairment at baseline and in those older than 60, renal outcomes are worse with TDF compared with ETV. Clinicians treating HBV-infected patients should avoid TDF use in those populations.

Source: https://doi.org/10.1016/j.cgh.2018.08.037.
Contributed by Molecular Technology Applications Division

Mammography in Preventive Oncology

Since 1990, the mortality rate from breast cancer has been declining approximately 2% per year. A study using several statistical models estimates that use of screening mammograms accounts for 28-65% of that reduction (median, 46%). A meta-analysis of randomized controlled trials showed a significant 34% reduction in breast cancer mortality at 7 years in those who had mammographic screening. A subsequent review indicated that the survival benefit from mammography was greater in women older than 50 years than in those between the ages of 40 and 49 years. However, numerous other studies have
demonstrated decreased mortality in women in their 40s as well. Most experts agree that screening mammography should be performed routinely in women between the ages of 50 and 69 years. The frequency of screening in this population has been a controversial issue. Despite this evidence of a mortality benefit, mammogram screening rates in the US decreased between 2000 and 2005. Types of mammograms in use include film mammograms and digital mammograms. Images from digital mammograms are electronically captured and stored, whereas those from film mammograms are provided via traditional radiographic films. Overall, cancer detection rates are similar regardless of which type of mammogram is used. The exceptions to this rule are that digital mammography is more accurate in premenopausal women and in women with dense breasts. Data that directly address this question are sparse, but one observational study comparing annual and biennial screening showed no significant disadvantage from the biennial schedule in terms of detection rate or stage at time of diagnosis. For women age 40 to 49, the breast cancer incidence and the sensitivity of mammograms are both lower than they are in women aged 50-69 years. The ACS recommends that average-risk women start annual mammograms at age 45 and consider transitioning to biennial screening at age 55. The American College of Physicians (ACP) and the Advisory Committee on Cancer Prevention in the European Union advise discussion of screening with patients and shared decision-making. The American College of Obstetricians and Gynecologists (ACOG) recommends offering mammography at ages 40 to 49 and, if after counseling the patient desires it, initiating annual or biennial screening. Recommendations for when to stop mammography also vary. It has been suggested that bone mineral density (BMD) be incorporated into decision-making for breast screening for individuals in this 70-79 year age group, as those with higher bone density have an increased risk of breast cancer compared with those with low bone mineral density. A general rule that has been suggested for this population is that screening continue for those who have a life expectancy of 10 years or greater.

Some women express concern regarding the radiation associated with regular mammographic screening. Direct data regarding the risk associated with this level of radiation exposure are lacking, but a study of a risk model comparing the risk of radiation and the mortality benefit of mammographic detection concluded that the net effect of mammograms was positive for women older than age 40 years. However, it is important to note that women with BRCA mutations may be more susceptible to the effects of radiation to the breast. Studies of BRCA carriers showed that those with exposure to chest x-rays were 54% more likely to develop breast cancer; this risk increased with multiple x-rays or x-rays done at an early age. In contrast, a study of mammograms in another BRCA population did not find an increased risk of breast cancer in a multivariate model.

Contributed by Pathology Research Division

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