PHARMANEXUS

THE ERODE COLLEGE OF PHARMACY

An Official Publication of The Department of Pharmacy Practice,
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Volume No.: 08
Issue No.: 01
JAN – MAR 2024

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DIABETES MELLITUS: UNDERSTANDING WHY A CURE REMAINS ELUSIVE

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Introduction:

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia due to defects in insulin secretion, insulin action, or both. The condition significantly impacts global health, leading to complications such as cardiovascular disease, neuropathy, nephropathy, and retinopathy. Understanding the pathophysiology of different types of diabetes provides insight into why curing the disease remains a major challenge.

Type 1 Diabetes: Autoimmune Destruction

Type 1 diabetes (T1D) is an autoimmune disorder where the immune system erroneously attacks pancreatic beta cells, leading to an absolute deficiency of insulin production [1]. This destruction is mediated by autoreactive T cells, with genetic and environmental factors playing a role in disease onset.

Challenges to a Cure

1. **Beta Cell Regeneration**: Once beta cells are destroyed, the body lacks mechanisms to regenerate them naturally [2].
2. **Immune System Dysregulation**: Even if beta cells are replenished through transplantation or stem cell therapy, the immune system may continue to attack them [3].
3. **Lifelong Immunosuppression**: Islet cell transplantation requires immunosuppressive therapy, which has long-term risks and limited efficacy [4].

Type 2 Diabetes: Insulin Resistance and Beta Cell Dysfunction

Type 2 diabetes (T2D) accounts for 90-95% of all diabetes cases and is characterized by insulin resistance and progressive beta cell dysfunction. Risk factors include obesity, sedentary lifestyle, and genetic predisposition [5].

Challenges to a Cure

1. **Complex Pathophysiology**: T2D arises from multiple mechanisms, including defective insulin signaling, chronic inflammation, and lipotoxicity, making it difficult to target a single curative approach [6].
2. **Beta Cell Exhaustion**: Prolonged hyperglycemia leads to beta cell apoptosis, limiting the pancreas's ability to restore insulin production [7].
3. **Lifestyle Dependence:** Even with pharmacotherapy, long-term glycemic control heavily depends on diet and exercise, reinforcing the need for ongoing management rather than a cure [8].

Gestational Diabetes: A Temporary but Significant Risk Factor

Gestational diabetes mellitus (GDM) occurs during pregnancy and typically resolves postpartum. However, it increases the risk of developing T2D later in life for both mother and child [9].

Challenges to a Cure

1. Hormonal Influence: Pregnancy-induced insulin resistance, driven by placental hormones, complicates long-term interventions [10].
2. Recurrence Risk: Women with GDM have a higher likelihood of developing diabetes in subsequent pregnancies or progressing to T2D later in life [11].
3. Fetal Programming: Intrauterine exposure to hyperglycemia can alter the child's metabolism, increasing their lifelong diabetes risk [12].

Current and Emerging Management Strategies:

Pharmacological Interventions

- **Insulin Therapy:** Essential for T1D and sometimes required in advanced T2D.
- **Oral Hypoglycemics:** Metformin, sulfonylureas, and SGLT2 inhibitors help manage T2D [13].
- **GLP-1 Receptor Agonists:** Improve insulin secretion and reduce appetite [14].

Technological Advancements

- **Continuous Glucose Monitoring (CGM)**: Improves glycemic control by providing real-time glucose data.
- **Artificial Pancreas:** Automated insulin delivery systems are advancing diabetes management but do not cure the disease [15].

Future Directions and Research

1. **Stem Cell Therapy:** Efforts to generate functional beta cells from stem cells are underway, but immune rejection remains a challenge [16].
2. **Gene Editing:** CRISPR technology offers hope in correcting genetic mutations associated with diabetes [17].
3. **Immunotherapy:** Strategies to modulate the immune response could prevent T1D progression [18].
4. **Beta Cell Encapsulation:** Protecting transplanted beta cells from immune attack may enhance their longevity [19].

Conclusion:

Despite extensive research, a definitive cure for diabetes mellitus remains elusive due to the irreversible destruction of beta cells in T1D, the complex etiology of T2D, and the transient but high-risk nature of GDM. Current management strategies aim to control blood glucose and prevent complications, while emerging therapies hold promise for future breakthroughs. Continued research in regenerative medicine, immunotherapy, and genetic engineering may one day lead to a cure.

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Optimizing the Management of Diabetic Ketoacidosis: A Comprehensive Approach

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Diabetic ketoacidosis (DKA) is a critical complication of diabetes mellitus, triggered by physiological, pathological, and drug-related factors, with the most common causes being suboptimal insulin therapy and infections. Suboptimal insulin causes uncontrolled hyperglycemia, lipolysis, and ketogenesis, leading to metabolic acidosis and dehydration [5,6]. Infections can worsen insulin resistance, exacerbating hyperglycemia [5]. Cardiovascular events, alcohol, and certain medications such as corticosteroids and diuretics also increase the risk of DKA [11,12].

The clinical presentation of DKA typically develops rapidly within hours and includes hyperglycemia, ketosis, and acidosis. Symptoms such as polyuria, polydipsia, weight loss, dehydration, and Kussmaul respiration are common [2]. Mental status changes can occur, ranging from mild confusion to coma, with acidosis considered a major driver of neurological impairment [19]. Euglycemic DKA, often induced by SGLT-2 inhibitors, can present with less pronounced hyperglycemia but still results in significant acidosis and electrolyte disturbances [13,14].

Laboratory Assessment in DKA

Diagnosis of DKA relies on lab tests, including plasma glucose, BUN, creatinine, ketones, electrolytes, and raise suspicion**.**

Electrolyte Imbalances and Fluid Therapy

Electrolyte imbalances, especially sodium and potassium, are common in DKA and require careful management. Sodium imbalances occur due to osmotic shifts, and corrected sodium helps guide fluid replacement. Potassium levels must be monitored closely, as insulin can cause hypokalemia.

For fluid resuscitation, isotonic saline (0.9% NaCl) is given initially at 15–20 mL/kg/hr, adjusted based on sodium levels. Insulin should only be started once potassium is above 3.3 mmol/L to prevent hypokalemia.

Insulin Therapy

Insulin plays a key role in managing DKA by inhibiting lipolysis and ketogenesis while promoting glucose uptake. Initial treatment involves an IV bolus of regular insulin (0.1 U/kg) followed by a continuous infusion at 0.1 U/kg/hr. Glucose levels should be monitored and reduced at a rate of 50–70 mg/dL per hour. Once glucose falls below 250 mg/dL, the insulin rate should be reduced to prevent hypoglycemia [1].

In cases of mild-to-moderate DKA, subcutaneous rapid-acting insulin (lispro or aspart) can be considered as an alternative, showing similar efficacy to IV insulin in controlled settings [30,32].

Conclusion

DKA is a life-threatening metabolic emergency that requires prompt identification and treatment. Fluid resuscitation, insulin therapy, and electrolyte

correction are essential components of management. While traditional IV insulin remains the gold standard for severe DKA, subcutaneous insulin may be effective for mild cases, potentially reducing hospitalizations and associated costs [30,32]. Accurate monitoring and a comprehensive, multidisciplinary approach can significantly improve patient outcomes and reduce recurrence.

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FREQUENT MOBILE PHONE USE AND NEW – ONSET HYPERTENSION

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In recent years, mobile phones have become a device of everyday life around the world, with an estimated 8.2 billion users worldwide in 2020. This poses serious concerns regarding the safety of making or receiving calls on a mobile phone, particularly for frequent users.

According to a research published on May 5, 2023 in European Heart Journal - Digital Health, a journal of the European Society of Cardiology (ESC), speaking on a mobile device for 30 minutes or more per week is associated with a 12% greater risk of high blood pressure compared with less than 30 minutes.

In order to determine if frequent use of mobile phones for making or receiving calls was connected with incident hypertension, a total of 2,12,046 people with a mean age of 54 years from the UK Biobank database were involved in the study. Among them, 38% and 62% were men and women respectively. 88% were mobile phone users i.e., uses mobile phone at least once a week. At the time of their recruitment, none of the participants had been diagnosed with hypertension.

Using a self-reported touchscreen questionnaire, data on years of use, hours per week, and use of a hands-free device/speakerphone for making and receiving calls was gathered at baseline.

13,984 (7%) of the trial participants who were followed up for 12 years experienced incident hypertension. With a hazard ratio (HR) of 1.07, mobile phone users had a greater chance of having new-onset hypertension. In comparison to those who used the mobile phone for calls for less than 5 minutes per week, the HR for weekly usage time of 30 to 59 minutes was 1.08; for 1 to 3 hours of use, 1.13; for 4 to 6 hours of use, 1.16; and for those with more than 6 hours of use, 1.25. The danger increased proportionally to the amount of time spent on phones each week.

When compared to those who used their phones for fewer calls or for shorter periods of time (less than 30 minutes) during the week and had a low genetic risk of hypertension, the risk was elevated by 33% among those who were genetically predisposed to hypertension.

This study demonstrated that mobile phone use for making or receiving calls was significantly associated with a higher risk of new-onset hypertension. The frequency of use influenced the risk of hypertension. This was rendered strong by a genetic predisposition to hypertension. Authors note that more research is needed to fully assess their findings and the underlying mechanisms. However, this study cautions regarding the responsible use of mobile phones.

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3.) Frequent Use of Mobile Phones for Calls Linked to Risk of New-onset Hypertension?

https://www.ijcp.in/Pages/Post_Detail.aspx?wid=20596&Frequent%20Use%20of%20Mobile%20Phones%20for%20Calls%20Linked%20to%20Risk%20of%20Ne

FREQUENT MOBILE PHONE USE AND NEW – ONSET HYPERTENSION

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Rattlesnakes, part of the Crotalus and Sistrurus genera within the pit viper subfamily, are found across the Americas, excluding Alaska and Hawaii. While other venomous snake species, such as Copperheads and Lanceheads, also belong to this subfamily, rattlesnakes are the most common in the U.S. Their main defense is hiding, though they may rattle and hiss to warn off threats. If threatened, they can bite and envenomate, leading to potentially fatal outcomes. Awareness of local snake species is crucial for proper snakebite management.

Most snakebites in the U.S. involve pit vipers, with rattlesnakes accounting for over half of these incidents. The venom, delivered through hollow fangs, contains enzymes that cause necrosis, increase cell permeability, and lead to coagulopathy. Crotalid venom is a complex mixture with over 50 proteins, metals, and macromolecules, including phospholipase A2 toxins, which have myotoxic, anticoagulant, and neurotoxic effects. Phospholipases harm platelet membranes, causing platelet lysis and thrombocytopenia.

Pre-hospital care is where the proper management of a rattlesnake bite should start. patients who report with a snake bite should first have their airway, breathing, and circulation evaluated.

Start the therapy at a 10 mL/hr rate while monitoring for side effects. If none, increase every few minutes till the administration is finished in an hour. Check patients for both local and systemic symptoms of edema. After gaining control, maintenance doses of 2 vials administered every 6 hours for 18 hours are advised for patients with rattlesnakes.On days 2-3 and days 5-7, repeat the coagulation panel (PT/PTT/INR), fibrinogen, platelets, and hemoglobin. It has been documented that recurrent coagulopathy can happen without clinically substantial bleeding. To normalization, some people repeat and follow the parameters. If coagulopathy develops between three and seven days after the last dosage of antivenom, the following are indications for repeat dosing:

INR > 3.0

PTT > 50 sec.

25,000 or less platelets

Fibrinogen 50 ug/ml or less

coagulopathy with several components

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LOTILANER OPHTHALMIC SOLUTION: A PROMISING BREAKTHROUGH IN DEMODEX BLEPHARITIS

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Demodex mites are the most common microscopic ectoparasite found in the human skin. The rate of Demodex infestation increases with age, being observed in 84% of the population at age 60 and in 100% of those older than 70 years these parasites are associated with dermatologic and ocular diseases including blepharitis (1) .

Anatomically, anterior and posterior blepharitis are the two subtypes of Demodex blepharitis. In the first, D. follicular infests eyelashes and follicles, clustering near the root of the lashes, whereas in the latter, D. brevis preferentially infests the meibomian gland. Factors like skin colour, sunlight exposure, alcohol consumption, smoking, stress, hot beverages, spicy foods, and sudden temperature changes might alter the environment to promote the growth of mites [2,3] .

Patients whose local or systemic immune state is weakened by the topical or systemic use of steroids or other immunosuppressive medications or by illnesses like leukaemia and HIV are more likely to experience an infestation of Demodex mites [4] .

1032 patients, had developed Demodex blepharitis (mean age, 60.2 ± 17.8 years).

Demodex blepharitis was more common in patients with blepharitis (69.1%) and glaucoma (64.8%) than it was in those with dry eye disease (DED) (58.9%) and cataract (55.7%) [5] . A team of investigators, led by Elizabeth Yeu, MD, from Virginia Eye Consultants in Norfolk, Virginia, reported the safety and efficacy of lotilaner ophthalmic solution, 0.25% (TP-03, Tarsus Pharmaceuticals Inc.) for treating Demodex blepharitis.

The Saturn-1 phase 2b/3 study is a prospective, randomized, controlled, double-masked clinical trial that evaluated the safety and effectiveness of lotilaner ophthalmic solution to treat Demodex blepharitis.

A total of 421 patients were included in the study and they were randomly assigned to active treatment or vehicle. Both eyes of each patient were treated twice daily for 43 days.

The participants were examined at 4 time points: days 8, 15, 22, and 43 after the start of treatment. At the end of the study, on day 43, instillation of lotilaner achieved the following results compared with the controls: significantly higher clinically meaningful collarette cure (81.3% vs. 23%), complete collarette cure (44% vs. 7.4%), mite eradication (67.9% vs. 17.6%), erythema cure (19.1% vs. 6.9%), and composite cure (13.9% vs. 1%) ($P < 0.0001$ for all comparisons).

The drops were considered to be “neutral to very comfortable” by about 92% of patients. Pain at the instillation site was the most common complaint reported and all ocular adverse events were mild. “Lotilaner ophthalmic solution, 0.25%, is the first drug designed to treat and target the underlying cause of Demodex blepharitis”.

On 25th July FDA had approved lotilaner for the treatment of demodex blepharitis.

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DEPARTMENTAL ACTIVITIES

1st ECPCON-2024: Bridging Pharma Research and Intellectual Property – A Pioneering Conference in Healthcare Innovations

ECPCON-2024, a three-day National Conference hosted by The Erode College of Pharmacy, Erode, held from 15th to 17th February 2024. This conference brought together experts, professionals, and enthusiasts to explore the critical intersection of pharmaceutical research and intellectual property.The conference was awarded 30 credit points under Category-I by The Tamil Nadu Dr. M.G.R. Medical University, Chennai, reflecting its academic excellence and importance in the field.This event served as a dynamic platform for insightful discussions, knowledge exchange, and collaborative efforts, highlighting the latest developments in pharmaceutical research and intellectual property.

Freshers' Day Celebration at The Erode College of Pharmacy

The I-Year Pharm.D students of The Erode College of Pharmacy were warmly welcomed by their seniors, the II-Year Pharm.D students, during the Freshers' Day celebration on February 10, 2024, at 2:00 PM in the college auditorium. The event began with a felicitation speech by Dr. V.S. Saravanan, the Vice-Principal, followed by inspiring addresses from Professor Mr. T.P. Sugumar, Dr. R. Natarajan, Dr. P. Balan, and Dr. S. Manokaran.

The II-Year students organized engaging games to help foster camaraderie, and the cultural segment showcased the talent of both I and II-Year students. The festivities included a cake-cutting ceremony to celebrate the day. The event concluded with a vote of thanks from Dr. M. Jambulingam, Associate Professor in the Department of Pharmaceutical Analysis, thanking everyone who contributed to the success of the event.

WEBINAR ON "CAREER OPPORTUNITIES IN CLINICAL RESEARCH"

A webinar on "Career Opportunities in Clinical Research" was conducted on 21st February 2024, organized by the Department of Pharmacy Practice in collaboration with TrueLessons! Bangalore.

Dr. Divya Sunil and Dr. Amrutha Babu delivered insightful lectures, exploring various career pathways in the clinical research field, including roles in clinical trials, regulatory affairs, data management, and more.

The webinar saw the participation of around 150 students from Pharm.D 1st to 6th year, held in the College Auditorium at The Erode College of Pharmacy, Erode. It was an excellent opportunity for students to gain val

uable insights into the diverse career opportunities within clinical research.

75th HAPPY REPUBLIC DAY

9th International Conference on Clinical Pharmacy – CPCON 2024

It was successfully conducted from 5th to 7th January 2024 at MAHE, Manipal.

This year's event featured a pre-conference workshop on Medication Therapy Management in Different Practice Settings, conducted by Dr. Johnson George, Associate Professor, Centre for Medicine Use and Safety, Monash University, Australia. The second workshop focused on Approaches in Regulatory Medical Writing, led by Dr. Avinash Laddha, Medical Writing Specialist, Novo Nordisk, Bangalore.

Mrs. Smitha Sarah Thambi, Assistant Professor, Department of Pharmacy, The Erode College of Pharmacy, attended both the pre-conference workshop and the main conference. She also presented a poster at the conference, contributing to the vibrant exchange of knowledge and ideas.