

RAPID COMMUNICATION

Quality of care for patients with inflammatory bowel disease in East China

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Abstract

AIM: To investigate the quality of care for a hospital based-cohort of patients with inflammatory bowel disease (IBD) from East China according to the current practice guidelines.

METHODS: A retrospective review was conducted, involving 177 patients with IBD admitted to Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University between June 2000 and June 2006. Data regarding demographic and clinical characteristics as well as medical therapy including use of oral aminosalicylates, topical therapy, corticosteroid agents, immunomodulatory agents (such as azathioprine) at admission and outpatient clinic visit were analyzed.

RESULTS: A total of 177 eligible patients were evaluated in this study, including 71 patients with Crohn's disease (CD) and 106 with ulcerative colitis (UC). All were the Han nationality Chinese with active disease at baseline. All the 106 patients with ulcerative colitis received optimal doses of aminosalicylate while 27 of 68 (39.7%) patients with ileal or colonic CD received the suboptimal doses of aminosalicylate. The incidence of suboptimal dose of aminosalicylate was significantly higher in CD patients with small intestine involvement only (52.8% vs 25.0%, $P = 0.019$). Thirty-one (54.4%) patients with active distal or left-sided ulcerative colitis received topical therapy, and 27.8% of patients suffering from severe inflammatory bowel disease did not receive oral or intravenous steroid therapy. Among the 51 patients for whom thiopurine was indicated, only 10 (19.6%)

received immunomodulatory agents, and more than half of the 8 patients received a suboptimal dose of azathiopurine with no attempt to increase its dosage.

CONCLUSION: The quality of care for IBD patients can be further improved. A suboptimal dose of aminosalicylate is used in treatment of patients with CD, especially in those with small intestine involved only. Topical mesalazine is inadequately used in patients with distal or left-sided colitis. Oral or intravenous steroid therapy is not used in some patients with severe IBD. Use of immunomodulatory medication is limited. Larger prospective studies are needed to investigate the quality of care for patients with IBD to establish our own evidence-based guidelines.

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Key words: Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Quality of care; Guidelines

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INTRODUCTION

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a chronic disorder of the gastrointestinal tract. The prevalence of IBD is about 1.0/1000 in Western countries^[1]. No large scale epidemiological investigation is available on the incidence and prevalence of IBD in China so far, but the diagnosed IBD in China has increased obviously in the past ten years^[2].

A number of national and international practice guidelines for management of inflammatory bowel disease are available^[3-5]. However, the essentials in a step-up treatment have not changed significantly. These practice guidelines are means of bringing evidence-based medicine into full play to improve IBD patient care. However, such

guidelines can improve the care of IBD patients only when they succeed in moving the actual clinical practice closer to the recommended practice.

The Sir Run Run Shaw Hospital is a teaching hospital affiliated to Zhejiang University, China. Together with 12 other large hospitals and numerous smaller district hospitals, it provides health care to 48 million people living in Zhejiang Province of East China. Our group has carried out a retrospective study to assess the demographic and clinical characteristics of IBD in Chinese patients^[2]. This study was to investigate the impact of such guidelines and the quality of care for a hospital based cohort of patients with IBD from East China.

MATERIALS AND METHODS

Subjects

IBD patients admitted to Sir Run Run Shaw Hospital, College of Medicine, Zhejiang University, between June 2000 and June 2006, were consecutively enrolled in this study. The diagnosis of IBD was confirmed by the criteria established by Chinese Society of Gastroenterology^[6] in 2000 and the guidelines issued by the Clinical Services Committee of the British Society of Gastroenterology (BSG)^[3] in 2004. The patients not under the care of a gastroenterologist were excluded.

Data collection

A retrospective review was performed. Clinical data on demographic information, clinical characteristics of IBD patients, as well as endoscopic, radiologic, surgical and pathological records, confirmed diagnoses, duration and severity of disease, medical therapy, were collected from the inpatient and follow-up clinic visit records and input into an IBD database. Medical therapy included use of oral aminosalicylate, topical therapy, corticosteroid agents, and use of immunomodulatory agents at admission and outpatient clinic visit.

Statistical analysis

Variables were expressed as mean, while categorical data such as proportion of patients receiving particular therapies and dose of medications were expressed as percentage. Association of patient gender, age, location and severity of disease with suboptimal therapy was analyzed by χ^2 test. $P < 0.05$ was considered statistically significant. All statistical analyses were carried out with the SPSS v. 13.0.

RESULTS

Patient characteristics

A total of 177 eligible patients were evaluated in this study, including 71 patients with CD and 106 with UC. All the patients were the Han nationality Chinese. Disease activity was assessed using the Harvey-Bradshaw index (HBI) for CD and the Sutherland index for UC. Active disease was defined as a HBI value ≥ 5 or a Sutherland index ≥ 3 . All the eligible patients had active disease at admission. Severity was broadly divided into mild, moderate or severe according to the Truelove & Witts' criteria for UC and the

Table 1 Characteristics of patients with CD or UC

Characteristics	CD (n = 71)	UC (n = 106)
Sex (male/female)	41/30	56/50
Age (yr) [mean (range)]	35 (13-70)	45 (15-80)
Disease duration (yr) [mean (range)]	5.3 (0.5-14)	5.8 (0.5-23)
Smoker/non-smoker	17/54	26/80
Disease severity		
Mild	13	53
Moderate	38	37
Severe	20	16
Previous surgery	34	4

Table 2 Distribution of CD and UC

Disease location	n
Crohn's disease (71)	
Small intestine	37
Colon	6
Ileocolon	27
Upper gastrointestinal	1
Ulcerative colitis (106)	
Distal colitis	35
Left-sided colitis	22
Extensive colitis	47
Missing information	2

criteria established by Chinese Society of Gastroenterology for CD^[6]. Mild CD was defined when the patient had no fever, abdominal tenderness, abdominal mass and obstruction, while severe CD was defined when the patient had persistent high fever, weight loss, nausea, vomiting, abdominal pain, diarrhea, anemia and complications. The characteristics of the patients and the information about the location of disease are given in Tables 1 and 2, respectively. Twenty-one gastroenterologists were involved in the treatment of the patients.

Medical therapy

Medical therapy for the patients including use of aminosalicylate, topical therapy, corticosteroids and immunomodulatory agents was analyzed, and the results are listed in Table 3.

Overall, 175 of 177 patients received oral aminosalicylate. Among them, 145 received mesalazine and 30 received sulphasalazine (SASP) (69/71 with CD, 106/106 with UC). The remaining 2 patients who did not receive oral aminosalicylate, had a history of adverse events, and therefore, received oral corticosteroids. A suboptimal dose of mesalazine or SASP was defined as a dose less than 4.0 g/d in patients with ileal or colonic CD or a dose less than 3.0 g/d in patients with UC. Among the 69 CD patients who received aminosalicylate, one had stomach involvement. Among the remaining 68 CD patients, 27 (39.7%) had a suboptimal dose. In contrast, all the 106 patients with UC were treated with an optimal dose. A further analysis was performed to elucidate factors associated with suboptimal doses of such medications. The variables were gender, age, location of disease, and severity of disease. It revealed no association other than a significantly higher incidence of

Table 3 Suboptimal dose used in treatment of CD and UC

Clinical parameters	Proportion (%)
Suboptimal dose of aminosaliclylate	
Crohn's disease	27/68 (39.7)
Ulcerative colitis	0/106 (0.00)
Failure to use topical therapy	26/57 (45.6)
Failure to use corticosteroid	10/36 (27.8)
Failure to use immunomodulatory agents	41/51 (80.4)
Suboptimal dose of AZA	4/7 (57.1)

suboptimal dose in CD patients with small intestine involved only ($P = 0.019$) (Table 4).

Of the 57 patients suffering from active distal (applies to colitis confined to the rectum or rectum and sigmoid colon) or left-sided (applies to colitis extending proximal to the sigmoid descending junction up to the splenic flexure) ulcerative colitis, 31 (54.4%) received topical therapy. Medications used in topical therapy included mesalazine ($n = 5$), corticosteroids ($n = 22$), antibiotics ($n = 12$) as well as traditional medications ($n = 15$).

Oral corticosteroid use was also assessed. Of the 177 patients (29/71 with CD, 31/106 with UC), 60 were treated with corticosteroids. No significantly different doses were applied in patients with mild to moderate disease or severe disease ($P = 0.391$) (mild to moderate disease: mean dose 35.4 mg/d, range 10-60 mg/d; severe disease: mean dose 38.7 mg/d, range 10-75 mg/d). Of the 36 patients with severe inflammatory bowel disease, 10 (27.8%) did not receive oral or intravenous steroid therapy.

Of the 177 patients, 51 were thiopurine indicated. Among these 51 patients, 23 were steroid-dependent (refers to a relapse when the steroid dose is reduced below 10 mg/d, or within 6 wk of stopping steroids), 4 were steroid-refractory (refers to active disease in spite of an adequate dose and duration of prednisolone > 20 mg/d for > 2 wk) and 24 had postoperative fistulation CD. However, only 10 (19.6%) patients received immunomodulatory agents (8 received oral azathioprine AZA, 2 received oral cyclosporine). The mean AZA dose used in the 8 patients was 1.52 mg/kg per day, ranging from 0.83 to 2.22 mg/kg per day. A suboptimal dose of AZA was defined as a dose less than 1.5 mg/kg in the absence of leukopenia or hepatotoxicity. Based on such criteria, one patient developed myelotoxicity and tolerated a lower dose. Of the remaining 7 patients receiving AZA, 4 (57.1%) received a suboptimal dose with no attempt to increase the dose. None of the patients was treated with methotrexate or inflixmab.

DISCUSSION

IBD, including UC and CD, is a complex disorder characterized by a wide range of variations in clinical practice. As the evidence is changing and rapidly growing, national and international societies are continuously updating the current diagnostic and treatment guidelines, for the sake of avoiding variations in clinical practice, and offering strategies for their effective implementation. Ultimately, the success of practice guidelines is determined

Table 4 Suboptimal dose of aminosaliclylate and location of CD

Location of CD	Suboptimal dose (n)	Optimal dose (n)
Small intestine ^a	19	17
Colon	2	4
Ileocolon	6	20

^a $P = 0.019$: A significantly higher incidence of suboptimal dose in CD patients with small intestine involved only.

by the physicians' acceptance, and perceived usefulness of the guidelines and their impact on patient care. Reddy *et al*^[7] have investigated whether patients with IBD receive optimal therapy in America according to the practice guidelines. Since general information about the quality of care for patients with IBD in China is lacking, we conducted this study to examine the quality of care for IBD patients in our hospital.

Abundant evidence suggested that higher doses of aminosaliclylates (4 g/day) are more effective for inducing remission in UC or CD. A dose-response trend for aminosaliclylates was also observed^[8]. Clinical improvement (but not necessarily remission) in ulcerative colitis is associated with the dose of aminosaliclylate (≥ 3 g/d)^[8]. Although the role of aminosaliclylate in the management of CD is less clear, it was reported that its higher doses (≥ 4 g/d) are effective on active CD of the ileum and colon^[9-11]. Compared with sulphasalazine (SASP), mesalazine is not significantly better, but has lower side effects^[12]. In our hospital, SASP is still widely used to induce and maintain remission of mild to moderate UC and CD, because of its comparatively lower price. Besides, the incidence of UC is relatively higher and the adverse events of SASP seem lower in China than those in Western countries. The mainstay of treatment, however, has shifted towards the use of mesalazine. In our study, all the patients with UC received the optimal doses of aminosaliclylate, while 39.7% patients with CD received its suboptimal doses. Furthermore, a significantly higher incidence of suboptimal dose was found in CD patients with small intestine involved only. This phenomenon may be explained by the relatively lower incidence of CD than that of UC in China and therefore the less understanding of this disease.

Topical therapy allows direct delivery of the active drugs to the site of inflammation, limiting systemic absorption and potential side effects. Topical therapy is the most effective approach, provided that the formulation reaches the disease. It also plays an important role in the maintenance of remission. Oral therapy combined with topical therapy is superior to a single agent^[13-15]. Furthermore, meta-analysis has shown that aminosaliclylate is significantly better than topical steroids in inducing clinical remission^[16,17]. However, in our study, only 31 (54.4%) patients with distal or left-sided colitis received topical therapy, and topical mesalazine was only used in 5 patients. There is a tendency that topical therapy is thought to be less effective in clinical practice, quite reverse to the evidence. Actually, its lower efficacy may be due to the lack of preparations such as liquid enemas, foams, gels and suppositories, rather than due to the medication itself.

Corticosteroids can effectively induce remission of UC and CD. Oral or intravenous corticosteroids are recommended for severe UC and CD^[3,4]. In our study, more than a quarter of patients suffering from severe inflammatory bowel disease did not receive oral or intravenous steroid therapy, possibly due to the lack of comprehensive evaluation of the patients' baseline states and reevaluation when exacerbations occurred. In addition, the patients' and even some physicians' fear of adverse effect played a part role. There is evidence that side effects of corticosteroid therapy are related to the dosage used and its duration. Short-term corticosteroid therapy is relatively safe.

Although corticosteroids are effective in inducing remission of CD and UC. More than 20% of patients may be steroid-refractory or become steroid dependent. Meta-analyses have shown that corticosteroids are not effective in maintaining medically or surgically induced remission of IBD. The frequency and severity of well recognized adverse effects also preclude their long term use. Immunomodulatory agents such as azathioprine (AZA) and mercaptopurine (MP) can induce and maintain remission of CD and UC and have steroid sparing effects in patients with steroid dependent or refractory IBD^[21,22]. Although lower doses had been favored in early clinical trials, a meta-analysis demonstrated greater efficacy of higher doses^[23,24]. In our study, the use of immunomodulatory agents was restricted to a minority of IBD patients (19.6%), which is distinctly less frequent compared with that in Western countries. Furthermore, more than half of the patients received a suboptimal dose of AZA with no attempt to increase its dosage. Biological agents such as infliximab have not been registered for the treatment of CD in our region, and their effect on CD in Han nationality Chinese needs to be further investigated.

The limited use of immunomodulatory medications may be due to the lack of evidence and limited experience with these drugs in Han nationality Chinese with IBD. Uncertainty regarding the risk for neutropenia deters some physicians from using AZA at effective doses and longer treatment with it. Experience abroad has shown that AZA can be safely used in treatment of CD and UC^[25-27]. Recently, thiopurine methyltransferase (TPMT) and its genotype have been applied in predicting the myelotoxicity and reducing the incidence of leucopenia in Europe and North America^[28-30].

In contrast, the data available on the management of IBD in China are rather limited. Guidelines published by the Chinese Society of Gastroenterology adhere mainly to the international ones. The lack of evidence holds back the use of these medications and therefore affects the quality of care for IBD patients. As the incidence of IBD has been increasing in China, it may be of interest to follow the temporal epidemiological trends and treatment policy for IBD in China.

Several factors limit the interpretation of our data. Firstly, we did not determine the duration or the frequency of visits. A longer period or more frequent contacts may provide more opportunities to achieve better care for IBD patients. Secondly, the patients' perspective and preference

were not taken into account, which may affect the decision. Finally, we did not study the association of the reported quality of care with patient outcomes.

In conclusion, the quality of care for IBD patients can be improved. suboptimal doses of 5-ASA was used in treatment of patients with Crohn's disease, especially those with small intestine involved only and Topical mesalazine is inadequately used in treatment of patients with distal or left-sided colitis. Oral or intravenous steroid therapy is not used in treatment of certain patients with severe IBD. Use of Immunomodulatory agents is limited. Larger prospective studies are needed to investigate the quality of care for patients with IBD and to establish our own evidence-based guidelines.

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COMMENTS

Background

As the evidence is changing and rapidly growing, a number of national and international practice guidelines for management of inflammatory bowel disease (IBD) are available, for the sake of avoiding variations in clinical practice and offering strategies for their effective implementation. However, guidelines for IBD treatment can improve patients' care only when they succeed in moving actual clinical practice closer to recommended practice.

Research frontiers

Reddy *et al* have investigated the quality of care for patients with IBD in America, and suggested that patients often do not receive optimal treatment of IBD, despite the availability of practice guidelines.

Innovations and breakthroughs

Although the incidence of IBD has been increasing in China, general information about the quality of care for patients with IBD in China is lacking. We investigated the impact of guidelines and the quality of care for IBD patients from East China.

Applications

The results of this study suggest that the quality of care for IBD patients can be improved. Larger prospective studies are needed to investigate the quality of care for patients with IBD and to establish our own evidence-based guidelines.

Peer review

This is an interesting paper addressing an important issue in Chinese IBD patients. The paper is well written.

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