NCD Newsletter

2021 - Issue 03

DOES SLEEP DEPRIVATION AFFECT HEART HEALTH?

Kannada actor Puneeth Rajkumar dies of heart attack at 46

Kannada actor Puneeth Rajkumar.

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Sidharth Shukla, Raj Kaushal, Amit Mistry: Cele from cardiac arrest

The recent passing of television and Bollywood actor Sidhar and peers shocked, the Bigg Boss 13 winner and Humpty S

Bollywood actor Inder Kumar won the heart of fans with his performances in movies like *Khiladiyon Ka Khiladi*, *Agnipath*, *Tumko Na Bhool Payenge* and Salman Khan's *Wanted*. But the actor's life was cut short at the age of 44 after he suffered a heart attack at his residence in Mumbai late at night on 28th July, 2017.

We can call agree that 2021 has been a disastrous year than 2020. Recently shocking news has hit us that the youthful Telugu producer Mahesh Koneru has passed away due to cardiac arrest on Tuesday at his home in Hyderabad. Superstar Jr. NTR took to his Twitter handle to share his sorrow at the death of his colleague.

The producer had just started his career as a film journalist and shortly became a publicist and marketing strategist for Telugu films Kanche and Baahubali series.

In recent years, a number of famous TV and film personalities have suffered from fatal cardiac arrests in their 30s and 40s. The list includes Rituparno Ghosh (aged 49), Raj Kaushal (49), Vivek Shauq (47), Amit Mistry (47), Inder Kumar (44), Abir Goswami (37) and Aarthi Agarwal (31).

The sad untimely demise due to cardiac arrest, colloquially called a heart attack, is a phenomenon witnessed at large in India. While heart attacks were a danger mostly attached to older adults till a couple of decades ago, the 21st century has brought about a rise in untimely heart attacks in people under 50 years, particularly in India.

Substantial evidence demonstrates that sleeping problems such as sleep deprivation and fragmented sleep harm heart health. Sleep provides time for the body to restore and recharge, playing an essential role in nearly all aspects of physical fitness. For the cardiovascular system, insufficient or fragmented sleep can contribute to problems with blood pressure and heighten the risk of heart disease, heart attacks, diabetes, and stroke.

Poor sleep, whether from a lack of sleep or sleep disruptions, is associated with non-dipping. Studies have found that elevated night-time blood pressure is related to overall hypertension (high blood pressure). Sleep deprivation also causes raised daytime blood pressure.

Poor sleep triggers chronic inflammation, which contributes to plaque formation and hardening of the arteries. An observational study of over 400,000 people showed that people who slept less than seven hours per night had an elevated risk of heart failure. Heart failure was also more common in people who had other indicators of unhealthy sleep such as insomnia symptoms, daytime sleepiness, snoring, and being an evening person.

Sleep deprivation heightens the risk of heart attacks. In one study, people sleeping less than six hours per night had a 20% higher chance of a heart attack. While the NREM sleep stage helps the heart slow down and recover, REM sleep involves heightened stress and activity. Insufficient sleep can throw off the balance of these stages, increasing heart attack risk. An analysis of existing research found that lack of sleep is related to obesity. People who sleep less than seven hours per night are more likely to have a higher body mass index (BMI) or be obese. Poor sleep is also associated with prediabetes.

Health Risk	Study or Author	Subject	Age (Year)	Follow-up period	Result
Hypertension (HT)	NHANES (2006)	4810 subjects without HT	25~74	8 - 10 (years)	Increased risk of HT in subjects with 5 or fewer hours of sleep.
Coronary Heart Disease (CHD)	Nurses' Health Study (2003)	71,617 females without CHD	45~65	10 (years)	Increased risk of CHD in subjects with 5 or fewer, 6, 7 and 9 or more compared with those with 8 hours of sleep. U-shaped phenomenon (+).
Myocardial Infarction (MI)	Liu et al. (2006)	260 males with AMI and 422 males without AMI	40~79	(-) (case-control study)	Increased odds ratios of AMI in subjects with 5 or fewer compared with those with 6 to 8 hours of sleep.
Diabetes Mellitus (DM) /Impaired Glucose Tolerance (IGT)	SHHS (2005)	722 males and 764 females	53~93	(-) (cross-s ectional design)	Increased odds ratios of DM and IGT in subjects with 5 or fewer, 6, and 9 or more compared with those getting 7 to 8 hours of sleep. U-shaped phenomenon (+).
None	MMAS (2006)	1709 males without DM	40~70	15 (years)	Increased risk of DM in subjects with 5 or fewer, 6 and 8 or more compared with those getting 7 hours of sleep. U-shaped phenomenon (+).

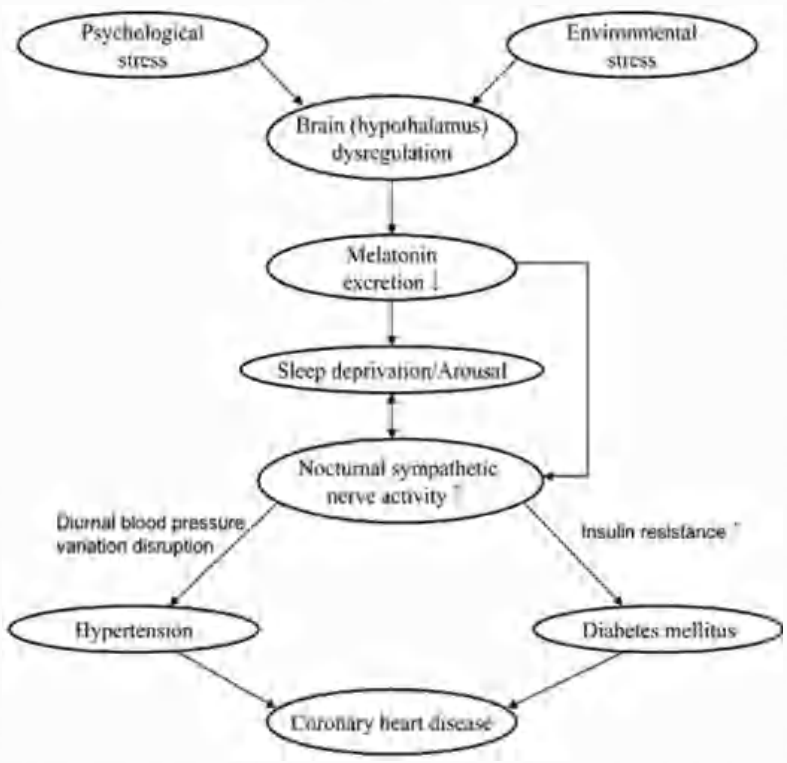
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2845795/

Sleep Duration And Hypertension (HT)

- The prevalence of HT has increased over the past decade despite improvements in awareness, treatment, and control of this disease. During the same period, the average sleep duration in the United States has steadily declined.
- In the First National Health and Nutrition Examination Survey (NHANES), Gangwischetal. conducted longitudinal analyses for 8 to 10 years on 4810 subjects from 25 to 74 years of age to determine whether or not short sleep duration increased HT incidence. of these, 647 subjects were diagnosed with HT in that period. Sleep duration of ≤ 5 hr per night was associated with a significantly increased risk of HT in subjects between the ages of 32 and 59 years. However, this significant relationship was not found in subjects between aged of 60 to 86 years.
- This result would suggest a strong association between short sleep duration and the development of HT, especially in middle-aged subjects.

Mechanism Underlying the Relationship between Sleep Duration and HT

Short sleep duration was associated with the development of HT. This may be attributable in part to autonomic dysregulation that changes the predominant neutral interaction of sympatho vagal balance during sleep into increased sympathetic tone. In 24 hr ambulatory blood pressure monitoring (ABPM) studies, BP tended to rise the day after sleep deprivation in both normotensives and hypertensives.



Correlation of sleep deprivation and CVD

Sleep Duration and Coronary Heart Disease (CHD)

Short sleep duration imposed on a group of healthy subjects increased sympathetic nervous system activity and blood pressure elevation. Therefore sustained short sleep duration could lead to adverse cardiovascular consequence.

A prospective study in the United States showed that the standardized mortality ratio of CHD was highest among those who worked 67 hr or more a week. Case-control studies in The Netherland, Denmark, and Sweden also reported that prolonged working time was associated with an increased risk of acute myocardial infarction (AMI). Another case-control study in Japan found significantly increased odds ratios of AMI for those who worked more than 11 hr a day.

It is possible to think that sleep deprivation caused by overtime work is associated with an increased risk of AMI. The American Cancer Society Study showed that men sleeping 4 hr or less had higher mortality from CHD than those sleeping 7-7.9 hr. The Alameda County Study and the study by Partinen et al. also noted that men who slept less than 6 hr had a greater risk of developing CHD than men sleeping 7-8 hr.

In the Nurses' Health Study, Ayas et al. investigated the relationship between self-reported sleep duration and the incidence of CHD in 71,617 female health professionals aged 45-65 years in the United States. A total of 934 coronary events were documented (271 fatal and 663 nonfatal) during the 10 years of follow up. The age-adjusted relative risks of CHD, with 8 hr of daily sleep being considered the reference group, for individuals reporting 5 or fewer, 6, and 7 hr of sleep were 1.82, 1.30, and 1.06, respectively. The relative risk for 9 or more hr of sleep was 1.57.

Sleep Duration and Diabetes Mellitus (DM)

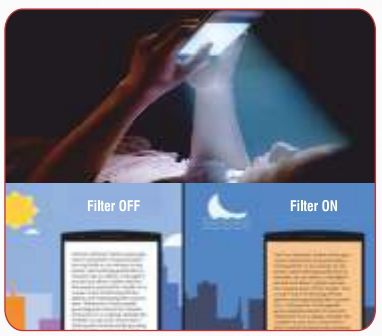
Spiegel et al. assessed the activity of the hypothalamo-pituitary-adrenal axis and sympatho vagal balance in 11 young men under two different sets of conditions: after their time in bed had been restricted to 4 hr per night for 6 consecutive nights, and after a sleep-recovery period when the participants were allowed 12 hr in bed per night for 6 consecutive nights. Lower glucose tolerance, higher evening cortisol concentration, and increased activity of the sympathetic nervous system occurred in the sleep deprivation experiment than in the fully rested condition. Similar results, that sleep deprivation was associated with lower glucose tolerance and increased insulin resistance, were found elsewhere.

In the Sleep Heart Health Study (SHHS), 722 men and 764 women, aged 53 to 93 years, were assessed to determine the cross-sectional relationship between usual sleep time and both DM and impaired glucose tolerance (IGT). Compared with those sleeping 7 to 8 hr per night, subjects sleeping 5 hr or less and 6 hr per night had adjusted odds ratios of 2.51 and 1.66 for DM and of 1.33 and 1.58 for IGT, respectively. Subjects sleeping 9 hr or more per night also had increased odds ratios for DM and IGT. These associations persisted when subjects with insomnia were excluded.

In the Massachusetts Male Aging Study (MMAS), a cohort of men without DM at baseline were followed for the development of DM for 15 years. When those reporting 7 hr of sleep per night served as the reference group, men reporting less sleep (≤5 and 6 hours sleep per night) were twice as likely to develop DM, and men reporting long sleep duration (>8 hours of sleep per night) were more than three times as likely to develop DM during the follow-up period. The risk elevation remained essentially unchanged after adjustments for age, hypertension, smoking status, self-rated health status, education, and waist circumference.

How to get better sleep?

- Stick to a regular sleep schedule. Go to bed at the same time each night and get up at the same time each morning, including on the weekends.
- Get enough natural light earlier in the day. Try going for a morning or lunchtime walk.
- Get enough physical activity during the day. Try not to exercise within a few hours of bedtime.
- Avoid artificial light, especially within a few hours of bedtime. Use a blue light filter on your computer or smart phone.
- Avoid eating or drinking within a few hours of bedtime; avoid alcohol and foods high in fat or sugar in particular.
- Keep your bedroom moderate, dark, and quiet.
- Develop strategies for relaxation: If heart concerns spur anxiety, they can keep your mind racing when you want to ease into sleep.



https://www.sleepfoundation.org/sleep-deprivation/how-sleep-deprivation-affects-your-heart

INNOVATIONS IN MEDICAL DEVICES

1. FDA clears first imaging device advancement for computed Tomography after a decade

The U.S. Food and Drug Administration cleared the first new major technological improvement for Computed Tomography (CT) imaging in nearly a decade.

Computed tomography is an important medical imaging tool that can aid in diagnosing disease, trauma or abnormality; planning and guiding interventional or therapeutic procedures; and monitoring the effectiveness of certain therapies.

The device uses the emerging CT technology of photon-counting detectors which can measure each individual X-ray that passes through a patient's body, as opposed to current systems which use detectors that measure the total energy contained in many X-rays at once. By 'counting' each individual X-ray photon, more detailed information about the patient can be obtained and used to create images with less information that is not useful in the review and analysis.

The new diagnostic imaging device, called Siemens NAEOTOM Alpha, is designed to transform the information from X-ray photons that pass through a patient's body, and are received by a detector, into a detailed 3-dimensional image. The images delivered by the system can be used by a trained physician as an aid in diagnosis or can be used by trained staff as an aid in diagnosis, treatment preparation and radiation therapy planning.

The Siemens NAEOTOM Alpha diagnostic imaging device provides more detailed information about a patient by utilizing an emerging CT technology that employs photon-counting detectors.

Siemens' novel device makes use of a rapidly emerging CT technology known as photon-counting. Unlike current systems, which measure the total energy of a large number of X-rays at once, this new diagnostic device counts individual X-rays to provide more detailed information and images.

The technology has transformed the current two-step process of converting X-rays into visible light, which is then detected by a light sensor, into a single-step process of directly converting X-ray photons into digital electrical signals that are counted, producing into a detailed 3-D image with greater clarity and contrast.

The images generated by the Siemens NAEOTOM Alpha can be used to aid in diagnosis, treatment preparation, and radiotherapy planning by trained physicians and staff.

Source: USFDA – Medical Devices Approvals 2021

2. HFX (Spinal Cord Stimulation Therapy) for Painful Diabetic Neuropathy

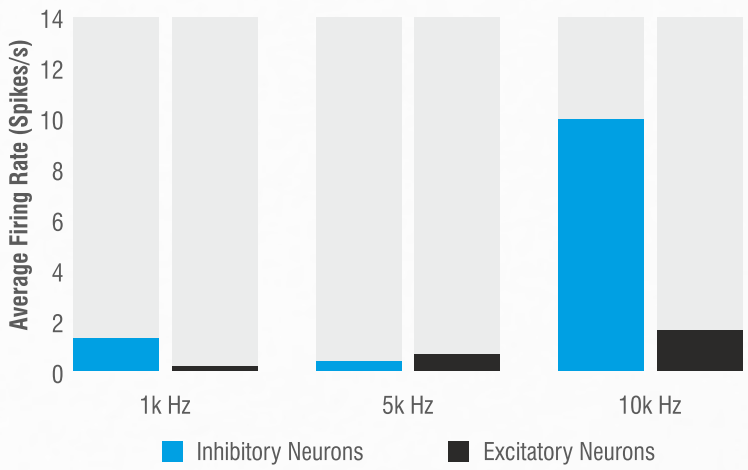
HFX is a Spinal Cord Stimulation Therapy for treatment of chronic pain associated with Painful Diabetic Neuropathy (PDN). Diabetic neuropathy is one of the most prevalent and debilitating chronic complications of diabetes, and for years, PDN patients have struggled with a lack of effective treatment options when conventional medications are not tolerated or fail.

HFX for PDN is a Cord stimulation system that uses 10 kHz Therapy. The approval by FDA is specific to Nevro's unique 10 kHz stimulation, being the only spinal cord stimulation system with specified indications to treat PDN.

Evidence shows that delivering mild electric pulses to the nerves interrupts pain signals to the brain, alleviating pain and improving quality of life. Spinal cord stimulation, or SCS, is a straightforward, well-established treatment for chronic pain, used for over 30 years. SCS involves a minimally invasive implant procedure that allows you to go home the same day. Within the Senza-PDN, 10 kHz Therapy demonstrated exceptional outcomes across responder rates, pain relief, and even sensory response.

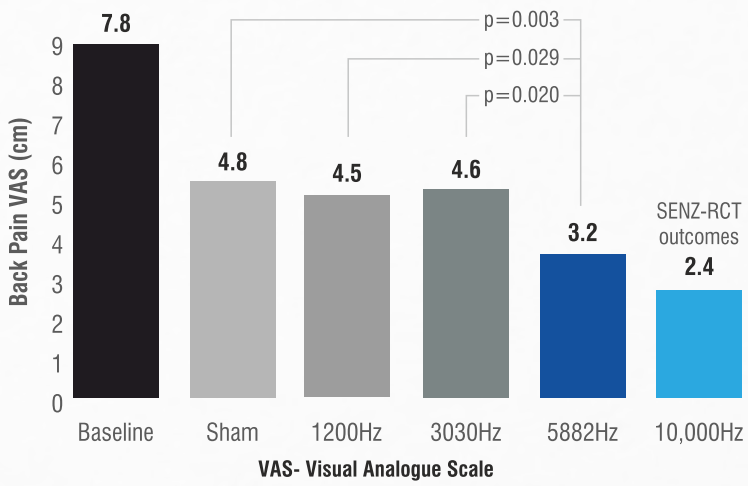
PDN patients have struggled with a lack of treatment options when CMM fails. 10 kHz Therapy and a unique mechanism of action offer new potential for relief. Rather than stimulating the dorsal column, 10 kHz Therapy directly targets inhibitory neurons in the dorsal horn, providing pain relief without paresthesia. Frequencies above 5,000 Hz have a unique inhibitory effect on pain circuitry in the dorsal horn. The stimulation drives inhibitory neurons without activating the excitatory neurons. This selective activation, called Direct Neural Inhabitation, reduces the hyperactivity of a wide dynamic range of neurons implicated in chronic pain.

Inhibitory Neurons Selectively Activated at 10,000 Hz



In the first frequency titration study in humans, patients were exposed to a range of frequencies to compare clinical outcomes. Only 5,882 Hz demonstrated improved pain relief versus sham. Additional studies on 10 kHz Therapy validate the importance of frequencies.

Frequency Titration Cross-Over Trial



HFX for PDN offers the ability to treat patients with direct neural inhibition and dorsal column stimulation. So that the patients receive the broadest range of solutions, Waveforms can be paired or delivered independently.

The 6-month results for the SENZA-PDN randomized controlled trial (RCT) were published previously in JAMA Neurology2 in April 2021. 12-month follow-up results and 6-month crossover patient data was presented recently at the American Diabetes Association 81st Scientific Sessions in June 2021.

Reference: Pain. 2014 Nov;155(11):2426-31

PATIENT COUNSELLING

Patient counselling, a process of providing vital information, advice and assistance to help with medications and includes important information about the patient's illness and lifestyle. Medicines play an important role in medical care. The Effectiveness of treatment depends on both the efficacy of the medication and patient adherence to the therapeutic regimen. Adherence to medications is essential to achieve the best possible pharmacotherapy outcomes. Counselling ensures proper use and the best therapeutic action of the medications.

The patient Counselling process involves, establishing caring relationships with patients, assessing the patient's knowledge about his or her health problems and medications, providing information orally and using visual aids or demonstrations, verifying patients' knowledge and understanding of medication use.

The counselling session should include information regarding the medication's trade name, its use and expected benefits and action, what to do if the action does not occur and directions for preparing and administering the medication. Session must include information regarding precautions to be observed during the medication's use and potential common and severe adverse effects with any other information unique to an individual patient or medication.

Guidelines of patient counselling in elderly people

Elderly patients are at the highest risk of experiencing ADRs (Adverse Drug Reaction), many of which are preventable. Actual, perceived, or even fear of ADRs increases the likelihood of medication non-adherence. Psychological factors such as predetermined medication views, lack of belief in treatment necessity, the anticipation of ADRs, conditioning based on past experiences, and misattributing symptoms as ADRs. The Clinician and pharmacist awareness of these factors helps to reduce the risk for ADRs and optimize management.

Patient counselling vs patient education

Patient education includes Basic medical information, Side effects and interactions and how to store drugs properly whereas patient counselling includes clinical information including the disease state, lifestyle modification and monitoring as well follow up of the drug.

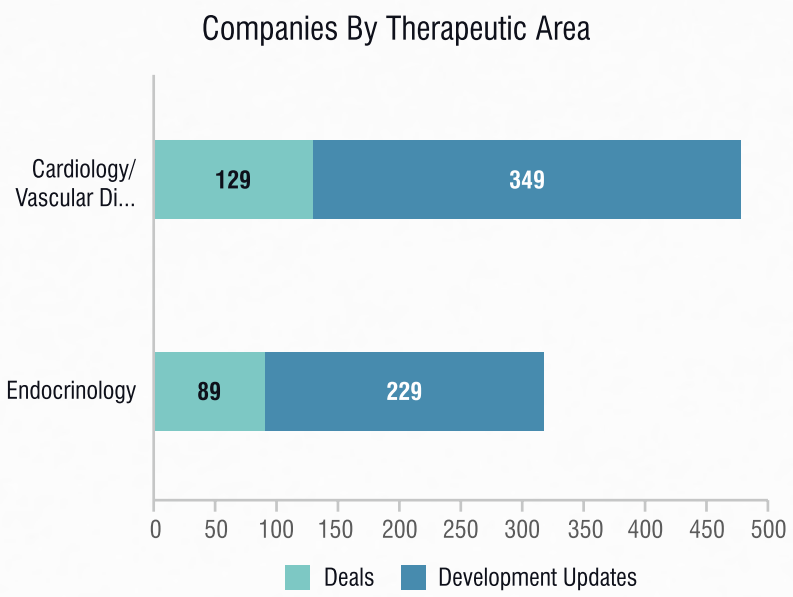
Ways of effective patient counselling

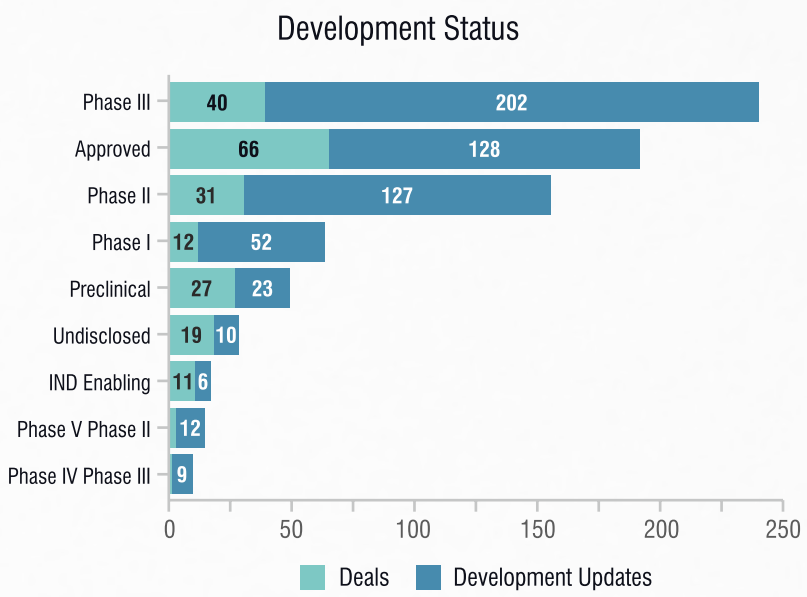
1. Establish Trust
2. Communicate Verbally
3. Communicate Nonverbally
4. Listen
5. Ask Questions
6. Remain Clinically Objective
7. Show Empathy and Encouragement
8. Provide Privacy and Confidentiality
9. Tailor Counselling to Meet Patient Needs
10. Motivate Patients

Studies have shown that patient counselling can improve patient care by reducing medication errors, Increasing patients' understanding and management of their medical condition and also minimizing the incidence of adverse drug reactions and drug-drug interactions and Improving patient outcomes and satisfaction with care.

https://fadic.net/important-outcomes-and-benefits-of-the-patient-counseling/

NEW PRODUCT PIPELINE





Developer Name: Dr Reddys

Molecule: Icosapent Ethyl

Trial Phase: Approved

Approved indication: As an adjunct to diet to reduce triglyceride levels in adult patients with severe hypertriglyceridemia, and as an adjunct to statin therapy to reduce the risk of cardiovascular events.

Proposed indication: To be used together with lifestyle changes (diet, weight loss, exercise) to reduce the number of triglycerides (a fat-like substance) in the blood.

Mode of action: Increased ß-oxidation; inhibition of acyl-CoA:1,2-diacylglycerol acyltransferase (DGAT); decreased lipogenesis in the liver; and increased plasma lipoprotein lipase activity.

Developer Name: Novo Nordisk

Molecule: Semaglutide

Trial Phase: Phase III

Approved indication: An adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus, to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease.

Proposed indication: From a mean baseline body weight of 99.3 kg, people treated with semaglutide 2.0 mg experienced a statistically significant and superior weight loss of 6.9 kg compared with 6.0 kg with semaglutide 1.0 mg.

Mode of action: It works by binding to and activating the GLP-1 receptor, thereby stimulating insulin secretion and reducing blood glucose.

Developer Name: Zucara

Molecule: ZT-01

Trial Phase: Undisclosed

Approved indication: —

Proposed indication: Promising results in a preclinical model of T2D and represents the potential to benefit a substantially larger population.

Mode of action: It works by binding to and activating the GLP-1 receptor, thereby stimulating insulin secretion and reducing blood glucose.

GLP-1 analogue exerts its main effect by stimulating glucose-dependent insulin release from the pancreatic islets. It has also been shown to slow gastric emptying, inhibit inappropriate post-meal glucagon release and reduce food intake.

Developer Name: Daewoong pharmaceutical co.

Molecule: Enavogliflozin

Trial Phase: Phase II

Approved indication: —

Proposed indication: Type 2 diabetes mellitus

Mode of action: It functions through a novel mechanism of reducing renal tubular glucose reabsorption, producing a reduction in blood glucose without stimulating insulin release. Other benefits may include favourable effects on blood pressure and weight.

Developer Name: Orion

Molecule: Levosimendan

Trial Phase: Phase II

Approved indication: Levosimendan is an inodilator indicated for the short-term treatment of acutely decompensated severe chronic heart failure, and in situations where conventional therapy is not considered adequate.

Proposed indication: An oral formulation of levosimendan for use with Type 2 pulmonary hypertension in heart failure patients with PH-HFpEF, or other heart-related indications

Mode of action: This sensitizes troponin C to calcium in a manner dependent on the calcium concentration, thereby increasing the effects of calcium on cardiac myofilaments during systole and improving contraction at a low energy cost

Developer Name: Vertex

Molecule: VX 100

Trial Phase: Phase II

Approved indication: –

Proposed indication: Fully differentiated pancreatic islet cell therapy to treat T1D.

Mode of action: Allogeneic human stem cell-derived islet cell therapy that is being evaluated for patients who have T1D with impaired hypoglycaemia awareness and severe hypoglycemia.

CASE STUDY

Case Presentation

The patient is a 60-year-old white female presenting to the emergency department with acute onset shortness of breath. Symptoms began approximately 2 days before and had progressively worsened with no associated, aggravating, or relieving factors noted. She had similar symptoms approximately 1 year ago with an acute, chronic obstructive pulmonary disease (COPD) exacerbation requiring hospitalization. She uses BiPAP ventilatory support at night when sleeping and has requested to use this in the emergency department due to shortness of breath and wanting to sleep.

She denies fever, chills, cough, wheezing, sputum production, chest pain, palpitations, pressure, abdominal pain, abdominal distension, nausea, vomiting, and diarrhea.

She reports difficulty breathing at rest, forgetfulness, mild fatigue, feeling chilled, requiring blankets, increased urinary frequency, incontinence, and swelling in her bilateral lower extremities that are new-onset and worsening. Subsequently, she has not ambulated from bed for several days except to use the restroom due to feeling weak, fatigued, and short of breath.

There are no known ill contacts at home. Her family history includes significant heart disease and prostate malignancy in her father. Social history is positive for smoking tobacco use at 30 pack years. She quit smoking 2 years ago due to increasing shortness of breath. She denies all alcohol and illegal drug use. There are no known foods, drugs, or environmental allergies.

Past medical history is significant for coronary artery disease, myocardial infarction, COPD, hypertension, hyperlipidemia, hypothyroidism, diabetes mellitus, peripheral vascular disease, tobacco usage, and obesity. Past surgical history is significant for an appendectomy, cardiac catheterization with stent placement, hysterectomy, and nephrectomy.

Her current medications include fluticasone-vilanterol 100-25 mcg inhaled daily, hydralazine 50 mg by mouth, 3 times per day, hydrochlorothiazide 25 mg by mouth daily, albuterol-ipratropium inhaled every 4 hours PRN, levothyroxine 175 mcg by mouth daily, metformin 500 mg by mouth twice per day, nebivolol 5 mg by mouth daily, aspirin 81 mg by mouth daily, vitamin D3 1000 units by mouth daily, clopidogrel 75 mg by mouth daily, isosorbide mononitrate 60 mg by mouth daily, and rosuvastatin 40 mg by mouth daily.

Physical Exam

Initial physical exam reveals temperature 97.3 F^0, heart rate 74 bpm, respiratory rate 24, BP 104/54 mmHg, BMI 40.2 Kg/m^2, and O_2 saturation 90% at room air.

Constitutional: Extremely obese, acutely ill-appearing female. Well-developed and well-nourished with BiPAP in place. Lying on a hospital stretcher under 3 blankets.

HEENT:

- Head: Normocephalic and atraumatic
- Mouth: Moist mucous membranes
- Macroglossia
- Eyes: Conjunctiva and EOM are normal. Pupils are equal, round, and reactive to light. No scleral icterus. Bilateral periorbital edema present.
- Neck: Neck supple. No JVD present. No masses or surgical scarring.
- Throat: Patent and moist

Cardiovascular:

- Normal rate, regular rhythm, and normal heart sound with no murmur. 2+ pitting edema bilateral lower extremities and strong pulses in all four extremities.
- Pulmonary/Chest: No respiratory status distress at this time, tachypnea present, (+) wheezing noted, bilateral rhonchi, decreased air movement bilaterally. Patient barely able to finish a full sentence due to shortness of breath.

Abdominal:

Soft, Obese, Bowel sounds are normal. No distension and no tenderness

Skin:

Skin is very dry

Neurologic:

Alert, awake, able to protect her airway. Moving all extremities. No sensation losses

Initial Evaluation

Initial evaluation to elucidate the source of dyspnea was performed and included CBC to establish if an infectious or anemic source was present, CMP to review electrolyte balance and review renal function, and arterial blood gas to determine the PO_2 for hypoxia and any major acid-base derangement, creatinine kinase and troponin I to evaluate the presence of myocardial infarct or rhabdomyolysis, brain natriuretic peptide, ECG, and chest x-ray. Considering that it is winter and influenza is endemic in the community, a rapid influenza assay was obtained as well.

CBC

Largely unremarkable and non-contributory to establish a diagnosis.

CMP

Showed creatinine elevation above baseline from 1.08 base to 1.81, indicating possible acute injury. EGFR at 28 is consistent with chronic renal disease. Calcium was elevated to 10.2. However, when corrected for albumin, this corrected to 9.8 mg/dL. Mild transaminitis is present as seen in alkaline phosphatase, AST, and ALT measurements which could be due to liver congestion from volume overload.

Initial arterial blood gas with pH 7.491, pCO_2 27.6, pO_2 53.6, HCO_3 20.6, and oxygen saturation 90% at room air, indicating respiratory alkalosis with hypoxic respiratory features.

Creatinine kinase was elevated along with serial elevated troponin I studies. In the setting of her known chronic renal failure and acute injury indicated by the above creatinine value, a differential of rhabdomyolysis is determined.

Influenza A and B

Negative

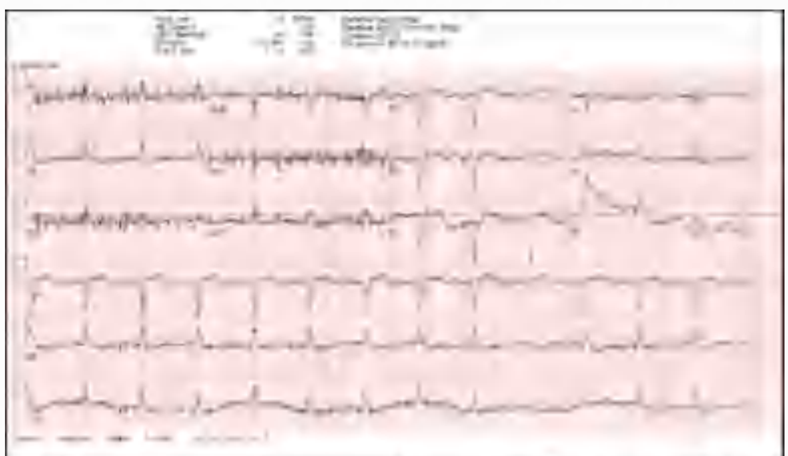
ECG

Normal sinus rhythm with non-specific ST changes in inferior leads. Decreased voltage in leads I, III, aVR, aVL, aVF.

Chest X-ray

Findings: Bibasilar airspace disease that may represent alveolar edema. Cardiomegaly noted. Prominent interstitial markings noted. Small bilateral pleural effusions

Radiologist Impression: Radiographic changes of congestive failure with bilateral pleural effusions greater on the left compared to the right



CBC
Table-1

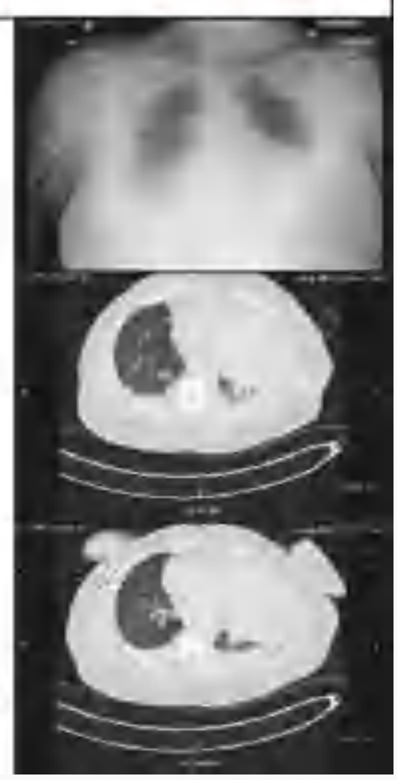
Lab	Units	01/19/18 0322
WBC	10^3/mm3	9.40
HEMOGLOBIN	g/dL	14.3
HEMATOCRIT	%	42.7
MCV	fL	[illegible]
MCHC	g/dL	33.5
PLATELETS	10^3/mm3	225
INR		0.99

CMP Table-2

Lab	Units	[illegible]
SODIUM	[illegible]	[illegible]
POTASSIUM	[illegible]	3.5
CHLORIDE	[illegible]	[illegible]
CO2	[illegible]	[illegible]
BUN	mg/dL	[illegible]
CREATININE	mg/dL	[illegible]
EGFR	[illegible]	28
CALCIUM	mg/dL	[illegible]
GLUCOSE	mg/dL	[illegible]
ALBUMIN	g/dL	4.50
BILIRUBIN	mg/dL	[illegible]
ALK PHOS	U/L	[illegible]
AST (SGOT)	U/L	[illegible]
ALT (SGPT)	U/L	[illegible]

Table-3

Lab	Units	[illegible]	[illegible]	[illegible]
CK TOTAL	U/L	-	-	[illegible]
TROPONIN I	ng/mL	[illegible]	[illegible]	[illegible]
[illegible]	%	-	-	[illegible]



Differential Diagnosis

- Acute on chronic COPD exacerbation
- Acute on chronic renal failure
- Bacterial pneumonia
- Congestive heart failure
- NSTEMI
- Pericardial effusion
- Hypothyroidism
- Influenza pneumonia
- Pulmonary edema
- Pulmonary embolism

Confirmatory Evaluation

On the second day of the admission patient's shortness of breath was not improved, and she was more confused with difficulty arousing on conversation and examination. To further elucidate the etiology of her shortness of breath and confusion, the patient's husband provided further history. He revealed that she is poorly compliant with taking her medications. He reports that she "doesn't see the need to take so many pills."

Testing was performed to include TSH, free T4, BNP, repeated arterial blood gas, CT scan of the chest, and echocardiogram. TSH and free T4 evaluate hypothyroidism. BNP evaluates fluid load status and possible congestive heart failure. CT scan of the chest will look for anatomical abnormalities. An echocardiogram is used to evaluate left ventricular ejection fraction, right ventricular function, pulmonary artery pressure, valvular function, pericardial effusion, and any hypokinetic area.

- TSH: 112.717 (H)
- Free T4: 0.56 (L)
- TSH and Free T4 values indicate severe primary hypothyroidism.
- BNP: 187

BNP can be falsely low in obese patients due to the increased surface area. Additionally, adipose tissue has BNP receptors which augment the true BNP value. Also, African American patients with more excretion may have falsely low values secondary to greater excretion of BNP. This test is not that helpful in renal failure due to the chronic nature of fluid overload. This allows for desensitization of the cardiac tissues with a subsequent decrease in BNP release.

Repeat arterial blood gas on BiPAP ventilation shows pH 7.397, pCO_2 35.3, pO_2 72.4, HCO_3 21.2, and oxygen saturation 90% on 2 L supplemental oxygen.

CT chest without contrast was primarily obtained to evaluate the left hemithorax, especially the retrocardiac area.

Radiologist Impression

Tiny bilateral pleural effusions. Pericardial effusion. Coronary artery calcification. Some left lung base atelectasis with minimal airspace disease.

Echocardiogram

The left ventricular systolic function is normal. The left ventricular cavity is borderline dilated.

The pericardial fluid is collected primarily posteriorly, laterally but not apically. There appeared to be a subtle, early hemodynamic effect of the pericardial fluid on the right-sided chambers by way of an early diastolic collapse of the RA/RV and delayed RV expansion until late diastole. A dedicated tamponade study was not performed.

The estimated ejection fraction appears to be in the range of 66% to 70%. The left ventricular cavity is borderline dilated.

The aortic valve is abnormal in structure and exhibits sclerosis.

The mitral valve is abnormal in structure. Mild mitral annular calcification is present. There is bilateral thickening present. Trace mitral valve regurgitation is present.

Diagnosis

1. Myxedema coma or severe hypothyroidism
2. Pericardial effusion secondary to myxedema coma
3. COPD exacerbation
4. Acute on chronic hypoxic respiratory failure
5. Acute respiratory alkalosis
6. Bilateral community-acquired pneumonia
7. Small bilateral pleural effusions
8. Acute mild rhabdomyolysis
9. Acute chronic, stage IV, renal failure
10. Elevated troponin I levels, likely secondary to Renal failure
11. Diabetes mellitus type 2, non-insulin-dependent
12. Extreme obesity
13. Hepatic dysfunction

Management

The patient was extremely ill and rapidly decompensating with multisystem organ failure, including respiratory failure, altered mental status, acute on chronic renal failure, and cardiac dysfunction. The primary concerns for the stability of the patient revolved around respiratory failure coupled with altered mental status. In the intensive care unit (ICU), she rapidly began to fail BiPAP therapy. Subsequently, the patient was emergently intubated in the ICU. A systemic review of therapies and hospital course is as follows:

Endocrine

Considering the primary diagnosis of myxedema coma, early supplementation with thyroid hormone is essential. Healthcare providers followed the American Thyroid Association recommendations, which recommend giving combined T3 and T4 supplementation; however, T4 alone may also be used. T3 therapy is given as a bolus of 5 to 20 micrograms intravenously and continued at 2.5 to 10 micrograms every 8 hours. An intravenous loading dose of 300 to 600 micrograms of T4 is followed by a daily intravenous dose of 50 to 100 micrograms. Repeated monitoring of TSH and T4 should be performed every 1 to 2 days to evaluate the effect and to titrate the dose of medication. The goal is to improve mental function. Until coexistent adrenal insufficiency is ruled out using a random serum cortisol measurement, 50 to 100 mg every 8 hours of hydrocortisone should be administered. In this case, clinicians used hydrocortisone 100 mg IV every 8 hours. Dexamethasone 2 to 4 mg every 12 hours is an alternative therapy.

Neurologic

The patient's mental status rapidly worsened despite therapy. In the setting of her hypothyroidism history, this may be myxedema coma or due to the involvement of another organ system. The thyroid supplementation medications and hydrocortisone were continued. A CT head without contrast was normal.

Respiratory

For worsening metabolic acidosis and airway protection, the patient was emergently intubated. Her airway was deemed high risk due to having a large tongue, short neck, and extreme obesity. As the patient's heart was preload dependent secondary to pericardial effusion, a 1-liter normal saline bolus was started. Norepinephrine was started at a low dose for vasopressor support, and ketamine with low dose Propofol was used for sedation. Ketamine is a sympathomimetic medication and usually does not cause hypotension as all other sedatives do. The patient was ventilated with AC mode of ventilation, tidal volume of 6 ml/kg ideal body weight, flow 70, Initial fraction of inspired O_2 100 %, rate 26 per minute (to compensate for metabolic acidosis), PEEP of 8.

Cardiovascular

She was determined to be hemodynamically stable with a pericardial effusion. This patient's cardiac dysfunction was diastolic in nature, as suggested by an ejection fraction of 66% to 70%. The finding of posterior pericardial effusion further supported this conclusion. The posterior nature of this effusion was not amenable to pericardiocentesis. As such, this patient was preload dependent and showed signs of hypotension. The need for crystalloid fluid resuscitation was balanced against the impact increased intravascular volume would have on congestive heart failure and fluid overload status. Thyroid hormone replacement as above should improve hypotension. However, vasopressor agents may be used to maintain vital organ perfusion targeting a mean arterial pressure of greater than 65 mm Hg as needed. BP improved after fluid bolus, and eventually, the norepinephrine was stopped. Serial echocardiograms were obtained to ensure that the patient did not develop tamponade physiology. Total CK was elevated, which was likely due to Hypothyroidism compounded with chronic renal disease.

Infectious Disease

Blood cultures, urine analysis, and sputum cultures were obtained. The patient's white blood cell count was normal. This is likely secondary to her being immunocompromised due to hypothyroidism and diabetes. In part, the pulmonary findings of diffuse edema and bilateral pleural effusions can be explained by cardiac dysfunction. Thoracentesis of pleural fluid was attempted, and the fluid was analyzed for cytology and gram staining to rule out infectious or malignant causes as both a therapeutic and diagnostic measure. Until these results return, broad-spectrum antibiotics are indicated and may be discontinued once the infection is ruled out completely.

Gastrointestinal

Nasogastric tube feedings were started on the patient after intubation. She tolerated feedings well. AST and ALT were mildly elevated, which was thought to be due to hypothyroidism, and as the TSH and free T4 improved, her AST and ALT improved. Eventually, these values became normal once her TSH level was close to 50.

Renal

Her baseline creatinine was found to be close to 1.08 in prior medical records. She presented with a creatinine of 1.8 in the emergency department. Since hypothyroidism causes fluid retention in part because thyroid hormone encourages excretion of free water and partly due to decreased lymphatic function in returning fluid to vascular circulation. Aggressive diuresis was attempted. As a result, her creatinine increased

initially but improved on repeated evaluation, and the patient had a new baseline creatinine of 1.6. Overall she had a net change in the fluid status of 10 liters negative by her ten days of admission in the ICU.

Hematology

Mildly anemic otherwise, WBC and platelet counts were normal. Electrolyte balance should be monitored closely, paying attention to sodium, potassium, chloride, and calcium specifically as these are worsened in both renal failure and myxedema.

Daily sedation vacations were enacted, and the patient's mental status improved and was much better when TSH was around 20. The bilateral pleural effusions improved with aggressive diuresis. Breathing trials were initiated when the patient's fio2 requirements decreased to 60% and a PEEP of 8. She was eventually extubated on to BiPAP and then high flow nasal cannula while off of BiPAP. Pericardial fluid remained stable, and no cardiac tamponade pathology developed. As a result, it was determined that a pericardial window was unnecessary. Furthermore, she was not a candidate for pericardiocentesis as the pericardial effusion was located posterior to the heart. Her renal failure improved with improved cardiac function, diuretics, and thyroid hormone replacement.

After extubation patient had speech and swallow evaluations and was able to resume an oral diet. The patient was eventually transferred out of the ICU to the general medical floor and eventually to a rehabilitation unit.

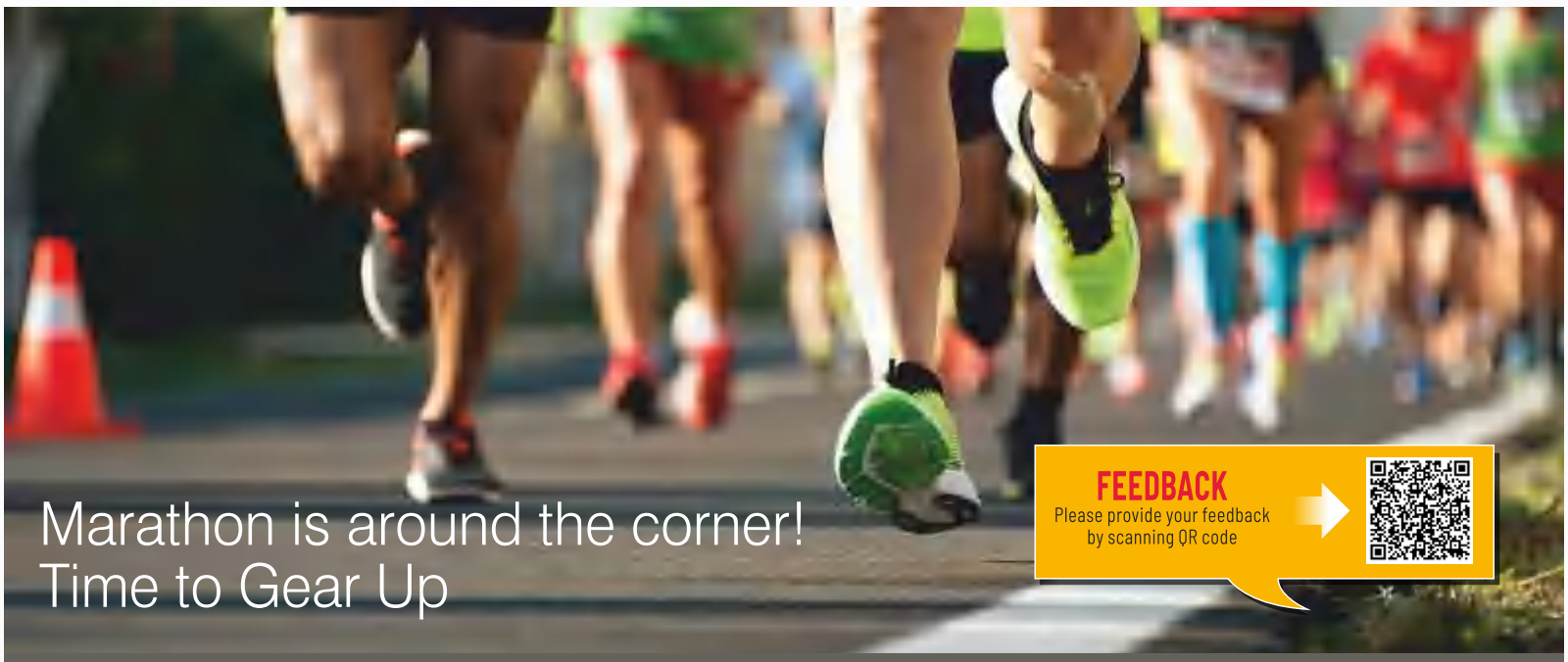
Pearls of Wisdom

- Not every case of shortness of breath is COPD or congestive heart failure (CHF). While less likely, a history of hypothyroidism should raise suspicion of myxedema coma in a patient with any cognitive changes.
- Myxedema is the great imitator illness that impacts all organ systems. It can easily be mistaken for congestive heart failure, COPD exacerbation, pneumonia, renal injury or failure, or neurological insult.
- Initial steps in therapy include aggressive airway management, thyroid hormone replacement, glucocorticoid therapy, and supportive measures.
- These patients should be monitored in an intensive care environment with continuous telemetry.

Enhancing Healthcare Team Outcomes

This case demonstrates how all interprofessional healthcare team members need to be involved in arriving at a correct diagnosis, particularly in more challenging cases such as this one. Clinicians, specialists, nurses, pharmacists, laboratory technicians all bear responsibility for carrying out the duties pertaining to their particular discipline and sharing any findings with all team members. An incorrect diagnosis will almost inevitably lead to incorrect treatment, so coordinated activity, open communication, and empowerment to voice concerns are all part of the dynamic that needs to drive such cases so patients will attain the best possible outcomes.

DON'T JUST CHASE YOUR DREAMS. RUN THEM DOWN!



Marathon running has been shown to improve markers of cardiovascular health. It can decrease blood pressure and resting heart rate. It may also reverse the aortic stiffening process that naturally occurs with ageing.

HOW TO PREPARE FOR A MARATHON?

Training for a marathon takes intense preparation, dedication and skill. Poor race-time decisions can counteract all of your months-long hard work and planning. Here are a few basic guidelines to minimize any excess damage to your body - and make the race experience more pleasant.

- Restore your muscles, focus on sleep the week prior to the race
- Make sure you are well-hydrated prior to the start of the race. Drink lots of water during the week before the race.
- Eat a diet rich in complex carbohydrates, such as breads, rice, pasta and starchy vegetables.
- Be sure to have on hand your hydration and food sources for the race, including an electrolyte source.
- There should be no strength training for the week of an event.
- Avoid wearing a new outfit and new shoes for the race. Schedule of all Marathons and running events in India

DATE	EVENT	PLACE, STATE
04-Dec-21	Chandigarh Freedom Ultrarun 6.0	Chandigarh, PB
05-Dec-21	Millennium City Marathon 2021 Gurugram	Gurugram, HR
05-Dec-21	Tuffman Beach Ultra & Half Marathon Goa (5th Edition)	South Goa, GA
05-Dec-21	BMG Elegant City Rewari Half Marathon 2021	Rewari, HR
11-Dec-21	SRT Ultra 2021	Pune, MH
12-Dec-21	6th SuperSikh Run, Delhi (NCR)	South East Delhi, DL
12-Dec-21	Celebrate Life! Bengaluru Half Marathon & 10K	Bengaluru Urban, KA
18-Dec-21	The Border 100 - 2021	Jaisalmer, RJ
26-Dec-21	The Last Sunday Run	Gautam Buddh Nagar, UP
26-Dec-21	Aravali Trail Run 2021	Gurgaon, HR
09-Jan-22	Air Heroes Half Marathon 2022 (2nd edition)	South West Delhi, DL
23-Jan-22	Celebrate Life! Mysuru Half Marathon & 10K	Mysuru, KA
06-Mar-22	HM Jaipur Half Marathon	Jaipur, RJ
27-Mar-22	Be Healthy Noida Half Marathon	Gautam Buddh Nagar, UP