Mini-Review

Irritable bowel syndrome (IBS): a treatable form of peripheral neuropathy

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Abstract: Irritable bowel syndrome (IBS) has long been considered a diagnosis of exclusion with no clear pathogenesis. With an estimated prevalence of 20% in the Western world, understanding this disease has been a major topic of interest in the medical and non-medical community. Data suggests the pathogenesis is multifactorial. More recently, the role of the mesentery, both on a structural and neurological level, has been postulated as well as the necessity of healthy gut flora. These are emerging as key factors in ensuring adequate levels of serotonin in the intestine, in turn regulating bowel motility. With IBS affecting a large patient population, further research is required to characterise relationships between the mesentery, peripheral nerves, bowel flora and gut motility to help identify an optimal treatment regimen for patients with IBS.

Keywords: Irritable bowel syndrome (IBS); peripheral neuropathy; serotonin; mesentery; microbiome; flora motility

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Irritable bowel syndrome (IBS) has long been considered a diagnosis of exclusion with no clear pathogenesis. With an estimated prevalence of 20% in the Western world (1), understanding this disease has been a major topic of interest in the medical and non-medical community. The specific pathogenesis is yet to be confirmed. As a result, patients are either not treated appropriately or are placed on restrictive diets in hopes of alleviating symptoms. With a vast array of theories, data suggests the pathogenesis to be multifactorial. Understanding pathogenesis is essential to optimize treatment for patients suffering from IBS.

The bowel is a two metres (2) long tube of muscle and functions at the motor level by peristalsis. It is suspended within the abdominal cavity by the mesentery (3). Without this attachment, it is postulated the bowel would fold on itself and disrupt transit of bowel contents. Although little is fully understood regarding the true function of the mesentery and its role in disease, it is possible that structural changes in this organ may lead to IBS.

For proper function, the bowel requires normal peristaltic motion and circadian rhythm. The bowel muscle, like all muscles of the body, requires hormonal input for movement. If these are imbalanced, gut function is suboptimal and may lead to IBS.

Peripheral nerve dysfunction is a common issue for endocrinologists who often find themselves managing nerve dysfunction due to poorly controlled diabetes. In these patients, suboptimally controlled diabetes leads to peripheral nerve root irritation causing, amongst other symptoms, burning of feet and cramps. Interestingly, these patients also exhibit signs and symptoms of IBS. It is thought these symptoms are due to peripheral nerve dysfunction caused by pituitary and adrenal fatigue. In patients with pituitary and adrenal fatigue, circadian inputs into intestinal mobility are disrupted causing the symptoms of IBS (bloating, cramping, flatulence, diarrhea/constipation).

Serotonin is the major hormone regulating bowel sensory and motor function. It is secreted by enterochromaffin cells (ECs) of the bowel when enteric nerves are stimulated. Not only does serotonin have a direct effect on the bowel, it also

influences the function of the mesentery as serotonergic neurons constitute 2% of mesenteric neurons (4).

With serotonin being the major hormone involved in bowel function at the nerve junction, regulating optimal serotonin levels in IBS patients often resolves patient symptoms. Oftentimes in practice it is found that treating these patents with low dose tricyclic anti-depressants or selective serotonin re-uptake inhibitors (SSRIs) regulates hormonal changes, alleviating peripheral nerve dysfunction and resolving the symptoms of IBS. Amitriptyline (a tricyclic antidepressant), functions by blocking the reuptake of serotonin and noradrenaline at the post synaptic cleft. This results in increased levels of serotonin in the bowel, allowing peristalsis and bowel sensory function to be restored. A similar mechanism occurs with SSRIs, which inhibit the reuptake of serotonin from the synaptic cleft.

In addition to the above, the microbiome has been intensively researched in recent years and evidence supports a link between it and regulation of homeostasis and metabolism. For this reason, the microbiome is providing alternate strategies for treating diseases (5) and adjusting microbial ecology in the intestine of patients with IBS, could play a major role in the treatment plan. With the human gut containing more than 1 kg of bacteria and inhabited by 10^{13} to 10^{14} microorganisms, it is highly likely the intestinal microbiota plays a major role in regulating proper bowel function (6).

Intestinal microbes are known to influence EC cells, i.e., major producers of serotonin within the intestine. 90% of serotonin production in the body in general is mediated by gut microbes in the bowel (7). With serotonin being a key factor in intestinal function both at a pre and post synaptic level (8), appropriate hormonal regulation is essential for improving IBS.

The creation of a diet that promotes a healthy microbiota is likely to be beneficial. It is feasible this could be achieved through the adoption of a variety of health foods including probiotics. It is also possible these may act at the EC interface to regulate mesenteric serotonin levels, thereby influencing bowel motility and related symptoms.

In lieu of this research, pharmacological management of IBS with drugs that prevent serotonin and noradrenaline breakdown at the neuromuscular junction may not be sufficient to fully ameliorate symptoms. Dietary regimens aiming to beneficially regulate the intestinal microbiota may also be required in tandem with pharmacological therapies. As IBS affects a substantial proportion of the population, further research is required to unravel the link between mesenteric inputs, peripheral nerve activity and intestinal mobility. This, in turn, could greatly assist in the treatment of IBS.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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