EMJ EUROPEAN MEDICAL JOURNAL

GASTROENTEROLOGY

EMJ Gastroenterol. 2019 Suppl 2 • europeanmedical-journal.com

INSIDE

Key Considerations in the Management of Inflammatory Bowel Disease: Interviews with Key Opinion Leaders

Supported by Fresenius Kabi

Key Considerations in the Management of Inflammatory Bowel Disease: Interviews with Key Opinion Leaders

Interviewees: Ian Arnott,[1] Manuel Barreiro-de Acosta,[2] Eduard Stange,[3] Antonio Tursi,[4] Frank Ruemmele[5]

1. Western General Hospital, Edinburgh, UK
2. Gastroenterology Department, Inflammatory Bowel Disease Unit, University Hospital of Santiago de Compostela, Santiago de Compostela, Spain
3. Internal Medicine I - Gastroenterology, Hepatology and Infectious diseases, University of Tübingen, Tübingen, Germany
4. Gastroenterology Service, Azienda Sanitaria Locale Barletta Andria Trani, Andria, Italy
5. Medical Faculty of the Université Paris Descartes, Sorbonne Paris Cité, Hôpital Necker Enfants Malades, Assistance Publique - Hôpitaux de Paris, Paris, France

Disclosure: Dr Arnott has received travel costs, editorial board fees, and speaking remuneration from Vifor Pharma and speaking remuneration from Takeda. Dr Barreiro-de Acosta has served as a speaker, consultant, and advisory member for or has received research funding from MSD, Abbvie, Hospira, Takeda, Janssen, Pfizer, Ferring, Faes Farma, Shire Pharmaceuticals, Dr Falk Pharma, Chiesi, Gebro Pharma, Otsuka Pharmaceuticals, and Tillotts Pharma. Prof Stange has served as a consultant for Amgen, CureVac, Falk, Janssen, Merck, and Takeda and has given lectures supported by Abbvie, Falk, and Ferring. Prof Antonio Tursi has declared no conflicts of interest. Prof Ruemmele has received speaker fees from Shering-Plough, Nestlé, Mead Johnson, Ferring, MSD, Johnson & Johnson, Centocor, AbbVie; serves as a board member for SAC:DEVELOP (Johnson & Johnson); and has been invited to MSD France, Nestlé Nutrition Institute, Nestlé Health Science, Danone, Mead Johnson, Takeda, Cellgene, Biogene, and Arkopharma.

Support: The publication of this feature interview was supported and reviewed by Fresenius SE & Co. KGaA.

Acknowledgements: Medical writing assistance was provided by James Coker, European Medical Journal, London, UK.

Disclaimer: The opinions expressed in this article belong solely to the named interviewees.

Citation: EMJ Gastroenterol. 2019;8[Suppl 2]:2-11.

Summary

Treatment advances in inflammatory bowel disease (IBD), as well as the development of new biomarkers and technologies to enhance monitoring of the disease and response to treatment, are providing new possibilities in the management of ulcerative colitis (UC) and Crohn's disease (CD). Awareness of the impact of IBD on patients beyond clinical endpoints is also increasing, including the prevalence and extent of extra-intestinal manifestations, psychological issues, and nutritional deficiencies. This means that the role of physicians in IBD is more important than ever, with continuous investigation required for every patient and a wealth of considerations to take into account when deciding on the most suitable treatment approach to undertake.

For this article, the European Medical Journal conducted a series of interviews with five key opinion leaders from across Europe, each with a wealth of experience and expertise in managing IBD, to gain their perspectives on a range of topics in this area. From the UK, we spoke to Dr Ian Arnott, Consultant Gastroenterologist, Edinburgh IBD Unit, Western General Hospital, Edinburgh, UK; from Spain, Dr Manuel Barreiro-de Acosta, Gastroenterology Department, Inflammatory Bowel Disease Unit, University Hospital of Santiago de Compostela, Santiago de Compostela, Spain; from Germany, Prof Eduard Stange, Internal Medicine I - Gastroenterology, Hepatology and Infectious diseases, University of Tübingen, Tübingen, Germany; from Italy, Prof Antonio Tursi, Gastroenterology Service, Azienda Sanitaria Locale Barletta Andria Trani, Andria, Italy; and from France, Prof Frank Ruemmele, Professor of Paediatrics, Medical Faculty of the Université Sorbonne, Hôpital Necker Enfants Malades, Assistance Publique - Hôpitaux de Paris, Paris, France.

The article begins by discussing monitoring of treatment response and detection of extra-intestinal manifestations, followed by considerations in making treatment decisions before outlining novel therapy options in both UC and CD. Optimal use of anti-TNF therapy, the impact and challenge of psychological issues in IBD, and nutrition and diet in this disease are also explored.

AIMS OF TREATMENT

Interviewees: Prof Frank Ruemmele (FRA), Prof Antonio Tursi (ITA)

A paradigm shift has occurred in IBD management, whereby reducing inflammation and mucosal healing has become a the key endpoint that clinicians strive to meet. This strategic change in IBD management has been experienced first-hand by Prof Ruemmele during his career. "When I was training, the main aim was to control clinical symptoms and we were told not to treat inflammatory markers in otherwise well patients, but that approach is completely wrong," he commented. "The paradigm has changed so that we not only treat symptoms but treat inflammation to heal the lesions. So the gold standard today is mucosal healing, meaning patients who have inflammation in the gut and in whom the inflammatory lesions can't be completely healed will have less favourable evolution compared to patients who do have complete mucosal healing."

This type of approach requires continuous monitoring of the disease in patients to understand disease severity and treatment response. This is something that Prof Tursi attested to: "The targets of treatment in IBD have changed significantly in recent years, moving from symptoms control to disease control," he said. "This means that the doctor's attention has moved from the simple control of abdominal pain or diarrhoea, to assessing how to control the disease by endoscopy, laboratory, and radiology methods. This approach requires a significant effort by doctors in daily practice, but it leads to better patient management."

DISEASE MONITORING

Interviewees: Prof Eduard Stange (DEU), Dr Ian Arnott (UK), Prof Antonio Tursi (ITA), Dr Manuel Barreiro-de Acosta (ESP)

A 'top-down' approach, whereby the strongest treatments available are used in IBD patients at the earliest possible stage, is advocated by some but is not a method that Prof Stange adheres to: "The downside is that you are treating a lot of patients who don't need it: about 40–50% of IBD patients have a rather uncomplicated course and don't need these drugs," he explained. In an era when health services are subject to increasing economic constraints, clinicians should also be mindful of the financial costs of using the most expensive and powerful drugs in the early stages of disease onset.

Prof Stange instead emphasised the importance of regularly analysing markers such as inflammation levels, before reacting quickly with an appropriate treatment if the condition changes, and reacting again if that treatment does not have the desired effect. Concurring with this view, Dr Arnott added:

"Our decisions are increasingly going to be driven by objective markers and numbers."

While there is some exciting research emerging with regard to the use of genetics to predict outcomes of specific IBD treatments, this is not currently at a point where it can be applied to clinical practice. "There's lots of tests we can do to individualise treatment but we're not at the stage yet of actually assessing people's DNA and it making a big change to treatment," said Dr Arnott.

Advances have, however, occurred in the quality of surveillance options available to clinicians. Endoscopy, particularly colonoscopy, has been recognised for some time as vital in assessing IBD in individual patients. The techniques have also continuously improved in quality over the years, for instance with features such as high definition starting to come to the forefront: "I think colonoscopy remains the gold standard for assessing inflammation," confirmed Dr Arnott. The Edinburgh-based clinician also expressed his expectation that the quality of colonoscopies will continue to improve in the future, including the potential for artificial intelligence to play a significant role. Dr Barreiro-de Acosta added: "Endoscopy is compulsory for the follow-up of patients, especially in UC, in order to see how they respond to a treatment."

Nevertheless, frequent use of colonoscopies is expensive for health systems and can be difficult to access for clinicians on a regular basis. Another consideration for clinicians in regard to this method is that it is invasive and unpopular with many patients. As a result, there has been a substantial increase in the use of noninvasive monitoring over recent years. The most impactful of these methods is faecal calprotectin, which enables clinicians to effectively monitor patients on a regular basis. Prof Tursi commented: "The best method is colonoscopy, because it enables the monitoring of healing of lesions. But since we cannot advise a colonoscopy every 2–3 months just to monitor endoscopic lesions, we can effectively use faecal calprotectin as a tool to monitor therapeutic response. Faecal calprotectin has been shown to be effective in monitoring clinical response and mucosal healing."

This can also be observed in Dr Arnott's own clinical practice: "It's interesting that, as time goes on, you really value faecal calprotectin in supporting your treatment decisions," he stated. "Back when I was training, somebody would come in with symptoms and you would do a few blood tests and say 'right we'll give a treatment'. And sometimes that treatment would work and sometimes it wouldn't. And in a number of those people, the treatment wouldn't work because the symptoms were not driven by inflammation."

This is also the experience of Dr Barreiro-de Acosta in regard to monitoring loss of response: "In our group, we have observed that in patients with elevated faecal calprotectin levels twice in 2 months, they are going to have loss of response to the biological treatment," he said.

EXTRA-INTESTINAL MANIFESTATIONS

Interviewees: Dr Manuel Barreiro-de Acosta (ESP), Dr Ian Arnott (UK)

As well as closely analysing severity of disease and response to treatment, IBD specialists must also closely assess patients for extra-intestinal manifestations (EiM), a regular occurrence in IBD which should form part of an overall disease management strategy. EIM are thought to affect approximately 6–47% of adult IBD patients and around 25–29% of paediatric IBD patients.[1]

"In our department we have found that, independent of the disease activity, if a patient has an EiM they have poorer quality of life, emotionally and fiscally," stated Dr Barreiro-de Acosta. Such an impact on quality of life is also capable of contributing to serious psychological problems for patients, a topic analysed later in this article.

In Dr Arnott's experience, the most common EiM of IBD are joint pain and skin problems, followed by ocular and liver issues, emphasising the crossover IBD has with many other therapeutic areas. Dr Arnott emphasised how it is incumbent upon physicians to regularly address the issue of EiM with patients. "Clinicians need to make patients aware that they can happen and need to specially ask people how they feel as part of their assessment of a patient's response to treatment," he noted.

A widely discussed issue is that the duration of the consultations clinicians have with patients is

often extremely limited. In this context, physicians must find novel ways to make the short time they have with patients as productive as possible. In Dr Arnott's clinical practice, IBD patients often fill out questionnaires describing their current symptoms and are also encouraged to write down the areas they are especially keen to discuss prior to the consultation. "It's good to get them into a mindset of thinking about what they want to get out of the meeting, so it's just making sure that people get the opportunity to discuss what they want to talk about," he added.

IBD also significantly increases the risk of colorectal cancer, which is something clinicians need to be particularly mindful of. Indeed, it is believed to account for 10–15% of all-cause mortality in IBD patients.[2] Therefore, extensive monitoring is required to check for this, in particular, regular colonoscopies. "Colonoscopy with dye spray is the current standard of care for assessing the risk of colon cancer," said Dr Arnott. "This may change in the near future to HD colonoscopy alone or for this technique to be supported by molecular markers or even faecal tests."

SELECTING THE APPROPRIATE THERAPEUTIC APPROACH

Interviewees: Dr Manuel Barreiro-de Acosta (ESP), Prof Frank Ruemmele (FRA)

Selecting the best strategy for each patient depends on numerous factors, not only limited to clinical endpoints. Personal characteristics and also preferences of the patients are particularly vital in an age when patient centricity is a key treatment goal.

The patient's age should be taken into account, since the disease manifests differently across different age groups. In particular, elderly patients have their own distinct set of considerations. "These patients have different problems; they normally have more comorbidities than other patients that we have, and most will need help with their other pathologies," confirmed Dr Barreiro-de Acosta. "The other thing is that these patients normally have more infections so we may have to treat with monotherapy or if we are looking for a biological therapy, we need one with a lower risk of infections."

Prof Ruemmele, a paediatric IBD specialist, outlined the general ways in which CD manifests and should be managed in paediatric patients. "In the majority of paediatric patients, the disease is more active, with a more extensive location compared to adult-onset CD. This means the disease is more inflammatory, which necessitates a faster use of immunosuppressants and biologics," he explained. "The second difference relates to growth retardation, which is very common in paediatric CD. So we avoid using steroids if possible because they do have a negative effect on growth."

EVOLVING TREATMENT LANDSCAPE

Interviewees: Dr Ian Arnott (UK), Prof Antonio Tursi (ITA)

The treatment landscape is evolving quickly, and this is providing new prospects for individualising care. "Since I became a consultant 15 years ago, the therapies have changed immeasurably. And our whole attitude and approach to the disease has changed completely," outlined Dr Arnott. "It's exciting times. There are lots of new treatments and I think as time goes on we're learning about how to use these treatments most effectively. And then there's other treatment options that are emerging, for example, for a small number of people, stem cell transplant may be used and faecal transplantation is also an exciting non-drug-based possibility. Again, we're learning about the best way of using these treatments."

As alluded to previously, a key aim of IBD therapy is the reduction of inflammation levels. Dr Arnott stated: "The paradigm has changed completely where we're aiming for mucosal healing and the absence of mucosal inflammation; so really trying to suppress the inflammation." As well as anti-TNF and antibiotics, immunosuppressants such as azathioprine, methotrexate, and ciclosporin are another common form of therapy used in IBD.

In the view of Prof Tursi, there is an opportunity for immunosuppressants to be used more often than is currently the case: "Physicians are still afraid about the risk of using these therapies, in particular because of the risk of neoplasia," he said. "Although the literature has clearly identified who the patients at risk are and who are not, immunosuppressors are still only used in patients

with steroid-dependent or resistant disease. However, they should be taken into consideration also in patients with frequent recurrences of the disease."

Prof Tursi opined that the most effective therapies for achieving mucosal healing induction are monoclonal antibodies. "They should be used more frequently, especially in patients with severe disease at onset or in patients with frequent recurrences. Economic considerations have limited their use until now but the wider availability of biosimilars could permit their use more frequently," he elucidated.

Ulcerative Colitis

Interviewees: Prof Eduard Stange (DEU), Dr Ian Arnott (UK)

In UC, there have been some particularly exciting advances in treatment in recent times. Only last year, the first JAK inhibitor, tofacitinib, was approved by the U.S. Food and Drug Administration (FDA), providing an alternative form of therapy for clinicians to consider. "Overall it's a major advance because there are no antibodies to this drug because it's not a monoclonal antibody, it's just a pill," said Prof Stange. "There have been some cases of pulmonary embolism and heart failure, but that is very rare and can be circumvented by giving a lower dose."

Another intriguing therapy approach in UC is to boost the patient's mucosal barrier by administering antimicrobial peptides. This form of therapy aims to prevent the inflammation occurring, as it is a secondary response against bacterial invasion, by increasing the patient's bacterial diversity, making it a particularly proactive approach to care. In Prof Stange's view, this type of approach in UC will become increasingly important in the future, with data suggesting it could be effective in around 25% of those with the condition. "A way to go is to change the microbiota and thereby change the defence system through methods like faecal transfer, and that is the right direction to go," he stated. "It's not something we would use in every patient and it doesn't work in CD, but there's a lot of future in that."

Likewise, Dr Arnott believes that in time, methods that use the body's microbiota in this way will become increasingly sophisticated. "As we know more, treatment will go increasingly towards targeting the microbiome. We're not there yet, but therapeutic modulation of the microbiome is something that will come," he outlined.

Crohn's Disease

Interviewees: Prof Eduard Stange (DEU), Prof Frank Ruemmele (FRA), Dr Ian Arnott (UK)

In CD, vedolizumab has become a viable option for patients in whom other therapies, such as anti-TNF, have failed. "Vedolizumab does not work as rapidly as anti-TNF, but it's relatively stable over time if you keep infusing the drug," said Prof Stange. "And it's more or less free of side effects which is good because with anti-TNF you have a significant risk of severe opportunistic infections."

Prof Ruemmele is particularly excited by the potential for clinicians to use exclusion diets as a means of treating and even preventing CD in the future. "The exclusion of potentially proinflammatory or harmful food ingredients might be a way to treat our patients," he elucidated. "Food is one of the triggers of inflammation and that is why I like the idea of excluding inflammatory food ingredients as a treatment."

He cited two studies that have recently been published on this topic. One by Levine et al.,[3] showed that a CD exclusion diet plus partial enteral nutrition induces remission in paediatric CD patients in a manner similar to exclusive enteral nutrition alone. However, exclusive enteral nutrition is significantly less well accepted due to its exclusivity principle (no food other than a sole liquid milk-based product). Another, by Svolos et al.,[4] demonstrated that an individualised food-based diet called CD-TREAT with a similar composition to exclusive enteral nutrition is potentially effective in active CD patients. Prof Ruemmele added: "This is one of my dreams: to prevent disease onset in high-risk patients." A more detailed analysis of nutritional and dietary issues in IBD will take place later on in this article.[5]

Surgery is another option in CD in certain circumstances. "It should be considered when there is obstruction, which is usually scar tissue, meaning it is not amenable to medical therapy. And then obviously it is an option when there is failure of medical therapy," said Dr Arnott.

Prof Stange added: "In those patients who have had previous infections, you should consider the surgeon very seriously and consider whether that would be a better option because surgery, especially limited surgery, like ileocecal resection, has been shown to be equivalent to the best medications that we have."

ANTI-TNF DRUGS

Interviewees: Prof Eduard Stange (DEU), Dr Manuel Barreiro-de Acosta (ESP), Prof Antonio Tursi (ITA)

A treatment modality which has had the most transformative impact on treating IBD in recent times is anti-TNF therapy, which has become a mainstay of treatment in IBD. Indeed, it is often a first-line treatment for moderate-to-severe UC and CD.[6] There is, however, much for clinicians to take into account when deciding the circumstances under which these drugs are appropriate for use in IBD patients. "Anti-TNF have turned the system: they are effective in some patients, both initially and long-term, but the big downside is that there is loss of response over time which happens in just about every patient sooner or later," stated Prof Stange.

Common contraindications associated with anti-TNF include the risk of infections and cardiological and neurological problems. There remains some debate about the extent to which this form of therapy should be used, with careful analysis of patients required both before these drugs are prescribed and during the course of treatment. "With anti-TNF, there are tight controls of their use regarding latent TB, prior immunisation, and hepatitis B and C etc.," explained Prof Stange. "It's now becoming more common to control serum levels of these drugs because it helps you understand whether the levels are sufficient or not and whether the patient is developing antibodies to the drug which will neutralise the therapy."

In Dr Barreiro-de Acosta's view, there are certain patients in whom anti-TNF should be avoided. "In my opinion, patients who have a history of severe and continuous infections, or in those who have had a cancer in the last 5 years, anti-TNF are not the drugs we should use because we now have safer drugs for these kinds of patients."

For Prof Stange, anti-TNF should, generally, not be the first line of therapy. "The best indication in my view are those relatively rare patients who are steroid nonresponsive," he outlined.

In UC, anti-TNF drugs, such as infliximab and cyclosporine, are used as a rescue therapy when other treatments have failed. When considering their use, however, physicians must be sure the safety and health of the patient is not compromised. Prof Tursi stated: "Close surveillance of the clinical picture is the main factor when considering the use of rescue therapy in UC. The Truelove criteria are widely used in defining an attack of severe UC and has to be used also when using infliximab or cyclosporine as a rescue therapy in those patients."

A preponderance of research has improved knowledge of the relative efficacy of the different anti-TNF drugs on the market for both UC and CD, and Prof Stange provided his perspective on this topic: "In UC, you have to be careful because there is a difference which is not the case in CD," he said. "In UC, adalimumab is inferior to infliximab and has also been shown to be inferior to vedolizumab so adalimumab is not an ideal drug for UC. In CD, it's totally equivalent to infliximab as far as we know, and there we can use them interchangeably."

Frequent checking of biomarkers of response to anti-TNF therapy is essential for physicians to ascertain whether there is any loss of response to anti-TNF therapy. "The markers that I trust are C-reactive protein (CRP) and calprotectin in CD, and calprotectin in UC," said Prof Stange. "CRP is not a good marker for UC because in many patients it's completely normal. So that is what I tend to look at in those patients. If calprotectin, in particular, is going up, that is an indicator of high risk of early relapse and you should respond early."

Measuring trough levels are another way of assessing the efficacy of an anti-TNF therapy, a method strongly advocated by Dr Barreiro-de Acosta. "In my opinion, it is very important to have the trough levels because it will help to see if you're going to go with an anti-TNF or swap with another mechanism of action," he outlined.

Making a decision about whether to reintroduce an anti-TNF following a drug holiday is another pertinent topic in IBD management. "You must

look at antibodies here; if you have antibodies to a drug that you have given previously, then you have a high risk of complications, even shock," said Prof Stange. "In this situation you should refrain from this particular drug and switch. If there was a good response, for example to infliximab, and the patient during his drug holiday develops an antibody to infliximab, I would switch to adalimumab because there is no cross-response there and it's safer."

In general, Prof Tursi believes the opportunities afforded by new biological drugs should be used by physicians on a more regular basis: "Unfortunately there is no simple way of managing IBD patients and the treatment remains individual, based on clinical, endoscopic, and radiology characteristics," he said. "Generally speaking, my advice is to avoid recurrent use of steroids, and try to use biologics more than we have been doing so far. The current availability of infliximab and adalimumab biosimilars, which are much cheaper, will help doctors in making this choice."

PSYCHOLOGICAL MALAISE

Interviewees: Dr Manuel Barreiro-de Acosta (ESP), Prof Frank Ruemmele (FRA)

Conversations about the extent to which psychological issues affect patients with IBD, and how they can impact treatment, are gaining traction. A study by Byrne et al.[7] found that 30.3% of IBD patients experience depression or anxiety. In the view of Dr Barreiro-de Acosta, it is critical that doctors consider psychology as essentially part of the disease itself, and therefore regularly assessing a patient's psychological state should become a normal part of IBD management.

"We have seen that if a patient has psychological issues, such as anxiety and depression, they are going to have worse quality of life," he explained. "This is independent of disease activity so I believe we need another step beyond biological remission: we also need psychological remission." He added: "We need to try and make doctors understand that even patients whose bowel has healed and calprotectin is good, they may have other problems which require further investigation."

Now that access to information about health is vast, and often from unverified sources, the psychological aspect of IBD is becoming exacerbated further. "Patients will be thinking that there is going to be a big change in their life and now with social media and the internet, they will read many things," commented Dr Barreiro-de Acosta.

Psychological conditions, such as depression, directly affect efficacy of treatment, further emphasising the need for clinicians to pay close attention to this area. "IBD patients with depression are going to respond worse to the medication, and will be less tolerant and adherent to treatment, which is a real problem," elucidated Dr Barreiro-de Acosta.

Other psychological disorders that Dr Barreiro-de Acosta and his team frequently observe in IBD patients include chronic fatigue, particularly in those undergoing anti-TNF therapy: "This is very difficult to detect for us, because CRP levels and calprotectin are fine but have chronic fatigue," he said. Another is the personality disorder alexithymia, which makes it difficult for patients to come to terms and cope with having a chronic disease.

On the part of physicians, checking for signs of psychological problems throughout their relationship with all IBD patients, beginning from the point of diagnosis, is essential. There are certain situations in which patients are particularly susceptible which physicians should be mindful of: these include at diagnosis, when the patient is forced to come to terms with the fact they will be living with a chronic disease and when they are going to start with a stronger course of therapy, such as surgery.

If surgery is required, physicians must be very conscious that this is a situation in which there is an especially high risk of psychological issues taking shape. Surgery has the potential to seriously impact a patient's quality of life, such as relationships. Dr Barreiro-de Acosta picked out the example of ostomies as having a particularly profound psychological impact on paediatric and young adult patients.

"In our consultations, if we detect signs of depression, anxiety, or stress, we can arrange with them to meet a psychologist. And if we see that the patient is in remission but has problems and cannot normalise their quality of life, it may be because of a psychological issue

which we can detect," stated Dr Barreiro-de Acosta. Prof Ruemmele added: "There is a need for psychological support for all patients, but it depends on the individual situation if long-term psychological support is necessary or not."

Consideration of each patient's characteristics must also be made when assessing those particularly at risk of psychological issues. These include age and gender. In Prof Ruemmele's experience in the paediatric setting, there is no doubt that clinicians have to be acutely aware of the psychological impact a diagnosis of IBD can have. "Facing a lifelong disease is a major challenge for anybody, independent of age. Teenage adolescents, who are the majority of patients at our clinic, are in an unstable phase of their life. Having a severe, chronic disease during that period can translate to problems with self-esteem, acceptance of the disease, and adherence to medication," he explained. Studies involving Dr Barreiro-de Acosta have also demonstrated that the risk of psychological conditions such as anxiety and depression is higher in female patients, a factor clinicians must also be mindful of.

As well as detecting psychological problems throughout IBD management, consultations are also critical for preventing psychological issues emerging in the first place. It is vital that honest and accurate information is provided to patients to give them a realistic picture of what they may experience during treatment, as well as counter the danger of misinformation through unverified sources, to ensure the most appropriate treatment decision is reached. "In times when a patient is going to start with a stronger treatment, it is very important they know the potential adverse events so they can analyse whether it's best to take the risk," said Dr Barreiro-de Acosta. "And when a patient is going to have surgery, it is important for them understand that it's not necessarily going to alter their quality of life."

In the paediatric setting, Prof Ruemmele stressed the importance of having specialist IBD clinics that are geared towards this patient group. "You need healthcare professionals who are familiar with this sort of age to respond to their non-compliance and still be able to listen to them and make them listen to you, which is a big challenge," he said.

NUTRITIONAL CONSIDERATIONS

Interviewees: Prof Antonio Tursi (ITA), Prof Frank Ruemmele (FRA)

Another key area for clinicians to consider during the management of an IBD patient is the potential for malnutrition and nutritional deficiencies to occur. For instance, it has been estimated that between 20% and 85% of IBD patients have nutritional deficiencies.[8] Monitoring for signs that these may be taking place is another necessary step in IBD management.

To do so effectively, physicians should firstly be aware of notable differences between UC and CD in this regard. "Nutritional deficiencies are quite frequent in IBD, and occur more frequently in CD patients," explained Prof Tursi. "A complete nutritional status assessment should be advisable in IBD patients at least at onset of the disease, because it could be predictive of the outcome of the disease. In regard to nutritional monitoring, UC patients have to be monitored mainly about iron pattern and proteins, while CD patients have to be monitored also for macro and micronutrient deficiencies." Prof Ruemmele added: "It depends on disease location whether patients have major albumin and iron deficiency; this is something that is monitored on a routine basis through vitamin D levels."

There are also notable differences in nutritional deficiencies between paediatric and adult IBD patient populations. An important factor to consider is that the paediatric patients are in a state of physical development that can be stunted by IBD. "Energy requirements change depending on the growth period and age of the child and that is a major issue since inflammation during that period will reduce growth and have potential life-long consequences for the patients. So, it's more about the energy requirement and providing optimal energy support," said Prof Ruemmele.

Therefore, a continuous analysis is essential in paediatric patients in particular: "In the paediatric field of IBD we use nutritional therapy routinely in all patients; we follow the height and weight of all our patients on a growth chart, which differs from adult care," explained Prof Ruemmele.

To successfully manage weight loss and malnutrition in IBD patients, Prof Tursi is clear that gaining control of the disease and putting it into, and maintaining, remission is the most effective means of achieving this. However, in patients in whom there isn't this control, there are options for physicians to build up nutrition levels. "If this endpoint cannot be reached, nutritional support and micronutrient supplementation is advisable to fight malnutrition," he noted.

A well-established method of doing this is enteral nutrition: the administration of a nutritionally complete formula via the gastrointestinal tract. "Enteral nutrition is already advised by current guidelines in managing paediatric CD," said Prof Tursi. "And specific advice on how and what to eat during the active phase of the disease can be helpful for patients, for example, avoiding fibres and spices."

As has been evident earlier in the article, Prof Ruemmele has substantial interest in the potential of exclusion diets to become an established form of treatment for all IBD patients. He emphasised that enteral nutrition can be a useful technique in treating in all IBD patients: "Exclusive enteral nutrition is a liquid-only diet, so no food, just the milk product. This is efficacious in reducing inflammation and we use it as an induction therapy," he outlined.

Partial enteral nutrition, however, can be efficacious too, either for patients who have weight loss or nutritional deficiencies, or in patients who require something extra on top of their current medication to reduce inflammation: "Partial enteral nutrition does not have this potent anti-inflammatory effect. We use it if we already have a medication that is working well but needs something extra to reduce inflammation. So instead of combining several immunosuppressants, this is another option and we use it frequently in patients in the paediatric field," explained Prof Ruemmele.

CONCLUSION

What is evident from the insights of the five key opinion leaders is that the current and potential future treatment options in IBD places us in the midst of a very exciting period in the field. The plethora of available treatment options provides the opportunity to design treatment programmes that are increasingly tailored to individual needs and preferences. Other emerging therapies like exclusion diets and using a patient's microbiota have the potential for effective, and critically, less expensive approaches to care too. New insights and appreciation of the side effects of IBD, such as EiM, as well as psychological and nutritional issues, provide the basis for enhancing quality of life in patients. All of this means the role of physicians in IBD is broadening to far beyond a traditional approach of symptoms control to one in which individual patients are continuously monitored in a plethora of ways and treated according to their specific needs.

Biographies

Dr Ian Arnott

Consultant Gastroenterologist, Edinburgh IBD Unit, Western General Hospital, Edinburgh, UK

Dr Arnott is a consultant gastroenterologist and an Honorary Senior Lecturer at the University of Edinburgh. His clinical practice focusses on the assessment and treatment of patients with IBD. The Edinburgh IBD Unit is a tertiary referral centre for IBD with broad experience of currently available therapies. There is also an extensive programme of clinical research and clinical trials. Other positions Dr Arnott holds include Chair of the British Society of Gastroenterology (BSG) IBD section and lead of the UK IBD Audit for 10 years. He has published widely on many aspects of IBD.

Dr Manuel Barreiro-de Acosta

Gastroenterology Department, Inflammatory Bowel Disease Unit, University Hospital Complex of Santiago de Compostela, Santiago de Compostela, Spain

Dr Barreiro-de Acosta is a clinician focussing exclusively on IBD, working in his current department since 2002. He also has published extensive research in IBD, with a particular interest in subjects such as genetics, psychological issues, and anti-TNF therapy response. He has participated as an author in several European Crohn's and Colitis Organization (ECCO) Guidelines.

Prof Eduard Stange

Internal Medicine I - Gastroenterology, Hepatology and Infectious Diseases, University of Tübingen, Tübingen, Germany

Prof Stange has been a prominent figure in the field of IBD for many years and was formerly chief physician at the Robert Bosch Hospital in Stuttgart. As well as his extensive clinical, research, and teaching work, he has also held the position of Head of the Guideline Conferences of the German Society for Digestive and Metabolic Disorders (DGVS) and the European Crohn's and Colitis Organization (ECCO) on Inflammatory Bowel Disease.

Prof Antonio Tursi

Gastroenterology Service, Azienda Sanitaria Locale Barletta Andria Trani, Andria, Italy

A renowned clinical gastroenterologist from Italy, Prof Tursi is also very active in the research space, regularly publishing on the topics of diverticular disease, inflammation in the gut, IBD treatment efficacy, and nutritional deficiencies in IBD.

Prof Frank Ruemmele

Professor of Paediatrics, Medical Faculty of the Université Sorbonne, Hôpital Necker Enfants Malades, APHP, Paris, France.

An expert in paediatric IBD, Prof Ruemmele is also in charge of the Pediatric Intestinal Immunopathology Program and Head of the Pediatric Inflammatory Bowel Diseases Clinic at Necker Enfants Malades Hospital. His research interests include understanding inflammatory processes leading to intestinal immune pathologies such as IBD and autoimmune diseases, as well as genetically determined immune gastrointestinal pathologies.

References

1. Chams S et al. Inflammatory bowel disease: Looking beyond the tract. Int J Immunopathol Pharmacol. 2019;33.
2. Stidham RW, Higgins PDR. Colorectal cancer in inflammatory bowel disease. Clin Colon Rectal Surg. 2018;31(3):168-78.
3. Levine A et al. Crohn's disease exclusion diet plus partial enteral nutrition induces sustained remission in a randomized controlled trial. Gastroenterology. 2019;157(2):440-50.
4. Svolos V et al. Treatment of active crohn's disease with an ordinary food-based diet that replicates exclusive enteral nutrition. 2019;156(5):1354-67.
5. Ruemmele FM. Role of diet in inflammatory bowel disease. Ann Nutr Metab. 2016;68(Suppl 1):33-41.
6. Cohen BL, Sachar DB. Update on anti-tumor necrosis factor agents and other new drugs for inflammatory bowel disease. BMJ. 2017;357:j2505.
7. Byrne G et al. Prevalence of anxiety and depression in patients with inflammatory bowel disease. Can J Gastroenterol Hepatol. 2017;2017:6496727.
8. Prince A et al. Nutritional problems in inflammatory bowel disease: The patient perspective. 2011;5(5):443-50.