ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Diseases

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Is There a Role for Rectal Therapy in the Treatment of Inflammatory Bowel Disease?

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G&H What are the different kinds of rectal therapy?

RC Rectal therapy means medication administered rectally, and includes enemas, foams, and suppositories.

G&H For which patients is rectal therapy generally appropriate?

RC Ulcerative colitis (UC) always starts in the rectum, and approximately one third of patients have disease occurring in the rectum alone, referred to as proctitis. Another third of patients have disease extending up into the left colon and the splenic flexure, approximately 60 cm up from the anus, referred to as either left-sided colitis or proctosigmoiditis if the disease extends only to the area of the colon just above the rectum. In the remaining third of patients, UC involves most or all of the colon, referred to as pan-ulcerative colitis.

Typically, rectal therapies are mainly considered for patients with proctitis, proctosigmoiditis, and left-sided colitis because enemas can reach to the left colon. In cases where UC involves the entire colon, rectal therapy can still be an appropriate choice because the disease is often most severe in the rectum.

G&H What are the medications administered through these rectal modalities?

RC The two active medicines available to be given rectally are mesalamine and corticosteroids. Currently, in the United States, mesalamine is available as an enema or a suppository. In other countries, mesalamine is also available as a foam, but that modality has not yet been approved here. Hydrocortisone is available as an enema, a foam, or suppositories.

G&H Do these medications work as topical agents inside the colon and rectum?

RC Yes, mesalamine is thought to work topically, even when given in a pill form. The medication is released topically onto the lining of the bowels, where it has an anti-inflammatory effect.

G&H How does a clinician select from the various rectal therapy modalities?

RC The choice of rectal therapy should be made according to the location of the disease. For patients with proctitis, a suppository might be appropriate, though foams and enemas could also be effective. However, suppositories will not reach high enough to treat proctosigmoiditis, left-sided colitis, or pan-ulcerative colitis. Foam may reach to the sigmoid colon, but for disease extending into the left colon, either of the enema formulations would be the appropriate choice. When more than one modality could work, patient preference should also be taken into account.

G&H Are rectal therapies intended for long-term use?

RC UC is a condition where the immune system is attacking the bowels. The medications administered

with rectal therapy do not alter the immune system, so the cause of the disease is not treated with this approach. Therefore, patients need to remain on effective medication in order to stay well. In patients with mild UC, the disease may go away, in which case the treatment can be stopped. However, for most patients, a two-step approach is warranted: first, induce a remission with medication, and second, maintain that remission by continuing treatment.

For patients who achieve a remission with mesalamine therapy, the same treatment can be given to maintain the remission. Generally, steroids are not used long term because prolonged exposure can have severe consequences, and data do not support long-term use. The hydrocortisone enema is absorbed to some extent; the manufacturer has reported an absorption rate of 40%. In other words, if the enema contains 100 mg of hydrocortisone, then there is a systemic exposure of 40 mg, which is the equivalent of 10 mg of prednisone.

That being said, there are times when prolonged steroid use may be the only option. In some patients with distal UC, the disease can be very difficult to treat. The steroid absorption rate with the foam and suppository modalities is thought to be much lower than that associated with the enema, and there are some cases where long-term use of a steroid foam or suppository is the best treatment option.

G&H Is rectal therapy underused? If so, why?

RC Yes, and there are two main reasons. First, patients may not like to take this type of medication. Second, physicians tend not to prescribe it unless they are experienced in treating inflammatory bowel disease or had a mentor with this experience. In addition, prescribers may be reluctant to choose rectal therapy for their UC patients because these modalities can be embarrassing to discuss and/or because they assume that patients will not want to use them.

In reality, rectal therapies are extremely effective. I often reassure patients that I would not recommend this approach unless I was confident about its benefit. Rectal therapy is associated with very few side effects; in fact, these are the treatments of choice for pregnant women with distal UC because, aside from the hydrocortisone enema, there is very little systemic absorption and the effect on the lining of the bowel is maximized.

Many patients are suffering unnecessarily because of the underuse of rectal therapy. Importantly, when rectal therapy is given, it needs to be used continuously in the acute phase and then slowly tapered, if possible. I have seen many patients who reported excellent results from using an enema but suddenly stopped its use after just 2 weeks.

Unfortunately, the state of education when it comes to rectal therapy for UC is quite poor right now. There are few centers treating the numbers of patients needed in order for physicians to be trained effectively.

G&H Why is there a lack of education about these treatments?

RC Part of the reason is that industry-sponsored education is being eliminated around the country. Government and medical organizations are passing laws and rules against industry-funded programs but are not replacing them with other programs. Most doctors are practicing outside of a university setting. They rely on educational information from experts in various disease states, but these opportunities have been curtailed dramatically, resulting in a troubling decline in medical education.

This situation is unfortunate because doctors are capable of making their own decisions about what treatments to prescribe. They are aware of the potential for bias in industry-sponsored education. This factor is not always a bad thing. Many times, a new treatment is a genuine improvement over what was previously available, and can lead to savings in overall healthcare costs. For example, one of the common treatments for UC required up to 4 pills taken as often as 4 times per day. Now, similar medications are available with just 2–4 pills taken once a day. Patient compliance is far better with this new dosage, which leads to lower rates of relapse, surgery, and hospitalization. Unfortunately, this side of the story is conveniently "left out" of the ongoing debate in the halls of government, the policy committees of medical organizations, and the media.

G&H How does the lack of education lead to underuse of rectal therapy?

RC In my experience, doctors who use these topical therapies were trained at centers where there are experts in this treatment approach, and doctors who do not use them were trained at centers without experts in this area. Education is needed so that those without this knowledge can learn about rectal therapy and incorporate it into their practice.

G&H Are there any new rectal therapies on the horizon?

RC Yes. One of the challenges with mesalamine is that it can irritate the lining of the bowel. Not all patients experience this, but many do. Now, a sulfite-free mesalamine enema is available that is less irritating.

(Continued on page 316)

(Advances in IBD, continued from page 310)

In addition, there are ongoing efforts to make a mesalamine gel or foam, which are approved in Europe, available in this country. Gels and foams do not go as high up into the colon as enemas do, but these modalities can be easier to hold and patients may prefer them. Also, budesonide, a steroid that has far fewer systemic side effects than traditional agents such as prednisone and hydrocortisone, is available as a foam outside of the United States. This formulation could become available here in the future.

Finally, there are intriguing biological approaches currently under investigation. One agent, alicaforsen, was initially evaluated in intravenous, oral, and rectal formulations for the treatment of Crohn's disease and pouchitis. This therapy prevents cells from producing ICAM-1, an adhesion molecule that plays a key role in allowing white blood cells to pass through the lining of the bloodstream and in cell-cell interactions that lead to inflammation. There are some promising data on the use of this drug in left-sided colitis, though this approach is not yet close to regulatory approval.

Several other novel approaches with a variety of agents have been proposed or undertaken. Information on clinical trials can be obtained from the National Institutes of Health clinical trials website (http://clinicaltrials.gov). Other helpful websites include that of the Crohn's and Colitis Foundation of America (http://ccfa.org), the University of Chicago IBD Center (http://www.ibdcenter.uchicago.edu), and those of many pharmaceutical companies.

Suggested Reading

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