HYPERGLYCEMIA-INDUCED ALTERATIONS IN COLONIC MOTILITY AND SECRETION: ROLES OF 5-HYDROXYTRYPTAMINE SIGNALING AND TRANSLATIONAL IMPLICATIONS

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Abstract

Diabetes mellitus is frequently associated with gastrointestinal dysfunction, traditionally linked to gastric dysmotility. Recent evidence demonstrates that chronic hyperglycemia also disrupts colonic motility and epithelial secretion, contributing to constipation, diarrhea, and fecal incontinence. Experimental studies using streptozotocin-induced hyperglycemia reveal impaired coordination between smooth muscle contractility and epithelial ion transport within the colon. These processes are closely regulated by enteric serotonergic signaling. 5-Hydroxytryptamine (5-HT) plays a central role in enteric neuron activation, smooth muscle excitation, and epithelial secretory responses. Sustained hyperglycemia alters 5-HT receptor expression, serotonin transporter function, and enteric neuronal integrity. This review synthesizes current scientific advancements and discusses translational implications for targeted therapeutic development.

Keywords: Diabetes mellitus; Colonic motility; Epithelial secretion; Serotonin; Hyperglycemia

I. INTRODUCTION

Gastrointestinal complications are prevalent in diabetes mellitus and significantly impair quality of life. Although gastric dysmotility has been widely investigated, colonic dysfunction remains underrecognized despite the colon's critical role in fluid balance, stool formation, and defecation. Clinical manifestations such as altered bowel frequency, urgency, diarrhea, and constipation suggest disruption of coordinated motility and secretion. Understanding the mechanistic basis of colonic dysfunction is essential for improving diagnostic accuracy and therapeutic outcomes.

II. 5-HYDROXYTRYPTAMINE SIGNALING IN COLONIC MOTILITY AND SECRETION

5-Hydroxytryptamine is synthesized predominantly by enterochromaffin cells and released in response to mechanical and chemical stimuli. In the colon, 5-HT activates intrinsic primary afferent neurons and downstream motor circuits through receptor subtypes including 5-HT3 and 5-HT4. These signaling pathways coordinate smooth muscle contraction with epithelial chloride secretion, ensuring effective propulsion and luminal hydration.

III. MECHANISMS OF HYPERGLYCEMIA-INDUCED COLONIC DYSFUNCTION

Chronic hyperglycemia induces oxidative stress and low-grade inflammation within the enteric nervous system. Reactive oxygen species impair neuronal excitability and neurotransmitter release, including serotonergic signaling. Structural changes in smooth muscle cells and interstitial cells of Cajal further compromise peristaltic coordination, resulting in functional bowel disturbances.

IV. TRANSLATIONAL AND CLINICAL IMPLICATIONS

Recognition of colonic involvement in diabetic gastrointestinal dysfunction has important clinical implications. Targeting serotonergic pathways, particularly receptor modulation and serotonin transporter regulation, combined with optimized glycemic control, may restore coordinated motility and secretion. Such approaches hold promise for improving symptom control and patient quality of life.

V. FUTURE DIRECTIONS AND RESEARCH RECOMMENDATIONS

Future investigations should prioritize integrative and longitudinal study designs to characterize disease progression. Human translational studies and interventional trials evaluating serotonergic and microbiome-modulating therapies are necessary to advance precision treatment strategies.

VI. CONCLUSION

Hyperglycemia-induced disruption of serotonergic regulation in the colon represents a critical but underrecognized component of diabetic gastrointestinal dysfunction. Continued translational research is essential for the development of mechanism-based therapies that restore coordinated colonic motility and secretion.

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