



HORMONES AND IBS

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One of the common questions asked by individuals who suffer from irritable bowel syndrome is whether hormones might play a role in causing the problem. In particular, some women with IBS wonder about this based on their own observations of changes in their bowel symptoms with the menstrual cycle. The possible role of hormones in IBS has been investigated in recent years by several researchers, including our group.

Hormones are internal messenger chemicals in the body. They are released by special cells into the blood stream, in varying amounts that depend on how much activity is called for at each time. Hormones circulate through the body and regulate the activity and growth of cells and organs by stimulating or inhibiting specific functions.

The most widely recognized examples of hormones are the sex hormones estrogen and testosterone, as well as adrenaline, which is the hormone that increases strength and energy to prepare the body for action. However, numerous other hormones also play varied roles in ensuring the normal functioning of the human body.

SEX HORMONES

There are indications that sex hormones, and in particular estrogen and progesterone, influence irritable bowel syndrome. Receptors for these hormones have been found on gastrointestinal cells, which suggest that the gastrointestinal tract is designed to sense and react to them. There is also evidence that such reactions do indeed occur: Both women with and without IBS tend to experience systematic changes in gastrointestinal symptoms at the times in their menstrual cycle when the amounts of these hormones in the blood change most^(1,2). Symptoms such as stomach pain, diarrhea, nausea, and bloating are generally greatest during menses, when estrogen and progesterone drop down to the lowest levels in the body. Bloating is the only IBS-type symptom which also seems to be worse during the second half of the cycle (the luteal phase) before the beginning of menses⁽³⁾.

Although GI symptom changes related to the menstrual cycle are common in women in general, those who have IBS are significantly more likely to report an exacerbation of bowel symptoms during menses. Our group found that 50% of female IBS patients, compared to 34% of non-IBS patients, report worsening of bowel symptoms during menses⁽²⁾. Lee and colleagues⁽⁴⁾ similarly reported that 40% of their female IBS patients experienced menstruation-related worsening of GI symptoms.

It should be noted, however, that even though gastrointestinal symptoms are more responsive to sex hormone fluctuations in women with IBS, the amounts of these hormones in the body do not seem to be different in women with the disorder⁽¹⁾.

Interestingly, women who have IBS-type symptoms also appear to experience worse menstrual symptoms, such as water retention and concentration difficulties, compared to other women⁽¹⁾. It is unclear how changes in sex hormones cause gastrointestinal symptoms to change. However, balloon distention studies have shown that women who suffer from IBS are more sensitive to discomfort in the intestines during menses^(5,6). This suggests that heightened pain sensitivity in the gut, which many researchers think is a key factor in IBS, might play a role in the increase in symptoms due to hormonal changes. Epidemiological data suggest that IBS in women becomes less common after menopause. In a national survey of 5430 householders in the United States ⁽⁷⁾ conducted by our group under the direction of Dr. Drossman, we found that the frequency of IBS decreased after age 45 in women but remained unchanged in men. Decrease in IBS symptoms has similarly been reported by other researchers⁽⁸⁻¹⁰⁾ British data also show⁽¹¹⁾ that clinic consultations for IBS by women, which are generally more common than in men, decrease down to rates equal to men after age 65. The decline in IBS after menopause indicates again that sex hormone fluctuations play a part in producing the symptoms, because such fluctuations cease after menopause.

With all these indications of female sex hormones playing a role in IBS symptoms, one might ask whether the male sex hormone testosterone also influences IBS. Houghton and colleagues in England recently attempted to address this question, to our knowledge for the first time, by comparing testosterone levels in men with and without IBS⁽¹²⁾. These investigators did not find a significant difference in testosterone levels between IBS men and those without the disorder, but they did find that men with the highest testosterone levels also had the highest gut pain sensitivity in balloon inflation tests. They also noted that another hormone - luteinizing hormone - tended to be lower in men who had IBS, but that finding was not statistically significant once emotional variables (which can influence it) were taken into account.

GUT HORMONES

Even though several hormones (including gastrin, secretin, cholecystokinin, and motilin) specifically control the activity of the gastrointestinal tract, there has been curiously little research to date on the role these hormones might play in IBS. However, there are a few indications that aberrations in gut hormones may be a factor in IBS symptom production.

A substantial proportion of patients with IBS experience bowel symptoms soon after eating a meal. There is now some evidence indicate that these so-called postprandial symptoms may be brought on by abnormal reactivity in the hormones cholecystokinin (CCK) and motilin, which are thought to initiate the activity of different parts of the intestinal tract in response to eating.

Sjolund and colleagues in Sweden⁽¹³⁾ observed that patients with IBS had an exaggerated CCK response to a fat-rich meal, and a decreased motilin response to both a meal and water. Another Swedish group has found motilin to be elevated in IBS patients⁽¹⁴⁾. Japanese research by Fukudo and Suzuki⁽¹⁵⁾ furthermore reported 15 years ago that IBS patients show an increase in motilin in response to mental stress in a laboratory test, and that hormone rise is associated with abnormally increased gut activity. All of this may point to abnormal reactivity in the hormones that control the gut's reaction to internal stimuli being at fault to some degree in eliciting bowel symptoms in IBS patients after eating, and possibly (if the Japanese findings turn out to be replicable) in response to psychological stress.

Our group has conducted two small studies, which indicate that another gut hormone, vasoactive intestinal peptide, or VIP, is abnormally concentrated in IBS. In the first study⁽¹⁶⁾, we measured the concentration of several substances in samples of the mucosal lining of the rectum, looking for evidence of possible low-grade inflammation of the bowel. While we found no evidence of inflammation, we noted that the gut hormone VIP was twice as concentrated in the samples from 16 IBS patients compared to the 17 control subjects. This group difference was statistically significant.

We followed up on this finding with another study⁽¹⁷⁾ where we examined whether the amount of VIP circulating in the blood in IBS and control subjects was different, by taking blood samples from the arm of 30 IBS patients and 30 age- and gender-matched healthy individuals. We found again that VIP was present in greater concentration in IBS patients. Together, these two findings provide intriguing indications that elevated levels of VIP, which stimulates the bowels and can cause crampy and watery diarrhea when highly concentrated in the gut, may be characteristic of IBS. Further research will be needed to clarify the influence of this hormone in IBS.

STRESS HORMONES

It is widely recognized that stress has a negative influence on irritable bowel syndrome. The adrenal hormone Cortisol is central to producing many of the physical effects which emotional stress causes in the body. Heitkemper and her colleagues⁽¹⁸⁾ reported in 1996 that Cortisol was unusually high in women with IBS. It was unclear from their study, however, whether the increase was the result of greater psychological stress levels of women with the disorder, or whether the higher hormone level was independent of mental stress.

More recently, Patacchioli and colleagues in Italy⁽¹⁹⁾ have also reported exaggerated Cortisol activity in patients with IBS. Cortisol is generally higher in the morning and lower in the evening. These investigators found this natural pattern to be exaggerated in IBS patients compared to control subjects. They furthermore evaluated the psychological stress of the subjects, and found that these Cortisol differences in the IBS patients could not be explained by differences in psychological stress.

Another stress hormone that may be a promising lead for understanding how stress increases IBS symptoms is Corticotropin-releasing hormone (CRH), which has been shown to cause stress-related intestinal muscle activity in laboratory animals. Fukudo's group in Japan has reported⁽²⁰⁾ that the intestines of IBS patients show stronger and longer-lasting muscle contractions in response to this hormone compared to control subjects.

SUMMING UP WHAT WE KNOW

As we have detailed above, research has uncovered several clues indicating that hormones influence IBS, but to date these findings have done more to raise interesting new research questions than provide useful answers. Much more work is called for to sort out the exact role of different hormones in IBS. So far, what we know can be summarized as follows:

- fluctuation of female sex hormone levels appear to influence the severity of IBS symptoms, and the cessation of this fluctuation at menopause seems to have a beneficial effect on IBS;
- both male and female sex hormones influence the intestinal pain sensitivity of individuals with IBS;
- the stress hormone Cortisol may be over-reactive and intestinal responses to CRH exaggerated in IBS patients;

- the gut hormones motilin and CCK show abnormal reactions in IBS patients, and VIP appears to be elevated in IBS.

It must be kept in mind in reviewing this research that even though measurable differences in hormone levels are found in IBS, this might not mean that such changes play a critical role in the disorder. Furthermore, the observed abnormalities may only be an intermediate step in a chain of dysfunction; hormones are message chemicals, and the source of the abnormal "message" may lie elsewhere. Nonetheless, the accumulating findings of hormone involvement in IBS are encouraging. For if hormones play a significant role in producing the symptoms, it may provide hope for better control of IBS symptoms in the future with medications that neutralize or correct the disturbing messages carried by hormones to the gut.

FURTHER RESEARCH ON SEX HORMONES AND IBS

There are several common events in women's lives that cause their sex hormone levels to change dramatically. These include the use of birth control pills, pregnancy, surgical removal of the ovaries, hormone replacement therapy, and estrogen-suppression with drugs (sometimes used to reduce breast-cancer risk).

The influence of these events has not been studied systematically to date, and doing so is likely to provide important information about the relationship between sex hormones and IBS in women.

We are presently preparing a large survey to attempt to get a clearer picture of how hormone changing events in women's lives affect IBS.

We will be inviting thousands of women to participate in this important investigation.

We are also planning a study to measure directly in our laboratory the relationship between female hormones, pain sensitivity in the gut, and IBS symptoms at different times in the menstrual cycle. We hope that these efforts will soon help to provide more detailed knowledge about the exact role hormones play in the manifestation of IBS.

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