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Editroial

Impact of Myenteric Plexus Alterations on Diabetes Related Gastrointestinal Dysmotility

Kyung Sik Park

Department of Internal Medicine, Keimyung University School of Medicine, Daegu, Korea

Article: Gastrointestinal motility changes and myenteric plexus alterations in spontaneously diabetic biobreeding rats
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Diabetes mellitus (DM) is a group of chronic metabolic disorder that develops when pancreatic insulin production or utilization is imbalanced. In particular, long-term complications of DM such as renal, cardiovascular, neurologic, ophthalmic and gastrointestinal (GI) diseases constitute the major causes of death or impaired quality of life (QOL).[1,2] Among these, GI complications are so frequent that more than 75% of diabetic patients show one or more gastrointestinal symptoms such as early satiety, nausea, vomiting, constipation, diarrhea, abdominal pain and fecal incontinence.[3-7] It has been widely reported that these GI symptoms result from abnormal GI motility which occurs in the development of diabetes.[4-6,8]

Although autonomic neuropathy involving a diffuse GI tract has been thought as the main mechanism of GI dysmotility due to diabetes,[9-11] several factors such as abnormal glycemia, morphological changes of the GI tract, and psychiatric disease have been suggested as other causes of GI dysmotility in diabetic patients.[12-17] In addition, various recent reports have emphasized the importance of enteric apparatuses such as interstitial cells of Cajal (ICCs) or enteric nerves and their transporting systems in the regulation of GI motility.[18-21] It is well known that impairment of these systems ultimately result in GI dysmotility and associated GI symptoms in various diabetic animal models and patients.[22-24]

Several animal models have been developed to present the characteristics of type 1 (autoimmune destruction of pancreatic beta cells) and type 2 (insulin resistance and failure of compensation by beta cells) diabetes.[25] Among these models, spontaneously diabetic biobreeding (BB) rats, are considered as an useful model for studying human type1 diabetes because they show destruction of insulin producing pancreatic the beta cells around 2-3 months of age.[26]

In this issue of the journal, the authors investigated the presence of gastric and jejunal dysmotility in spontaneously diabetic BB rats,[27] and whether it correlates with autonomic neuropathy or with changes of myenteric innervation. The same group which included the authors of this issue has previously reported that decreased nitrergic motor control and neuronal nitric oxide synthase protein expression in the jejunum may be the primary dysfunction in spontaneously diabetic BB rats with supporting results from in vitro experiments.[28] In this issue, the authors supple-

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*Correspondence: Kyung Sik Park, MD
Department of Internal Medicine, Dongsan Medical Center, 194 Dongsan-dong, Jung-gu, Daegu 700-712, Korea
Tel: +82-53-250-7088, Fax: +82-53-250-7088, E-mail: seenae99@dsmc.or.kr
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mented the results from in vivo experiments including relative risk-interval variability on electrocardiography, gastric emptying time and small intestinal electromyography. With the results of small intestinal electromyography, the research group confirmed that altered inhibitory motor control in the small bowel can be attributed to the loss of nitrergic motor function in spontaneously diabetic BB rats, in a similar manner to the 2,4,6-trinitrobenzenesulfonic acid (TNBS)-induced post-inflammatory small intestinal dysmotility rat model.[29] Using the relative risk-interval variation study on electrocardiography, the authors concluded that vagal neuropathy is not associated with altered nitrergic motor function. Furthermore, there was no difference in gastric emptying rate between diabetic and control groups. These findings are not consistent with previous studies which showed an association between vagal neuropathy and delayed gastric emptying with altered motor function in a diabetic model.[30,31] In addition to the authors' conclusion, "short-term follow-up period" should be considered as a possible confounding factor that may lead to incorrect conclusions. The authors also found transient inflammatory infiltration of the jejunal wall in the 8 week-old diabetic group, which was found to disappear in the 16 week-old diabetic group. This finding is consistent with previous reports on the small intestine and colon of BB rats and a TNBS-induced model.[29]

In summary, the authors conclude that transient small intestinal inflammation followed by loss of myenteric nitric oxide synthase expression and continuing alterations of small intestinal motor function are ultimately associated with GI dysmotility and that this dysmotility is not dependent on hyperglycemia or vagal neuropathy.

There are 2 points which should be considered in future studies. First, it should be examined whether the duration of 16 weeks is long enough to develop long-term GI complications in spontaneously diabetic BB rats since such complications usually take more than several years to develop in human DM patients. Checking several indicators (for example, microalbuminuria or advanced glycation end-product level) which suggest the presence of long-term diabetic complications may be helpful since GI complications are frequently represented with other diabetic complications such as nephropathy or ophthalmopathy.

Second, investigation about ICCs and their communicating systems is recommended considering their important roles in the regulation of GI motility.

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