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Medical Bulletin

News You Can Use

Type 2 Diabetes Is Reversible: Newcastle University Study

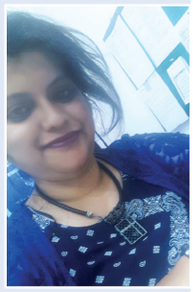
Type 2 Diabetes is a life changing condition that progresses over time, which can have devastating consequences. **Finding ways to put it into lasting remission could significantly reduce the cost of delivering diabetes care and treating serious complications such as cardiovascular disease, kidney disease and stroke.**

According to a study led by Professor Roy Taylor, from Newcastle University and Professor Mike Lean from Glasgow University, 45.6% of those who were put on a low calorie diet for three to five months were able to stop their Type 2 diabetes medications. The trial called *DiRECT (Diabetes Remission Clinical Trial)* funded by Diabetes UK, recruited 298 people between Newcastle and Glasgow University.

***DiRECT* is a two year trial which aimed to find an effective and accessible way to put Type 2 diabetes into remission for the long term.** The trial was delivered through GP practices across Tyneside and Scotland to find out if the benefits of structured weight management can be felt in a real life primary care setting. **Remission was defined as having blood glucose levels (HbA1c) of less than 6.5% (48mmol/mol) at 12 months without any Type 2 diabetes medications.**

Type 2 diabetes remission was found to be closely related to weight loss. Over half (57%) of those who lost 10-15 kgs achieved remission, along with a third (34%) of those who lost 5-10 kgs and only 4% of the control group achieved remission. Professor Lean said *"putting Type 2 diabetes into remission as early as possible after diagnosis could have extraordinary benefits, both for the individual and the NHS."*

Greetings from Blue Cross Laboratories!



Dear Colleagues,

Hope all of you are in the best of health and spirit, and I hope you have had a fabulous first and second quarter for 2018 !

It gives me immense pleasure and satisfaction to present you with the second issue of the Blue Cross Medical Bulletin for this current financial year.

This issue will have you updated on a few recent medical discoveries/developments, and novel clinical insights involving diverse therapeutic facets. We have also included, a tutorial on "What are the Different Types of Headaches?" and a new segment called "Beyond the Pharmacodynamic Frontier", in which we will highlight therapeutic benefits of molecules extending beyond the realm of their current indications. We hope all these topics make for interesting reading !

We hope you enjoy reading this edition of the Medical Bulletin as you have been in the past. Please feel free to send in your feedback, so that we can incorporate the same in future editions.

Happy Reading!

Best wishes & Warm regards,

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Vitamin D Linked To Fertility Outcomes

Adequate levels of vitamin D were associated with better fertility outcomes in women undergoing assisted reproduction treatment (ART), a meta-analysis of recent studies found.

The analysis of 11 studies including 2,700 women reported that **those with adequate vitamin D were 33% more likely to achieve live birth than those with deficient or insufficient levels** (OR 1.33, 95% CI 1.08-1.65), said researchers led by Justin Chu, PhD, of the University of Birmingham in the U.K.

Women with adequate vitamin D were also 34% **more likely to achieve a positive pregnancy test** (OR 1.34, 95% CI 1.04-1.73) and 46% more likely to achieve a clinical pregnancy (OR 1.46, 95% CI 1.05-2.02. However, the meta-analysis found no significant association between vitamin D concentrations and risk for miscarriage (OR 1.12, 95% CI 0.81-1.54), Chu and colleagues reported.

***"Vitamin D deficiency has been associated with an increased risk of abnormal pregnancy implantation as well as obstetric complications** such as pre-eclampsia and fetal growth restriction. However, the effect of vitamin D on conception and early pregnancy outcomes in couples undergoing ART is poorly understood,"* Chu's group wrote.

It could be that correcting vitamin D deficiency could benefit women undergoing ART, but further research is needed to test this.

We have long known the importance of vitamin D for bone health. **Recently, more and more studies have shown the importance of vitamin D for conceiving as well as having a healthy pregnancy. Additional functions of vitamin D that are being researched include its role in the immune system and preventing cancer.**

Tutorial

What are the Different Types of Headaches ?

There are many different types of headaches, and their causes and symptoms can vary. Although most are short-lived and rarely a cause for concern, being able to recognize which kind of headache a person is experiencing can inform them how best to treat it and whether to see a physician.

Headaches are a common complaint. According to the World Health Organization, most people will experience a headache from time to time.

While they can be sometimes painful and debilitating, the majority can be treated with simple analgesics and will go away within several hours. However, repeated attacks or certain types of headache could be a sign of something more serious.

The International Classification of Headache Disorders (ICHD) defines more than 150 different types of headaches. These are divided into two main categories: primary and secondary.

Primary headaches

A primary headache is one that is not caused by another condition — it is the condition itself. Examples include migraine and tension headache.

1. Migraines

Migraines are categorized as a primary headache, and are often accompanied by visual disturbances. A person who has a migraine will characteristically feel an intense throbbing pain on just one side of the head. The person may experience a heightened sensitivity to light, sound, and smell. Nausea and vomiting are also common.

Around a third of people experience an aura before the onset of a migraine. These are visual and sensory disturbances that typically last between 5 and 60 minutes. They can include: seeing zig-zag lines, flickering lights, or spots; partial loss of vision; numbness; pins and needles; muscle weakness; difficulty speaking. Aura symptoms could also indicate stroke or meningitis. Anyone experiencing them for the first time should see a doctor immediately.

Migraines tend to be recurrent, and each attack may last up to 3 days. For many, it is a life-long condition.

Although a migraine can occur in both adults and children, it is three times more likely to develop in females than males. Attack frequency can range from several times a week to once a year.

The causes of migraine are not fully understood. However, it often runs in families. Migraines are also more common in people with certain pre-existing conditions, such as depression and epilepsy.

Triggers of migraine could include: Stress and anxiety, sleep disruption, hormonal changes, skipped meals, dehydration, some foods and medications, bright lights and loud noise.

Analgesics like paracetamol and NSAIDs such as mefenamic acid or ibuprofen can reduce pain intensity. A person should take all medications as soon as migraine symptoms begin for best effect.

Physicians can prescribe an antiemetic drug to relieve nausea and vomiting, such as ondansetron. Migraine-specific combination drugs are also available.

Attacks may also be eased by:

- Resting in a dark, quiet place
- Placing an ice pack or a cold cloth on the forehead
- Drinking water

For more difficult-to-treat migraines, physicians may prescribe triptans, such as sumatriptan or rizatriptan. Triptans are chemically known as 5-hydroxytryptamine (5-HT) receptor agonists, also called 5-HT 1B/1D-receptor agonists.

A doctor may diagnose a person with chronic migraine if they have experienced headaches for more than 15 days per month, over a period of 3 months – of which at least 8 show symptoms of migraine.

Drug options for migraine prevention include topiramate, propranolol, and amitriptyline. Other management choices to consider are dietary supplements, meditation, acupuncture, and neuromodulation therapy (involves applying mild electrical pulses to the nerves).

2. Tension headaches

Tension headaches are very common, and present as a dull, constant pain felt on both sides of the head. Other symptoms can include:

- Tenderness of the face, head, neck, and shoulders
- A feeling of pressure behind the eyes
- Sensitivity to light and sound

These headaches normally last from 30 minutes to several hours. Severity can vary, but they rarely prevent normal activities. The cause of tension headaches is unclear, but stress, anxiety, and depression are common triggers. Other potential triggers include: dehydration, loud noise, lack of exercise, poor sleep, bad posture, skipped meals, eye strain.

Analgesics, such as acetaminophen, mefenamic acid, ibuprofen and aspirin are usually very effective in stopping or reducing pain. Individuals experiencing a headache on more than 15 days per month over 90 days should see a physician.

Lifestyle changes and some treatments may help prevent tension headaches. These can include: getting enough sleep, regular exercise, improving sitting and standing posture, having an eye test, management of stress, including anxiety and/or depression, acupuncture.

3. Cluster headaches

Cluster headaches are severe and recurrent headaches that are six times more likely to develop in men than in women.
People describe an intense burning or piercing pain behind or around one eye. Other symptoms include lacrimation, swollen eyelid, a blocked/runny nose, sensitivity to light and sound, restlessness or agitation.
Cluster headaches are usually sudden, without warning, and last between 15 minutes and 3 hours. People can experience up to eight attacks a day.
Attacks tend to occur in daily clusters that can persist for weeks or months. They typically take place at the same time of day, which can often be a couple of hours after falling asleep at night.
The cause of cluster headaches is unclear, but they are more likely to occur in smokers.
Treatment aims to reduce the severity and frequency of the attacks. Options include: topiramate, sumatriptan, verapamil, steroids, melatonin, oxygen therapy and lithium.

4. Exertional headaches

Exertional headaches are brought on by strenuous physical exercise and can be triggered by: running, jumping, weight lifting, bouts of coughing or sneezing.
These headaches are usually short-lived but can sometimes last up to 2 days. They present as a throbbing pain felt throughout the head and are more common in those with a family history of migraine.
Most attacks can be treated with analgesics.

5. Hypnic headaches

A hypnic headache is a rare condition that usually begins for the first time in a person's 50s, but can start sooner. Also known as "alarm clock" headaches, they wake people during the night.
A hypnic headache consists of a mild-to-moderate throbbing pain usually felt on both sides of the head. It can last for up to 3 hours, and other symptoms may include nausea and sensitivity to light and sound.
People can experience several attacks each week. The cause of hypnic headaches is not understood, and there are no known triggers.
The leading treatment choice is caffeine, taken as tablets or as cups of coffee before bedtime. Other drug options include NSAIDs, and lithium.

Secondary headaches

A secondary headache is a symptom of something else, such as a headache resulting from a head injury or sudden caffeine withdrawal.

6. Medication-overuse headaches

A medication-overuse headache (MOH) — sometimes known as a rebound headache — is the most common type of secondary headache. A MOH is marked by frequent or daily headaches with symptoms similar to those of either tension headaches or migraines.
These headaches initially respond to analgesics but then reoccur sometime later.
MOH can result from taking analgesics for more than 15 days in a month. Drugs that can cause MOH include:

- Opioids
- Acetaminophen
- Triptans, such as sumatriptan

A MOH can still occur despite taking these medications as directed. The only treatment for MOH is to stop taking the medication behind the headaches (under the supervision of a physician). Headaches will typically stop within 10 days.
Additional withdrawal symptoms usually go away within 7 days, but may take up to 3 weeks. These include: nausea and vomiting, increased heart rate, sleep disturbance, restlessness, anxiety, and nervousness. Most people revert to their original headache pattern within 2 months. After this, it should be safe to start retaking pain relief medication.
The following steps can help prevent MOH:

- Avoiding the use of codeine
- Taking painkillers for headaches on no more than 2 days in a week
- Using preventive medications for a chronic migraine

7. Sinus headaches

Sinus headaches are caused by sinusitis. The symptoms consist of a dull, throbbing ache around the eyes, cheeks, and forehead. The pain may worsen with movement or straining and can sometimes spread to the teeth and jaw.
These headaches are usually accompanied by a thick green or yellow nasal discharge. Other symptoms may include blocked nose, fever, nausea, and light or sound sensitivity.
Sinus headaches can be treated with OTC painkillers and nasal decongestants. People should see a physician for evaluation of sinusitis if symptoms do not improve within a week.

8. Caffeine-related headaches

In people consuming more than 200 mg of caffeine daily for over 2 weeks, withdrawal may result in migraine-like headaches. Other possible symptoms include: tiredness, difficulty concentrating, poor mood or irritability, nausea.
Symptoms are often relieved following caffeine intake or resolve spontaneously within 7 days of complete withdrawal.

9. Head-injury headaches

Head injuries, including those sustained in contact sports, may lead to headaches. These are often similar to migraine or tension headaches and can usually be treated with OTC analgesics and NSAIDs.
Always call an ambulance for serious head injuries, or if someone experiences unconsciousness, seizures, vomiting, memory loss, confusion and/or vision or hearing problems after a head injury. Post-traumatic headaches can also develop months after the original head injury, making them difficult to diagnose. They can sometimes occur daily and persist for up to 12 months.

10. Menstrual headaches

Headaches are often related to changes in hormone levels. In women, migraine is frequently linked with periods due to natural changes in estrogen levels.

These menstrual migraines develop in the days just before or during a period, or sometimes during ovulation. Symptoms are similar to migraine without aura, but can last longer or be more debilitating.

Hormone-related headaches can also be caused by oral contraceptives, menopause, and pregnancy.

Mefenamic acid is an effective migraine preventative and has been reported to be particularly helpful in reducing migraine associated with heavy and/or painful periods. A dose of 500 mg, three to four times daily, may be started either 2 to 3 days before the expected start of menses, but is often effective even when started on the first day (this is useful if periods are irregular). Treatment is usually only necessary for the first two to three days of menstruation.

In a double-blind clinical study (Al-Waili NS. *Eur J Med Res.* 2000) in women (18-35 years of age), mefenamic acid was significantly superior to placebo in treatment of acute menstrual migraine when considering mean pain scores, percentage of patients pain-free at 2 hrs post-dose, percentage of patients requiring rescue treatment, percentage of patients with headache recurrence and percentage of patients with their daily activities restored.

11. Hangover headaches

Consuming too much alcohol can lead to a throbbing headache the next morning or even later that day. These migraine-like headaches are usually felt on both sides of the head and are made worse by movement. Someone who has a hangover headache may also experience nausea and sensitivity to light. There are no cures for hangovers, but it is possible to relieve symptoms by drinking plenty of water and eating sugary foods. OTC painkillers may help reduce or stop the headache.

When to see a doctor

Most headaches are rarely a sign of something more serious and most people can manage them efficiently with analgesics and NSAIDs (e.g., mefenamic acid).

However, anyone who experiences severe, persistent, recurrent, or worsening headaches should consult a doctor. Medical assistance should be sought immediately for:

- Headaches that come on very suddenly and are extremely painful
- Recurring headaches in children
- Headaches following a significant blow to the head
- Headaches associated with confusion or disturbed vision, balance, or speech
- Headaches associated with numbness or weakness
- Headaches associated with fever, seizures, or unconsciousness
- Headaches accompanied by a stiff neck or rash
- Headaches associated with persistent vomiting

Beyond The Pharmacodynamic Frontier

Dual Therapy Appears Superior to Monotherapy for Low-Income Individuals With Newly Diagnosed Type 2 Diabetes.

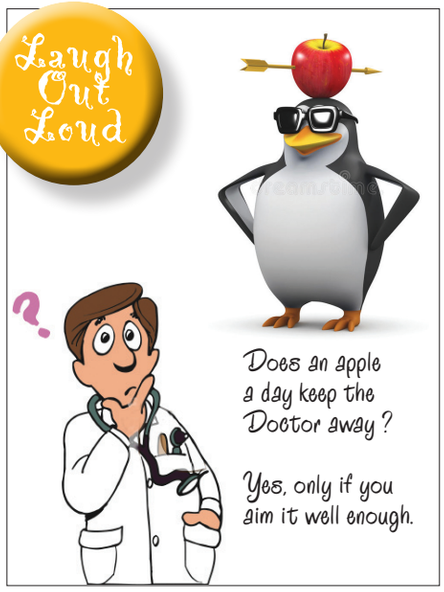
Vaughan EM, *et al. J Prim Care Community Health.* 2017; 8(4): 305-311.

- There are variable recommendations regarding initiating monotherapy or dual therapy in patients with newly diagnosed type 2 diabetes (T2DM). Clear initial strategies are of particular importance in underserved settings where access to care and financial burdens are significant barriers.
- A 12-month retrospective chart review of 309 low-income individuals with newly diagnosed T2DM initiated on oral anti-diabetic drugs (i.e., mono-, dual-, transition [from mono to dual or vice versa] therapy) indicated that patients on dual therapy had a greater change of HbA1c compared to those taking monotherapy with metformin. Patients who transitioned therapies did not differ in change of HbA1c vs. monotherapy. *Initiation of dual therapy was superior to metformin monotherapy or transitioning therapies and may be preferred for low-income individuals with newly diagnosed T2DM.*

Telmisartan improves vascular endothelial function, inflammation and insulin resistance in patients with coronary heart disease (CHD) and type 2 diabetes mellitus (T2DM).

Chen T, *et al. Exp Ther Med.* 2018; 15(1): 909-913.

- In a 12 week randomized, controlled study conducted in 80 CHD patients with coexisting T2DM, it was observed that subjects receiving telmisartan had significant improvements in levels of: Fasting blood glucose, insulin resistance, markers of vascular endothelial function (vascular endothelin [ET] levels; brachial artery diameter) and markers of inflammation (tumor necrosis factor-α [TNF-α], interleukin-6 [IL-6], C-reactive protein [CRP]).
- *Telmisartan can help patients with CHD coexisting with T2DM better regulate blood glucose, reduce insulin resistance and body inflammatory responses, and improve vascular endothelial functions.*



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