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Editorial

The Important Roles of Interstitial Cells of Cajal and Cholinergic Receptors on Diabetes Related Dysfunction of Colon

Jae Yeoul Jun

Department of Physiology, College of Medicine, Chosun University, Gwangju, Korea

Article: Alterations of colonic contractility in long-term diabetic rat model
Kim SJ, Park JH, Song DK, et al
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Diabetes mellitus (DM) is a chronic disease that develops at the time of inappropriate insulin production and utilization. Lifelong medical attention is required for inhibiting the development of potentially devastating late complications of DM.

Diabetic patients are generally affected with gastrointestinal (GI) disorders.[1,2] The common symptoms are dysphagia, satiety, reflux, constipation, abdominal pain, nausea, vomiting and diarrhea.[3-5] These symptoms are eventually caused by the neuropathy involving the entire GI tract. In particular, it has been well known that abnormal motility of the GI tract occurs in the development of diabetes.[6] So far many studies have demonstrated that DM patients have slow transit and abnormal motility. GI abnormalities such as motor dysfunction, autonomic neuropathy, inadequate glucose control, psychological factors, or morphological changing in the GI tract have been reported.[7-9] However, the underlying mechanism is not clearly understood.

Interstitial cells of Cajal (ICCs) are known as pacemaking cells, mediators of neurotransmission in GI tract and play a crucial roles in GI motility.[10-12] They are network-forming cells connected electrically with each other and with smooth muscle cells via gap junctions.[13] Recently, it has been shown that some populations of ICCs express the proto-oncogene c-Kit, and the antibodies to its gene product, the Kit (or c-Kit) receptor which a membrane receptor tyrosine kinase, are now available for use as an immunohistochemical label for ICCs in some species.[14] Many regions of the GI tract display spontaneous electrical rhythmicity.[15] Auto-rhythmicity in GI muscles is an exclusive property of ICCs and the spread of slow waves through GI muscles occurs electronically, not by active regeneration. Slow waves, pacemaking by ICCs, are organized into electrically coupled networks within discrete areas of the stomach, small bowel and colon.

Interestingly, some reports have recently suggested the loss of ICC networks in diabetic patients and animal models.[16,17] These showed the involvement of ICCs on DM-related GI motor abnormalities. Kim et al[18] examined the nature of colonic dysfunction in a long-term diabetic rat model. They found that the spontaneous contractility of proximal colon and the ICC networks were decreased in the diabetes rats. This result supports

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*Correspondence: Jae Yeoul Jun, MD
Department of Physiology, College of Medicine, Chosun University, 375 Seosuk-dong, Gwangju 501-759, Korea
Tel: +82-62-230-6412, Fax: +82-62-232-4943, E-mail: jyjun@chosun.ac.kr
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the previous findings that the involvement of ICCs has showed in diabetic patients and animal models.[16,17]

Kim et al[18] indicated that the response of carbachol or nitric oxide in proximal colon of the diabetic rats was significantly decreased. It is well known that acetylcholine plays important roles for modulation of GI motility and the existence of receptors for acetylcholine in ICCs and smooth muscle of the GI tract was mentioned in many reports.[19-21] Nitric oxide (NO) is also a major nonadrenergic, noncholinergic inhibitory neurotransmitter in GI tract and the release of NO causes relaxation of the smooth muscle.[22,23] It has been reported that NO has an effect on the electrical activity of ICCs as well.[24] However, Kim et al[18] did not show the exact mechanism what kind of cells is involved in the diabetic rats. Nevertheless, they proposes strong evidence regarding the role of ICCs on GI motor abnormalities in diabetic rats. The number of acetylcholine receptor and the production of nitric oxide can affect the DM-related motor symptoms.

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