NCD Newsletter

July 2023 - Issue 07

WONDER DRUG-CAPSULE MAY ONE DAY REPLACE INSULIN INJECTION FOR DIABETICS

Scientists in Melbourne have designed a new type of oral capsule that could mean pain-free delivery of insulin and other protein drugs.

Co-lead researcher Professor Charlotte Conn, a biophysical chemist from RMIT University, said protein drugs had proven challenging to deliver orally as the drugs degrade very quickly in the stomach - until now.

“These types of drugs are typically administered with an injection – thousands of diabetics in Australia need insulin injections up to several times a day, which can be unpleasant for the patient and results in high healthcare costs.

She said the new technology could also be used to deliver other protein drugs orally - including a new type of oral antibiotic developed by the RMIT team that can avoid resistance by dangerous superbugs.

Other protein drugs such as monoclonal antibodies have been developed to treat inflammatory conditions, cancer and other diseases. An international patent application has been filed for RMIT’s technology.

The oral capsule designed by the RMIT team, alongside the fatty nanomaterial filled with insulin that is inside the capsule.
Credit: RMIT University

Strong preclinical results provide optimism for a new way to deliver insulin

The team has tested the new oral capsule with insulin in a pre-clinical study and the results have been published in the international journal Biomaterials Advances.

The research paper assessed the performance of the oral capsules with both fast-acting and slow-acting insulin.

“When controlling the blood-sugar, one needs a very fast response if they are eating a meal. That’s known as fast-acting insulin. A slow-acting form acts over a much longer timeframe - up to a day or so - to keep the insulin in the body steady. Most diabetics take a combination of both types of insulin.

“We had excellent absorption results for the slow-acting form - about 50% better than injection delivery for the same quantity of insulin,” Conn said.

The capsule achieved good absorption results for fast-acting insulin, but the significant lag in the insulin taking effect compared with injection delivery would likely make it less practical.

The results show there is real promise for using these oral capsules for slow-acting insulin, which diabetics could one day take in addition to having fast-acting insulin injections.

“The oral capsules could potentially be designed to allow dosing over specific time periods, similar to injection delivery. We need to investigate this further, develop a way of doing so and undergo rigorous testing as part of future human trials.”

Dr Céline Valéry, Dr Jamie Strachan and Professor Charlotte Conn (left to right) in the RMIT team's lab. Credit: RMIT University

How does the drug capsule work?

Dr Jamie Strachan, the first author on the paper, said the capsule protected the drug inside so that it passed safely through the stomach to the small intestine.

"The capsule has a special coating designed to not break down in the low pH environment of the stomach, before the higher pH levels in the small intestine trigger the capsule to dissolve," said Strachan, from the School of Science.

The insulin is packaged inside a fatty nanomaterial within the capsule that helps camouflage the insulin so that it can cross the intestinal walls.

It's actually similar to how the Pfizer and the Moderna COVID vaccines work where the mRNA in those vaccines is also packaged within fats, helping to keep the drugs active and safe during delivery in the body.

These vaccines contain mRNA, which is similar to DNA, to safely carry the instructions for making a viral protein within the body, activating our immune system.

A cheaper and more efficient way to deliver protein drugs

Dr Céline Valéry, a pharmaceutical scientist from RMIT and study co-author, said they used the same amount of insulin in the oral capsules and in the injection delivery.

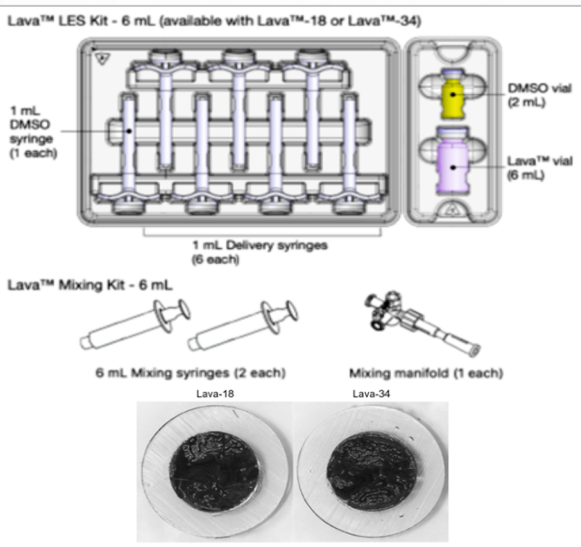
"For many pre-clinical trials the oral formulations by necessity contain much higher levels of insulin to achieve the same response as the injection delivery. This is not a very cost-effective way to deliver protein drugs which tend to be expensive," said Valéry, from the School of Health and Biomedical Sciences.

It's a great starting point but further trials are needed to develop an alternative, pain-free method for the delivery of insulin and other protein drugs.

'A promising new oral delivery mode for insulin using lipid-filled enteric-coated capsules' is published in Biomaterials Advances Jamie Strachan, Brendan Dyett, Stanley Chan, Brody McDonald, Ross Vlahos, Céline Valéry and Charlotte Conn are co-authors.

MEDICAL DEVICES

1. Lava Liquid Embolic System



The Lava Liquid Embolic System is used to stop severe bleeding (arterial bleeding or hemorrhage) in the blood vessels of the torso, arms, legs, hands, and feet (peripheral blood vessels). The system also includes particles that can be seen under fluoroscopy imaging when inside the body.

A doctor inserts the delivery catheterASA in an artery by making a small cut, or incision. The catheter is carefully guided through the blood vessels to the area of arterial bleeding using fluoroscopy imaging. When the liquid embolic is injected into the blood vessel, it forms a spongy solid material that stops active bleeding.

The device is used in people who have active arterial bleeding in peripheral vessels. Arterial bleeding, or hemorrhage, can be caused by injury or damage to the organs or blood vessels. Hemorrhage may require emergency medical attention to get bleeding under control.

The Lava Liquid Embolic System becomes solid when injected into a blood vessel to stop active arterial bleeding in peripheral blood vessels. In a study of 113 patients, the system successfully stopped bleeding 94% of the time.

This device should not be used in pregnant women, babies 4 weeks old or younger (neonates), or people who have problems with liver or kidney function.

2. Assert-IQ insertable cardiac monitor device

The device is intended to conduct diagnostic assessment and long-term monitoring of individuals with irregular heartbeats.

The US Food and Drug Administration (FDA) has approved Abbott's Assert-IQ insertable cardiac monitor (ICM) device.

The new device will enable physicians to carry out diagnostic assessments and long-term monitoring of individuals with irregular heartbeats (arrhythmias). Assert-IQ provides doctors with enhanced flexibility in diagnostic monitoring by offering two battery life options, ensuring a minimum lifespan of three or six years.

The three-year option is suitable for traditional monitoring such as diagnosis of fainting, heart palpitations or detection of abnormal heart rhythms. In contrast, the six-year option enables physicians to conduct long-term monitoring.

The monitoring is crucial for individuals who are undergoing therapy, have been recently treated for cardiac ablation or are vulnerable to additional arrhythmias including atrial fibrillation.

Until now, insertable cardiac monitors have allowed for remote monitoring of patients but lacked the longevity needed to monitor them long-term. Assert-IQ IQCM offers physicians a connected health device that will help them provide the best care for their patients while making more accurate and informed treatment decisions.

This device utilizes Bluetooth technology to stay connected to a transmitter, which is generally the individual's personal mobile phone. It continuously monitors heart rhythms at 20-second intervals and transmits the real-time results to the clinic's portal. Furthermore, certain models within the Assert-IQ ICM family support remote programming to improve connectivity with patients. This feature enables clinicians to modify the settings of the connected device, enhancing performance and minimizing unnecessary alerts or transmissions.

NEW FDA APPROVALS & INDICATIONS

Sr. No.	Brand Name	Generic Name	Approval Date	FDA approved Indication
1	Lantidra	Donislecel	6/28/2023	Allogeneic pancreatic islet cellular therapy for the treatment of type 1 diabetes mellitus
2	Inpefa	Sotagliflozin	6/26/2023	INPEFA is indicated to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with: • heart failure or • type 2 diabetes mellitus, chronic kidney disease, and other cardiovascular risk factors

INDIA IS EMERGING AS A FAVORABLE DESTINATION TO CONDUCT CLINICAL TRIALS, REVEALS REPORT

In the coming years, India has the potential to increase global clinical trials in the country by five times, according to a report.

According to the report, Biopharma can benefit from the critical enablers of innovation in the private healthcare system in India and leverage the rapidly expanding healthcare infrastructure in the country.

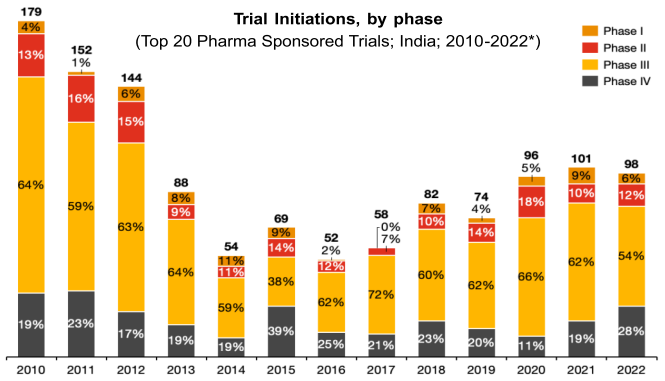
A joint report by PwC India & US-India Chamber of Commerce (USAIC), 'Clinical Trial opportunities in India,' has revealed that India is emerging as a favorable destination to conduct clinical trials. The report was released at the USAIC BioPharma & Healthcare Summit held virtually on May 3.

"Clinical trial activity in India has been increasing steadily since 2014 due to several key regulatory reforms aimed towards global harmonization, enabling open access to clinical trials in India. The country's diverse population, combined with its rapidly advancing healthcare infrastructure, provides a fertile ground for clinical trials to flourish. This is an opportunity for top biopharma companies to develop a long-term strategy that focuses on the key enablers of innovation and strategic partnerships in India," Sujay Shetty, Partner & Global Health Industries Leader, PwC, said in a statement.

According to the report, Biopharma can benefit from the critical enablers of innovation in the private healthcare system in India and leverage the rapidly expanding healthcare infrastructure in the country.

Clinical trial activity was historically low until 2014 due to non-favorable regulations; since 2014 India witnessed a reversal of historical decline

Key takeaway: While India's contribution to the global clinical trials has been ~4% in the last decade, top 20 pharma activity has increased by 10% since 2013



Actual annual trial initiation count may differ because not all trials were reported with phase distribution *2022 trial initiation counts are provisional and updated on December 15, 2022

Source: PwC Analyses, TrialTrove, December 2022

1. Growth Recovery

4% While bulk of the sponsored trials are Phase III, Phase IV trials have grown at 4% annually over the last decade

40% Following the new regulations, the number of sites increased by 40% between 2014 and 2022

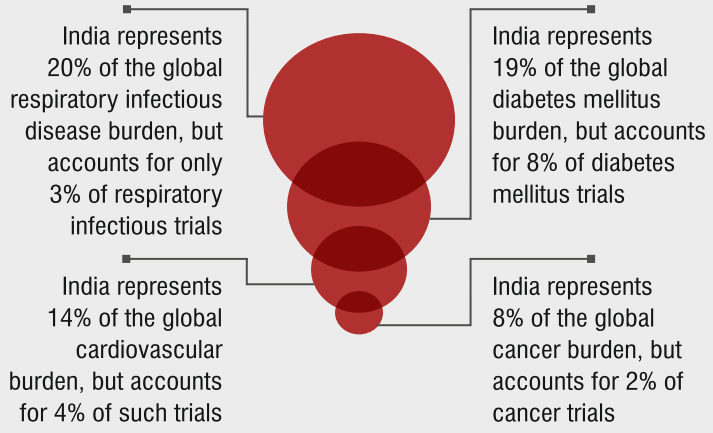
2. Catalysts of Growth

10+ Since 2013, 10+ regulatory updates (e.g., NDCT 2019, online platform, relaxation on approval processes) have catalyzed the growth in trial activity

2019 The 2019 NDCT** Rules established the principles and practices for clinical trials, including the continuous evaluation of data to achieve safety

**NDCT: New Drug & Clinical Trial Rules, 2019

MILES TO GO



CLINICAL TRIAL SCENE

In the top 20 pharma companies, AstraZeneca, Novartis, Eli Lilly, Pfizer and J&J are among the sponsors of clinical trials in India

Following the new regulations, the number of sites increased by 40% between 2014 & 2022

Total number of investigations has increased by 2x between 2015 & 2020

CDSCO now has 90 days to decide whether to approve global clinical trial applications

Revised timeline for approval to manufacture new drugs in India has been reduced to 90 days

Key takeaways from the report:

- The private sector is a well-suited channel for the top biopharma to conduct more efficient clinical trials with easier and faster access to investigators and patients.
- Indian states with high disease prevalence (e.g., cancer) also have the most number of tier-1 cities, with advanced medical infrastructure and availability of investigators. Targeting these states can provide biopharma companies with faster access to patients, sites, and investigators
- Total number of investigators has increased by 2x between 2015 and 2020, with the majority of the increase occurring in the internal medicine and oncology specializations. However, the growth in the number of investigators is largely restricted to tier-1 and 2 cities.
- While the top 20 pharma activity for the major therapy classes in India has remained largely constant in the last decade, growth opportunities exist across key diseases (e.g., pain, epilepsy, cervical cancer) and orphan diseases (β-thalassemia, Duchenne Muscular Dystrophy)
- India has an overall clinical trial participation of ~3% but contributes upwards of 15% to the global burden of most high prevalent diseases (e.g., respiratory infections, cardiovascular, diabetes, cervical cancer), representing an untapped potential for top pharma
- Top biopharma should align their strategy towards tier-1 cities (e.g., Mumbai, Delhi, Bengaluru, Chennai) where the higher bed capacity, number of doctors, and presence of tertiary care multi-city hospitals can support enablement efforts of running faster and more efficient clinical trials.

GOVT BANS 14 FIXED-DOSE COMBINATION DRUGS USED TO TREAT COUGH, FEVER

The Union Health Ministry has banned 14 irrational fixed-dose combination (FDC) medicines five years after the Supreme Court told the government to examine the health benefits of these drugs. In a series of notifications published

Sr. No	Combination
1	Nimesulide, paracetamol dispersible tablet
2	Amoxicillin, bromhexine
3	Pholcodine, promethazine
4	Chlorpheniramine maleate, dextromethorphan, guaiphenesin, ammonium chloride, menthol
5	Ammonium chloride, bromhexine, dextromethorphan
6	Chlorpheniramine maleate, codeine syrup
7	Bromhexine, dextromethorphan, ammonium chloride, menthol
8	Dextromethorphan, chlorpheniramine maleate, guaiphenesin, ammonium chloride
9	Paracetamol, bromhexine, phenylephrine, chlorpheniramine, guaiphenesin
10	Salbutamol, bromhexine
11	Chlorpheniramine, codeine phosphate, menthol syrup
12	Phenytoin, phenobarbitone sodium
13	Ammonium chloride, sodium citrate, chlorpheniramine maleate, menthol syrup
14	Salbutamol, hydroxyethyl theophylline, bromhexine

CASE STUDY 1

An Unusual Side Effect of Metformin-Nightmare and Abnormal Dreams

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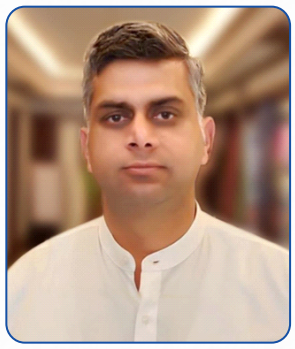
Diabetes & Thyroid Specialist



Introduction

Since medieval times, biguanides in the form of French iliac or goat's rue were used in Southern and Eastern Europe as a treatment for diabetes. French physician Jean Sterne translated the blood glucose lowering potential of metformin into a therapeutic reality in 1956. Although metformin was available in the United Kingdom in 1958 and in Canada in 1972, it got US Food and Drug Administration (FDA) approval in 1994. Metformin was introduced in 1957 and since then metformin has been the "uncrowned king." In the arena of antidiabetic drugs, day by day newer advantages and indications in the treatment strategies are coming up.

Case description

A 30-year-old male, who was a bank employee, presented to the medicine outdoor department with chief complaints of nightmares and abnormal dreams for the last 15-20 days. He was diagnosed with type 2 diabetes mellitus (T2DM) about a month back for which he was prescribed sitagliptin+metformin (50/500) combination twice daily. He told that he started having abnormal dreams and nightmares after 7-8 days of starting this drug therapy. He is married and satisfied with his job and family life. He denied any other concomitant drug intake (including ayurvedic and homeopathic)/abuse or any other illness. He is a nonsmoker, non tobacco chewer, and also refused any previous or present intake of alcohol. The patient also reported having frequent nightmares leading to awakening and lack of sleep, which affected his mental state and work performance throughout the subsequent day. Hamilton psychiatric rating scale for depression (HAM–D17) and Pittsburgh Sleep Quality Index (PSQI) showed a very good sleep quality and also negative results for any depressive symptoms.

Physical examination was found to be unremarkable. Renal function test (RFT), liver function test (LFT), complete blood count (CBC), and lipid profile were within normal limits. His blood sugar fasting and post prandial were 110 and 190mg/dL, respectively. His HbA1c was 7.2%. To rule out hypoglycemia, we performed a continuous glucose monitoring test (CGMS) and it showed glycemic levels between 106 and 192mg/dL. On searching the literature online, we found studies on sleep disorders with metformin. Therefore, we stopped the combination and switched the patient from sitagliptin + metformin to sitagliptin 100mg daily and glimepiride 0.5mg daily. On a follow-up visit on the 10th day, the patient denied of nightmare and abnormal dreams. So these symptoms were metformin induced.

On the Naranjo's Severity Assessment scale, the adverse event indicated a probable causality. On Hartwig's scale, the adverse drug reaction (ADR) falls under a mild severe reaction.

After 2 months, metformin was reintroduced by another physician and the patient again complained of nightmares and abnormal dreams; on stopping metformin, the problem of nightmares and abnormal dreams was resolved.

Discussion

Metformin is useful, safe, and one of the cost-effective drugs for diabetes. Beyond its effects on glucose and lipid metabolism, it has been shown to reduce cardiovascular mortality, morbidity, atherogenic process, insulin resistance, homeostasis, vascular function, and microcirculation. Dreaming is a very complex cognitive process in the human central nervous system during sleep that might be affected by a wide variety of variables, including psychological, medical, and social factors.Nightmares are defined as intensely disturbing dreams that awaken the dreamer to a fully conscious state and generally occur in the latter half of the sleep period.Despite the absence of a precise pathophysiology for disordered dreaming which might possibly involve a very complex neurochemical process, drugs affecting the neurotransmitters and those affecting the rapid eye movement (REM) sleep have been proved to cause nightmares. The occurrence of abnormal dreams and poor quality of sleep among those suffering from T2DM were found to be associated with poor glycemic control in such patients [Table 1].

Table 1: Drugs influencing adrenergic, aminergic, dopaminergic, and cholinergic neurotransmitter have a prominent role in abnormal dreams or nightmare

Sr No.	Class	Drugs
1.	Antihypertensive agents	B-blockers, B-blockers Guanethidine, reserpine ACE inhibitors, ARB Calcium channel blockers
2.	Statins	Atorvastatin, simvastatin, pravastatin
3.	Anti-Alzheimer's	Donepezil, rivastigmine, tacrine, memantine
4.	Antidepressants	MAO inhibitors, tricyclic antidepressants SSRI, fluoxetine, citalopram Mirtazapine
5.	Antipsychotic's agent	Chlorpromazine, thiothixene Clozapine
6.	Anti-Parkinsonian drugs	Levodopa, Bromocriptine, Pergolide Amantadine
7.	Antiepileptic drugs	Gabapentin, valproic acid, lamotrigine, ethosuximide
8.	Sedatives hypnotics	Benzodiazepines, zolpidem
9.	General anaesthetic	Propofol, thiopental, midazolam Isoflurane, ketamine
10.	Antihistamines	Chlorpheniramine
11.	Antimicrobial and immunosuppressant agents	Erythromycin, ciprofloxacin Ganciclovir, amantadine
12.	Analgesic drugs	Morphine, buprenorphine Naproxen
13.	Endocrinal agents	DHEA, testosterone

ACE = angiotensin-converting enzyme, ARB = angiotensin receptor blocker, DHEA = dehydroepiandrosterone, MAO = monoamine oxidase, SSRI = selective serotonin reuptake inhibitor

While there were reports of several meta-analyses and reviews of adverse effects of metformin, only a case report and a brief review mentioned nightmare and abnormal dreams as a possible causality of metformin. In our case, the patient complained of nightmare on combination of sitagliptin + metformin; however, when we switched the therapy to sitagliptin + glimepiride (omitting metformin) the patient denied nightmares and abnormal dream, so it is proven that the nightmares occurred due to metformin and also this was confirmed by drug rechallenge.

T2DM does not entirely explain why the symptoms such as abnormal dreams were ensued directly after metformin therapy but it might be an underlying cause of the symptoms. One factor playing a significant role in explaining

nightmares and abnormal dreams as an ADR in this case might be cerebral blood glucose levels during night. Nocturnal hypoglycemia is clinically asymptomatic most often, but it might cause problems related to poor sleep quality in certain individuals.

Conclusion

Metformin with low side effect profile and very few serious complications is considered to be a safe oral hypoglycemic drug though it may be associated with nightmares and abnormal dreams as rare side effects of the drug.

CASE STUDY 2

Pachydermoperiostosis (Touraine-Solente-Gole syndrome)

Dr. Shaqib Ahmad
DM Endocrinologist , Lucknow

Introduction:

Pachydermoperiostosis is a rare disorder characterized by progressive thickening of the skin, enlargement of the hands and feet, and clubbing of the fingers and toes. It is considered a differential diagnosis of acral enlargement and requires a distinct treatment approach compared to other causes of acromegaly or pseudoacromegaly. We present a case of pachydermoperiostosis in a young male patient and discuss the clinical features, investigations, differential diagnoses & treatment options.

Case Presentation

A 26-year-old male presented with a complaint of acral enlargement, coarsening of facial features, and increased sweating persisting for 6 years. The patient denied any history of diplopia, color blindness, visual field restriction, polyuria, polydipsia, carpal tunnel syndrome, behavioral dysfunction, autonomic dysfunction, seizure, cranial nerve palsy, deepening of voice and snoring, recurrent hypoglycemia/overeating, or any significant medical history. There was no family history of similar complaints or relevant medical conditions.

Upon physical examination, the patient's height was measured to be 167 cm, weight was 61.4 kg, and BMI was calculated as 22.01 kg/m^2. Blood pressure was recorded as 130/90 mm Hg.

The patient exhibited pronounced clinical features characteristic of pachydermoperiostosis. Clubbing of the fingers and toes was observed, graded as grade 4, and was present in all four limbs. The fingertips appeared bulbous and rounded, with the nails showing a convex curvature. The presence of clubbing can be indicative of underlying chronic diseases and is commonly associated with pachydermoperiostosis.

Acromegaloid facies were noted, characterized by coarse and thickened skin. The facial features included a prominent supraorbital margin, which contributed to the overall coarsening of the patient's facial appearance. However, there was no evidence of prognathism, and macroglossia was absent. The head circumference was measured as 57 cm, which was within the normal range. Laboratory investigations showed normal hemoglobin level and white blood cell count. (Hb: 12.3 gm/dl TLC: 7000/ cmm DLC: P 65 L 30 E 3 Platelet: 1.9 lac. PBF: RBC normocytic normochromic, S.Ca++: 1.20, S Bilirubin: 0.5 mg/dl, SGOT: 19, SGPT=23, S. Creatinine =0.9 mg/dl, S. Cortisol (8.00 am) = 13.5 µgm/ dl, S. Prolactin=8.08 ng/ ml, S. FSH: 2.02 mIU/mL, S. LH: 1.94 mIU/ml, S. Testo=1140 ng/dl, s.TSH =3.1 mciu/ml, s.T4 =1.3 ngm/ dl, S. IGF1= 107 ng/ml, S. Lipid profile; s.cholesterol=202 mg/dl, S.TG=175 mg/dl, S.HDL=65.3 mg/dl s.VLDL=35 mg/dl). The C-reactive protein (CRP) test was positive. Radiographic evaluation revealed periostitis in long bones, while X-ray of the skull was normal. Visual field analysis was within normal limits.

Diagnosis and Treatment

Based on the clinical features, physical examination findings, and investigations, a diagnosis of pachydermoperiostosis was made. The patient was prescribed naproxen tablets (30 mg once a day) for a duration of 2 months. The treatment resulted in a significant improvement in the coarsening of facial features without any joint pain or notable side effects.

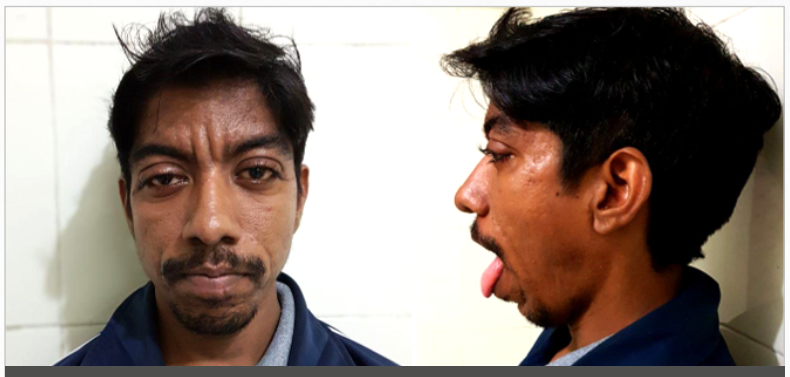


Fig 1: Acromegaloid facies with prominent supraorbital margin, thick lips and deep furrowing of his forehead skin

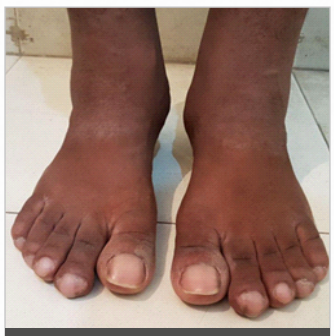


Fig 2: Spade-like feet with thick doughy soles and clubbing of toes

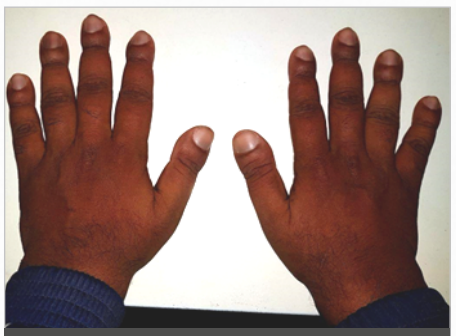


Fig 3: Spade-like feet with thick doughy soles and clubbing of toes

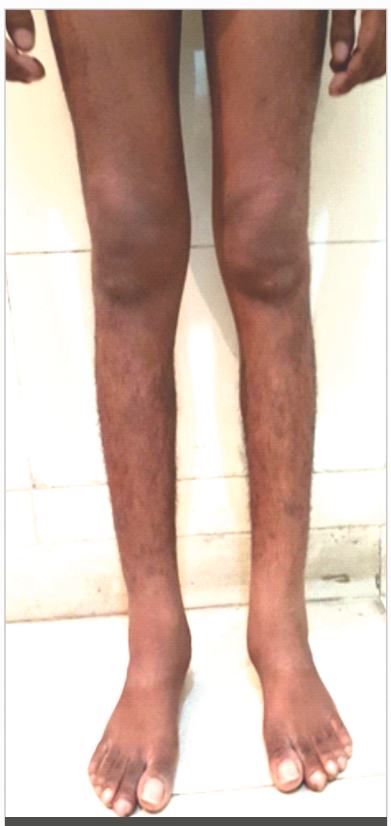


Fig 4: Bilateral knee effusions

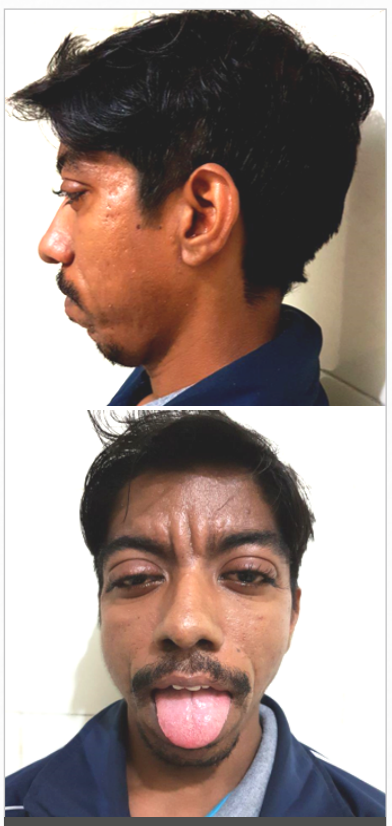


Fig 5: No prognathism, No macroglossia present

Outcome and Follow-up

The patient showed a gradual improvement in symptoms and remained asymptomatic during follow-up visits. There were no reports of joint pain or any significant side effects related to the treatment. The patient's condition continues to be monitored regularly.

Discussion

Pachydermoperiostosis is a rare condition characterized by thickening of the skin, enlargement of the hands and feet, and clubbing. It is important to differentiate pachydermoperiostosis from other causes of acral enlargement, such as pituitary acromegaly, hypothyroidism, drug-induced conditions, and hormone-secreting tumors. The response to treatment differs among these conditions. In the literature, various treatment modalities have been explored for pachydermoperiostosis, including oral isotretinoin, nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, indomethacin, coxibs,

bisphosphonates, and tamoxifen. The choice of treatment depends on the individual patient's symptoms, severity of the condition, and response to therapy.In this case, the patient showed a favorable response to NSAID treatment with naproxen.

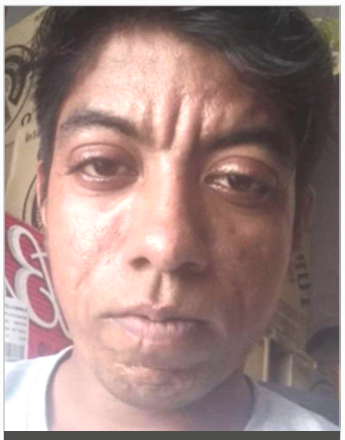


Fig 6: Recent image after 3 months of treatment

Conclusion

Pachydermoperiostosis should be considered as a differential diagnosis in cases of acral enlargement with clubbing. This case highlights the importance of a thorough clinical evaluation, appropriate investigations, and tailored treatment approaches for differentiating pachydermoperiostosis from other causes of acromegaly or pseudoacromegaly. Further studies are needed to explore the underlying pathogenesis and optimal treatment strategies for this rare condition.

Informed Consent:

The patient has provided written informed consent for the inclusion of their case details and images in this report.

GUIDELINE UPDATES

American Association of Clinical Endocrinology (AACE) has recently updated the Comprehensive Type 2 Diabetes Management Algorithm 2023.

This 2023 diabetes algorithm update emphasizes lifestyle modification and treatment of overweight/obesity as key pillars in the management of prediabetes and diabetes mellitus and highlights the importance of appropriate management of atherosclerotic risk factors of dyslipidemia and hypertension.

One notable new theme is an emphasis on a complication-centric approach, beyond glucose levels, to frame decisions regarding first-line pharmacologic choices for the treatment of persons with diabetes.

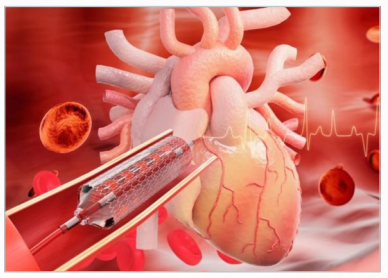
KEY POINTS

1. Glucose-lowering algorithms split into "complications-centric" and "glucose-centric". Accordingly, recommendations have been given for the choice of antihyperglycemic agents in T2M management.
2. Further, the glucose-centric algorithm considers obesity, hypoglycemia risk, and access / cost issues for the selection of OADs. (Patient-centric approach for decision making).
3. Prediabetes patients should be treated with metformin, pioglitazone, and acarbose to prevent the progression to T2DM, if not well controlled with lifestyle modification.
4. Considering the COVID pandemic in the past, the Vaccine Recommendations for Persons with Diabetes Mellitus section is added as advice for DM patients with the flu vaccine, pneumococcal vaccine, recombinant zoster vaccine etc. for secondary prevention.
5. Profiles of weight loss medications have been mentioned with details of Semaglutide, Liraglutide, Phentermine / Topiramate-ER, Naltrexone-ER / Buproprion-ER, Orlistat and Phentermine.
6. Guideline has mentioned some options for the treatment of hypoglycemia includes,soluble glucagon and a glucagon analog (dasiglucagon), Intranasal glucagon.

TRIAL UPDATE

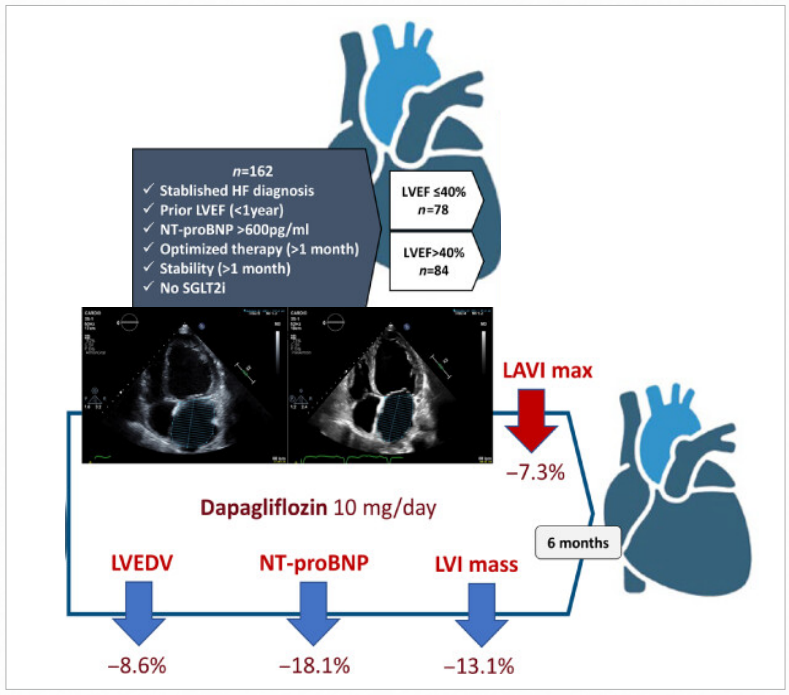
1. DAPA MODA Trial: Dapagliflozin Improves Multiple Parameters of Cardiac Remodeling

May 31, 2023



In the prospective DAPA MODA trial, therapy with dapagliflozin reversed left atrium and left ventricle remodeling over 180 days. The therapy also had a positive influence on biomarkers and the quality of life of patients with heart failure (HF).

Graphical Abstract:



The mechanisms underlying the positive effect of SGLT2 inhibitors on cardiac remodeling have not yet been fully understood. As the left atrium plays a critical role in cardiac function, Dr. Domingo Pascual-Figal and his team aimed to investigate the impact of dapagliflozin on echocardiographic parameters of cardiac remodeling, with special focus on geometry and function of the left atrium. The multicenter, single-arm, open-label, prospective DAPA MODA trial (NCT04707352) was specifically designed to assess the effect of dapagliflozin in cardiac remodeling parameters over a 6-month period in stable patients with chronic HF irrespective of left ventricular ejection fraction (LVEF) and diabetes status. The primary endpoint was the left atrial volume index (LAVI) maximal change from baseline to 180 days. Secondary endpoints included changes in other parameters of geometry and function of left atrium and left ventricle, and circulation biomarkers.

The 162 participants had a mean age of 70.5 years; 40% were 75 years or older. “Our trial population reflects a real-world population in terms of age and long-standing high rates of guideline-directed medical therapy,” Dr. Pascual-Figal commented. Atrial disease was present irrespective of LVEF phenotype. At baseline, the study population had a LAVI maximal of 48,1 ±22.64 mL/m2.

At 180 days, therapy with dapagliflozin reduced LAVI maximal by -6.6% (P=0.008). “Therapy with dapagliflozin led to an improvement of all left ventricular remodeling parameters,” Dr. Pascual-Figal said. Left ventricular mass was reduced by 13.9% at 180 days, a highly statistically significant change (P<0.001). The positive treatment effect was mirrored by a reduction of biomarkers: NT-proBNP concentrations were lowered by 18.2% compared with baseline (P<0.001). Therapy with dapagliflozin also improved the quality of life of patients.

Dr. Pascual-Figal concluded that these results support the concept of the left atrium as part of a global adverse remodeling in HF, regardless of LVEF. The benefit of dapagliflozin in HF patients may be partly explained by the ability to reverse cardiac remodeling.

REFERENCE: Pascual-Figal DA. DAPA MODA: Dapagliflozin and cardiac remodeling in chronic heart failure. Presented at: Heart Failure 2023; May 20-23, 2023; Prague, Czechia.

2. Sacubitril / valsartan and dapagliflozin combination exerts better effects in patients with diabetes and STEMI

May 2023

Announcing a new article publication for Cardiovascular Innovations and Applications journal. This study was aimed at observing the clinical effects of sacubitril/valsartan combined with dapagliflozin on cardiac function and ventricular remodeling in patients with type 2 diabetes and ST-segment elevation myocardial infarction (STEMI).

Between May 2019 and May 2022, the authors of this article retrospectively analyzed 57 patients with diabetes and STEMI receiving percutaneous coronary intervention: 32 patients receiving sacubitril/valsartan and dapagliflozin tablets comprised the observation group and 25 patients receiving angiotensin converting enzyme inhibition (ACEI) or angiotensin receptor blockers ARB) in combination with other hypoglycemic drugs comprised the control group. The authors of this article compared the left ventricular end diastolic diameter (LVEDD), right ventricular end diastolic diameter (RVEDD), left ventricular ejection fraction (LVEF), N-terminal pro-B-type natriuretic peptide (NT-pro BNP), and noninvasive hemodynamic parameters at baseline and 3-6 months after treatment between the groups.

Before treatment, the parameters were similar between the observation group and control group. However, after 3-6 months of treatment, serum NT-pro BNP levels showed a greater decline in the observation group than the control group. Moreover, the LVEDD and LVEF improved more substantially in the observation group than the control group ($P<0.05$). RVEDD did not markedly change after treatment ($P>0.05$). After treatment, in the observation group, the cardiac index (CI) and cardiac output (CO) were significantly higher, and the thoracic fluid conduction (TFC) and systemic vascular resistance index (SVRI) were significantly lower, than those in the control group ($P<0.05$).

Sacubitril/valsartan combination with dapagliflozin exerted better effects than ACEI or ARB with other hypoglycemic drugs in improving cardiac function and ventricular remodeling in patients with diabetes and STEMI.

REFERENCE: Wang, Z., et al. (2023) Clinical Effects of Sacubitril/Valsartan Combined with Dapagliflozin in Patients with Diabetes and ST-segment Elevation Myocardial Infarction. Cardiovascular Innovations and Applications. doi.org/10.15212/CVIA.2023.0032.

CASE STUDY - 3

Acute myocardial infarction with multi vessel thrombus containing lesions: An unusual presentation

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DM. (Interventional Cardiologist)
(Fellow SCAI) KMGU, Lucknow

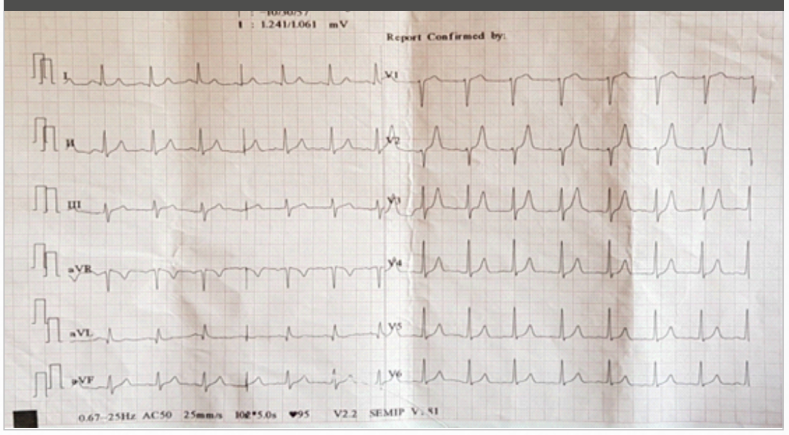
Introduction

Acute multiple STEMI (AMSTEMI) due to thrombotic occlusion of >1 major ECAs can be seen very rarely (2.5%) in STEMI-suffering patients. More than one third patients p/w cardiogenic shock & fatal arrhythmia. AMSTEMI is an extreme clinical condition on which there is limited information in the literature; most of them are case reports. The main pathophysiological mechanism is thrombotic occlusion due to atherosclerotic plaques. But, simultaneous multi-vessel thrombosis can be secondary to the following causes: coronary vasospasm, vasoactive drug abuse, increased thrombotic conditions, rheumatoid diseases, adenosine receptor agonist-induced complication.

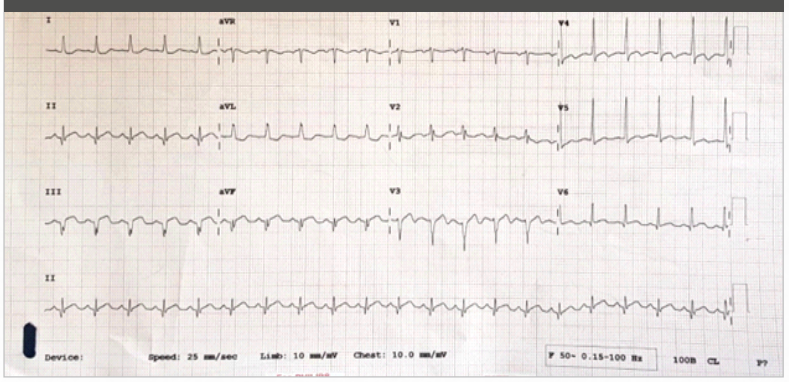
Case description

A 32-year-old male was admitted to the emergency department with severe chest discomfort, perspiration & vomiting which started 14 hours ago. He had no known history of coronary artery disease. No history of hypertension, diabetes mellitus , dyslipidemia. He is a chronic weed smoker for 15 years. He is unmarried and non-obese. His heart rate and blood pressure were 126/min , BP 80/50 mmHg respectively and had a cold extremity. EKG showed ST coving in anterior & inferior leads and sinus tachycardia. 2d echo showed LAD & RCA territory severely hypokinetic [EF 38%] with moderate MR & mild to moderate TR. ANGIO MVD with thrombus occluding lesions. Laboratory reports showed raised Troponin I, BNP, slightly raised LDL & TG levels, normal Homocysteine level, FBS , PPBS & HbA1c were also normal.

H/O mild chest & epigastric discomfort 5 Days back & normal EKG documented by local doctor



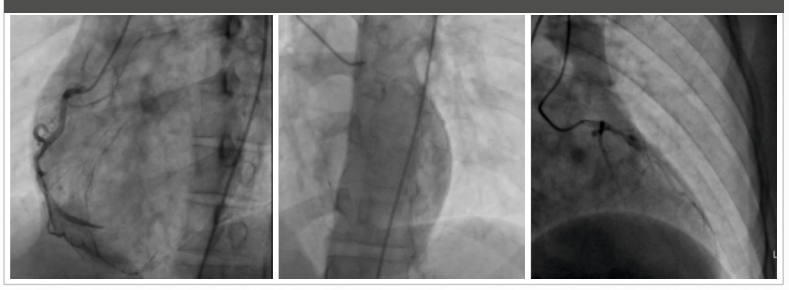
At time of presentation ST coving in inferior & anterior leads with reciprocal changes in 1, aVL & sinus tachycardia



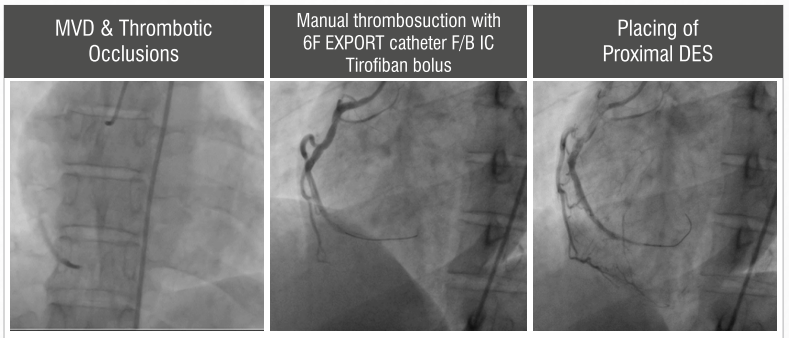
Patient was diagnosed with ACS (AMSTEMI), a coronary angiogram was planned immediately.

Acetylsalicylic acid (300 mg) and loading-dose ticagrelor (180mg) were administered. The patient was given Rosuvastatin LD 40 MG, IV fluids & IV vasopressor noradrenaline infusion. He was then Immediately shifted to the cath lab

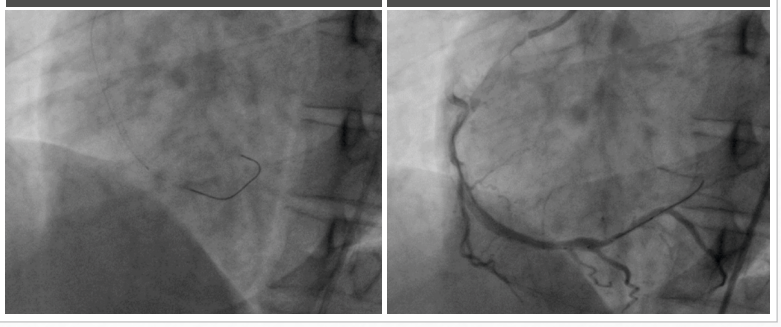
PROX LAD 70% f/b MID LAD 100%, D1 100%, PROX LCX 90%, DISTAL RCA 100%



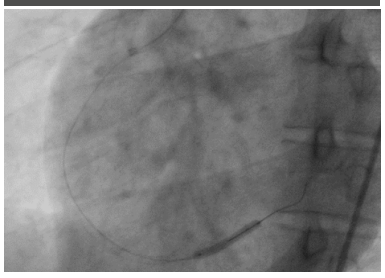
MVD & Thrombotic Occlusions | Manual thrombosuction with 6F EXPORT catheter F/B IC Tirofiban bolus | Placing of Proximal DES



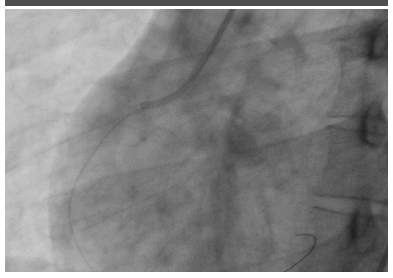
1st DES distal RCA to crux long stent (3 x 33) | 2nd DES after crux (2.75 x 18)



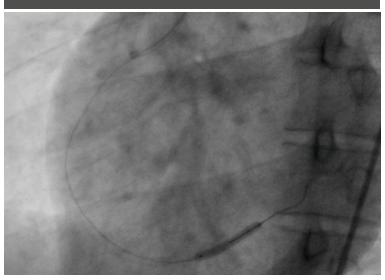
1st DES distal RCA to crux long stent (3 x 33)



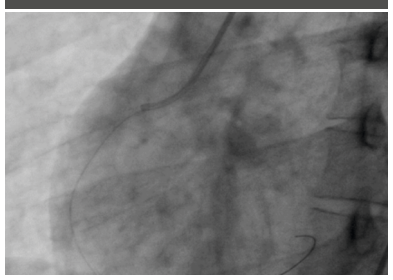
2nd DES after crux (2.75 x 18)



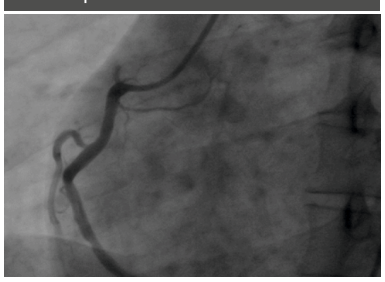
2nd DES Dilatation



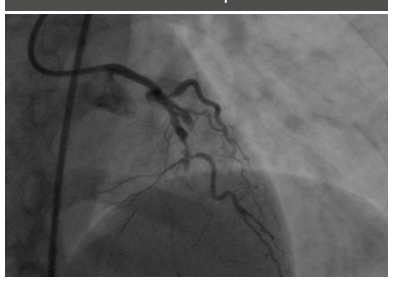
Post dilatation of proximal stent with NC balloon 3.5 x 12



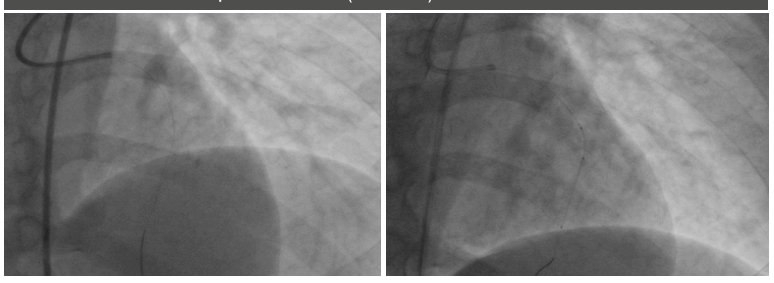
TIMI 3 flow, no sign of perforation & dissection



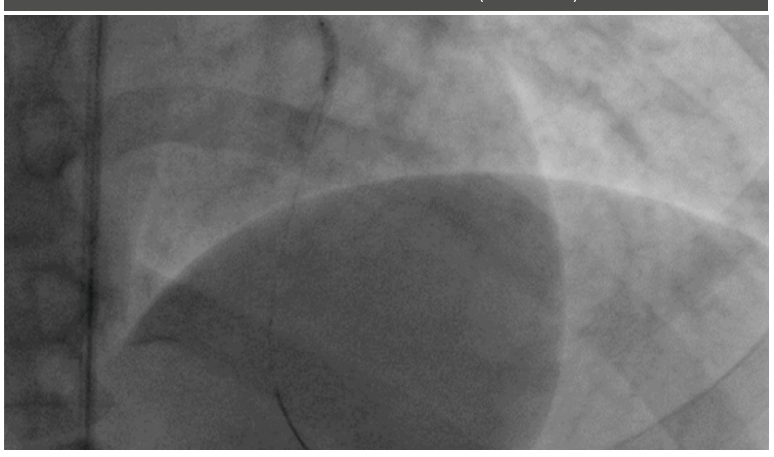
Manual thrombosuction done with same export catheter



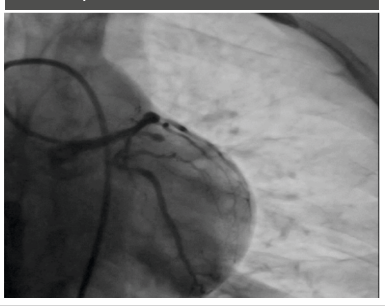
Predilatation in mid to distal LAD with small compliant balloon (2.0 x 15) IC tirofiban bolus



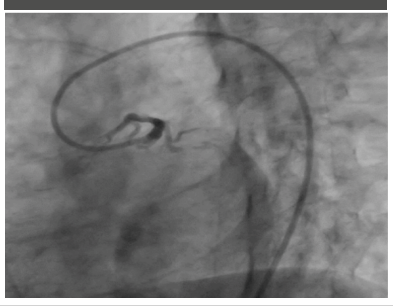
Post dilatation with NC balloon (2.75 X12)



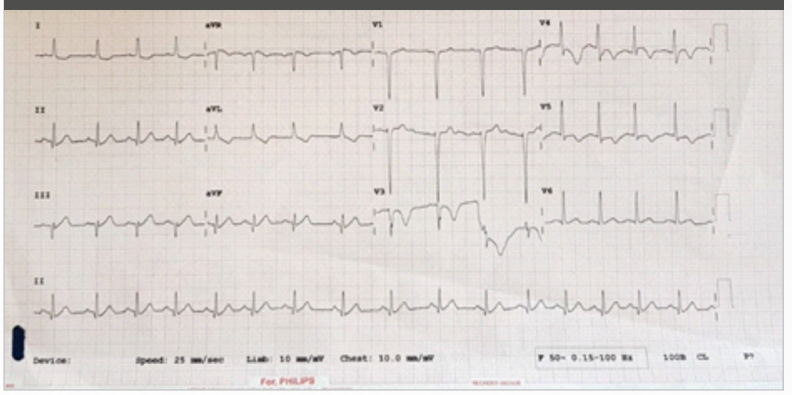
TIMI 3 flow, no sign of perforation & dissection



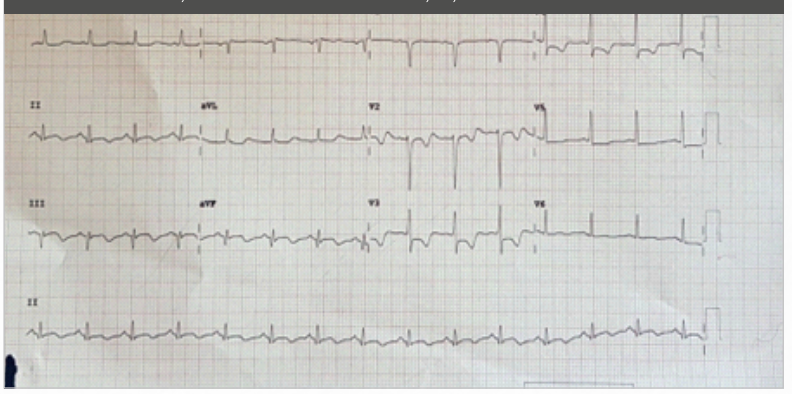
Stage procedure plan for Diagonal & Lcx Tirofiban Iv infusion for 24 hours



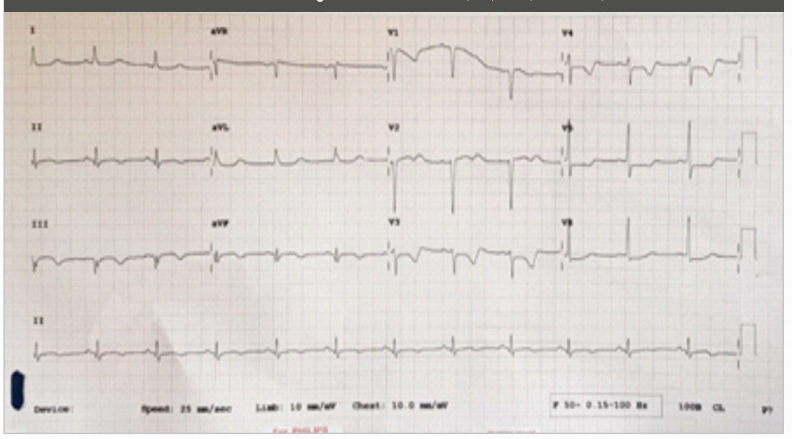
Post procedureEKG



DAY 2 EKG , Q wave with T inversion II, iii, aVF & T inversion in V2-V4



DAY 3 EKG at time of discharge T inversion in ii, iii, aVF, V2 –V4, Vitals stable



Conclusion

- Simultaneous multi-vessel coronary thrombotic occlusion is an extremely rare clinical condition.
- Most of the patients cannot be reached to a hospital, and patients who are admitted suffer from serious clinical outcomes of multiple myocardial infarctions.
- Urgent invasive treatment should be given to all eligible patients.

CASE STUDY - 4

A case of LQT Syndrome in a postpartum female presented with recurrent polymorphic ventricular tachycardia managed with atrial pacing and dual chamber Automatic implantable cardioverter-defibrillator (AICD)

Dr. Venkata Siva Krishna K
Consultant Interventional Cardiologist

Introduction

The Congenital Long QT is a rare congenital disorder characterized by delayed repolarization of the myocardium leading to QT-interval prolongation (QTc >480 msec) and repetitive episodes of syncope, seizures and sudden cardiac death related to rapid, polymorphic ventricular tachycardia in the setting of structurally normal heart and otherwise healthy adults. Genetic linkage mapping defines six types of LQTS (LQT1-LQT6) out of which, LQT1-LQT3 have been well characterized in clinical studies. Diagnosis of LQTS is based on clinical and electrocardiographic features. Patients with LQT may or may not

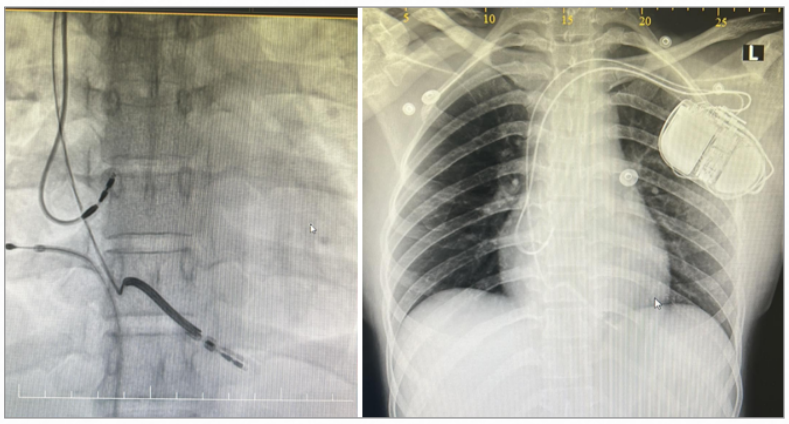
show QT prolongation on surface ECG. Sometimes specific triggers like exercise, swimming, emotion, auditory stimuli like alarm clock, postpartum period male heart electrically unstable and precipitate torsades de pointes that is sometimes lethal. Timely diagnosis and management with AICD prevents sudden cardiac death in these individuals. LQT 1 is precipitated by swimming, LQT2 postpartum period and LQT3 at rest and sleep. Recently genotype specific electrocardiographic patterns in the congenital LQTS have also been described. Here we describe a case of LQT in a postpartum female with recurrent episodes of Torsade de pointes treated successfully with Atrial pacing followed by AICD implantation.

Case report

22 yr old female, postpartum status, otherwise healthy with no comorbidities presented to the ER with complaints of multiple episodes of dizziness and seizure like events for the past 2 days. She was referred from a peripheral center where she was diagnosed to have multiple episodes of Ventricular tachycardia reverted with DC cardioversion. She was tried with Amiodarone and Lidocaine to prevent recurrence but –failed. At the presentation to the ER here baseline ECG showed Normal Sinus Rhythm with Prolonged QTc of 550 sec. Echo showed a structurally normal heart with normal EF. All baseline investigations were done. Serum Electrolytes were in normal range.

She was initially hemodynamically stable and got admitted to the ICU. After admission she again developed multiple episodes of VT, typical Torsade de pointes that needed Defibrillation as the patient is becoming unresponsive and hemodynamically unstable. Beta-blocker Propranolol was tried, but unsuccessful. Class IA drugs tried as they may prolong the QT further. As a last resort to prevent the recurrent arrhythmia atrial pacing with temporary pacing lead was attempted. She was shifted to cath lab and TPI done with lead in the RA and paced at a rate of 100 bpm. The lead position was secured properly and she was shifted to ICU. After atrial pacing the episodes of VT did not recur the QT got shortened to 480 msec.

Dual chamber AICD was planned on the 3rd day and successfully implanted and the base atrial rate was programmed at 90bpm. Patient improved symptomatically and got discharged 1 week after successful AICD implantation. She was in follow-up for the past 6 months with no episodes of VT further.



Discussion

The QT interval is a surface marker of cardiac electrical activity, specifically cellular repolarization. It is generally accepted that the absolute QT interval provides a surface rendering of the underlying cellular action potential durations. Despite overlap of the resting QT between healthy persons and patients with LQTS, the 12-lead EKG remains one of the principal tools in the LQTS evaluation, and the baseline QTc is still one of the most important diagnostic criteria.

The congenital LQTS is a potentially life threatening condition, caused by mutations in genes encoding cardiac ion channels which result in prolongation of ventricular action potential. Genetic screening of symptomatic patients or their asymptomatic family members may identify patients at risk for life threatening arrhythmias and the type of LQT as it has important implications in the management. Out of the several forms of congenital LQTS, three forms LQT1, LQT2, and LQT3 have been well characterized. Recent investigations suggest that even in patients with acquired LQTS (e.g. resulting from intake of QT- prolonging medicines), there are clinically silent gene mutations that lead to overt QT prolongation only with exposure to QT-prolonging medications. Provocative tests using catecholamine or exercise testing have long been considered to unmask some forms of congenital LQTS. LQT 1 can be diagnosed with Epinephrine Provocative test. Facilities for genetic analysis are not easily available. The characteristic ECG finding include Broad based T waves for LQT1 low amplitude notched or biphasic T waves for LQT2, long isoelectric segment followed by a narrow based T wave for LQT3.

In the above case a probable diagnosis of LQT 3 was made based on the ECG findings, clinical presentation and the response to treatment. Cervical ganglion sympathectomy is another treatment option for these patients. As the patient did not develop further VT episodes, cervical sympathectomy was deferred.

Conclusion

This case report demonstrates the successful management of recurrent polymorphic VT in a postpartum female with LQTS using atrial pacing and subsequent dual chamber AICD implantation. Timely diagnosis and appropriate interventions are crucial in preventing sudden cardiac death and improving outcomes in individuals with LQTS. Further research is warranted to optimize treatment approaches and enhance the management of this challenging condition.

EVERY EYE TELLS A STORY

Google's AI Revolutionizes Cardiovascular Predictions Through Eye Scans

Unveiling an era-defining breakthrough in health tech, Google's CEO Sundar Pichai is spearheading a paradigm shift with the tech giant's groundbreaking artificial intelligence (AI) technologies. Recent revelations showcase Google's AI prowess, as cardiovascular events can now be predicted through eye scans, potentially replacing conventional diagnostic methods like CT scans, MRIs, and X-rays.

Power of Google's AI in Health Tech

From diabetic retinopathy detection to comprehensive disease prediction, Google's AI has made remarkable strides in healthcare. Four years ago, a collaborative effort between Google and Aravind Eye Hospital led to the development of an automated tool capable of swiftly diagnosing diabetic retinopathy through retinal photos. The algorithm is poised to operate independently, revolutionizing eye disease detection. Further advancements emerged when Google introduced an algorithm that, based on retinal imagery, could identify an individual's sex, smoking status, and predict their five-year risk of a heart attack. This breakthrough offers potential early detection opportunities for various diseases, including dementia, multiple sclerosis, Parkinson's, Alzheimer's, and even schizophrenia.

AI and the Eye: A Window to Cardiovascular Health

The retina serves as a window into overall health, with blood vessels reflecting critical indicators of cardiovascular well-being. By analyzing retinal appearances, medical professionals can infer vital information such as blood pressure, age, and smoking habits, enabling prediction of cardiovascular risk. Google and Verily's scientists leveraged machine learning and neural networks to analyze a vast medical dataset, including eye scans and general medical data, training an algorithm to detect patterns that correlate with cardiovascular risk factors. When tested, Google's AI demonstrated a 70% accuracy in distinguishing retinal images of patients who experienced a cardiovascular event within five years, comparable to the established SCORE method's 72% accuracy.

Future of Health Diagnostics

The revolutionary approach to cardiovascular risk assessment not only streamlines the diagnostic process but also ushers in an AI-powered paradigm for scientific discovery. As AI algorithms delve into existing medical data, they uncover new insights and raise the possibility that artificial intelligence could generate novel medical discoveries autonomously. Additionally, this technology has the potential to transcend high-tech medical facilities, enabling affordable, portable solutions for vision centers. By utilizing smartphones, inexpensive condensing lenses, and DIY retinal cameras, remote areas can access vision screenings promptly. Patients can capture retinal images, upload them to the cloud, and receive swift diagnoses, illustrating the vast potential of this transformative technology.

Conclusion

Google's AI is propelling us toward a future where eye scans unveil hidden health issues and predict cardiovascular events, transforming healthcare and diagnostics. This paradigm shift challenges traditional diagnostic methods, highlighting the potential of the human eye as a rich source of invaluable medical insights. As we navigate this remarkable era of health tech, the adage "To understand the body, look to the eye" resonates more profoundly than ever. With Google's AI at the helm, every eye tells a story, propelling us closer to a healthier future.

HEALTHY LIVING

Balancing carbs, sugar, insulin: The power of good cholesterol foods and millets

Other than diet, the key to reducing insulin resistance is three types of exercise FAR-flexibility, aerobics, and resistance, says Dr. V Mohan, Chairman, Dr. Mohan's Diabetes Specialities Centre

Insulin resistance is a condition where the body's cells stop responding to the glucose control hormone. It can happen due to different foods in different countries. When it comes to India and broadly South Asia, the commonest cause of insulin resistance is the consumption of excess carbohydrates.

Nowhere else in the world, and we have data, so much rice is consumed. Not even in China now, they have reduced their rice intake. of course, in north and west India the major contributor is refined wheat flour, which is no better than rice.

To understand why the consumption of excess carbohydrates leads to insulin resistance-and diabetes-we need to understand why it happens. Excess carbohydrates can lead to obesity, particularly central obesity or fat in the abdominal area. While this fat itself can lead to the insulin not working properly, a person with central obesity is likely to have fat deposited on their liver and their muscle. Without all the fat, the insulin can work smoothly and easily burn off the glucose. The fat acts like an obstruction that slows down the activity of the insulin.

Coming back, rice and wheat when consumed in moderation do not lead to insulin resistance. But we do not consume it in moderation - it is the main part of our breakfast, lunch, and dinner. Rice or chapati is the main component of our meals and everything else is an accompaniment. Instead, there is a need to create a plate where vegetables make half of it, proteins a quarter, and carbohydrates just one quarter.

To improve the plate, the highly polished rice and refined wheat can be replaced with complex carbohydrates such as whole grains, millet, and oats. Now, let's come to foods other than these carbohydrates. Most of the fruits are okay in moderation. However, certain fruits like bananas, mango, and other highly sweet fruits, can also lead to insulin resistance. This happens particularly with fruit juices where there is no fiber left.

Next, we need to take a look at the fats that are used in our food. It is the saturated fats - such as high-fat dairy, ghee, vanaspati, coconut oil, and palm oil - that lead to insulin resistance. Broadly, remember any oil that remains solid at room temperature - including trans fats that are the greasy, solid layer seen on many desserts-can lead to insulin resistance.

The unsaturated fats - mainly mono-unsaturated fats like olive oil, corn oil, groundnut oil, sesame oil (gingelly oil), and mustard oil - don't produce insulin resistance. While mono-unsaturated fats are the best, poly-unsaturated fats such as sunflower oil and safflower oil are also quite good.

The other thing that can give you fat is meat - red meat has definitely been shown to produce insulin resistance. But lean meat like poultry or fish is good; in fact, fish contains omega-3 fatty acids that can actually reduce insulin resistance. Vegetarians can include Bengal gram, green gram, rajma, and mushrooms in their diet as they are low in carbohydrates, high in fibers, and high in protein. Soya is also very good, with a very high 40% protein content.

Then we come to vegetables - there has to be lots of fresh, green, leafy vegetables. Starchy vegetables such as potatoes, yams, beetroot, and tapioca should be avoided because they are almost the same as consuming rice and wheat. A broad rule can be to avoid vegetables that grow under the roots, they are usually the starchy ones, except for carrots - carrots are very fibrous and contain nutrients like carotenoids and vitamin A. And also try and eat vegetables like tomato and cucumber raw.

Next, we come to sugars - the World Health Organization recommends that less than 5% of total daily calories come from sugars. So, only one or two spoons of sugar should be consumed during the entire day. In fact, sweetened beverages are the commonest reason for insulin resistance in the West.

Coming to the surprising findings

We used to think nuts are bad, but for every nut that we have worked with so far - groundnut, pistachio, cashew, and almond - the finding has been consistent. It reduces insulin resistance and decreases weight. They contain a lot of calories, but they are also very satiating. You cannot eat too much – you end up eating less rice and roti. If you have say a fistful of nuts at 11 o'clock before your lunch at 1, you are likely to eat less at lunch. They give you fat, but the right type of fat - the mono-unsaturated fat mentioned earlier.

But while eating nuts, two things have to be kept in mind.

First, the quantity – you cannot polish off a huge amount. Have only a fistful of nuts a day. In fact, Indians have low good cholesterol or HDL levels and the nuts can increase it. For the first time in the world, we showed that cashews can not only increase the HDL level, they can also bring down the blood pressure. Then a study from the US confirmed these findings. Second, the nuts have to be unsalted.

The other thing that we found in our studies from Chennai is that dairy seems to be actually protective against insulin resistance, obesity, and diabetes. Initially, we doubted it, we thought there may be some confounders. Then we did a 15-year follow-up prospective study of people who did not have diabetes at the beginning of the study and divided it into whether they consumed dairy or not and found that dairy was actually protective, thereby confirming our previous finding.

Among the dairy, yogurt came out to be the best, milk was good, cheese was okay, but butter was neutral. So, you need not give up dairy. Not only is it protective, but it also gives you a lot of protein and calcium. But, again no one should go overboard - don't drink two or three glasses of milk a day. One glass of milk gives 500 mg of calcium, which is half the daily requirement even for a pregnant woman and okay for a man.

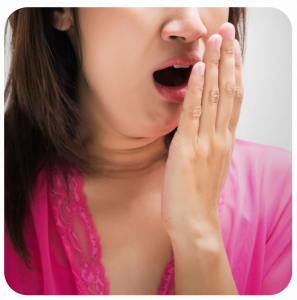
In addition, yogurt also improved the gut microbiota. The foods that we consume affect the gut microbiome. When you have high-fat, salt, and sugar food, it destroys the good bacteria and replaces them with the bad ones. This leads to leakiness of the gut which causes inflammation, which again leads to insulin resistance.

Other than diet, the key to reducing insulin resistance is three types of exercise FAR - flexibility, aerobics, and resistance.

ON A LIGHTER NOTE

SOME INTERESTING FACTS

ANXIETY CAN MAKE BAD SMELLS EVEN WORSE



A 2013 study published in The Journal of Neuroscience examined the way certain emotions affect your sense of smell. After exposing subjects to anxiety-inducing images like car accidents and war, researchers found that neutral scents became unpleasant and bad smells became even worse.

PUPILS CAN HINT AT YOUR ALZHEIMER'S RISK

In a 2019 study published in the journal Neurobiology of Aging, researchers noted that the disease affects the locus coeruleus, a cluster of neurons in the brainstem responsible for pupillary responses, among other things. As a result, individuals with cognitive impairment who are at risk of developing Alzheimer's have greater pupil dilation while performing cognitive tasks.

HUMANS ARE THE ONLY ANIMALS WITH CHINS

Humans are the only animals with chins. Of course, other animals have jaws, but as anthropologist James Pampush told The Atlantic, "only humans have chins." Though scientists aren't entirely sure why we have this feature.

RIDING A ROLLER COASTER COULD HELP YOU PASS A KIDNEY STONE

The researchers from Michigan State University, conducted tests with a model kidney and found that there was a 64 percent kidney stone pass rate for those seated in the rear of the roller coaster. That number was 16 percent for those seated in the front.

FINGERNAILS GROW FASTER ON YOUR DOMINANT HAND

The American Academy of Dermatology (AAD) says that a fingernail takes around six months to grow from base to tip and that toenails can take up to a year to do the same. According to the AAD, fingernails grow faster on your dominant hand, as well as on your bigger fingers.

TAKING PICTURES MESSES WITH YOUR MEMORY

One 2018 study published in the Journal of Applied Research in Memory and Cognition tested the effects of photo-taking on memory by asking students to remember a series of paintings in three situations: with no camera, with a camera, and with a Snapchat-like app where photos disappear. Researchers found that those who took pictures always had a harder time remembering the details of the painting.

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