TURKISH INFLAMMATORY BOWEL DISEASE SOCIETY RECOMMENDATIONS ON SELECTED TOPICS OF CROHN'S DISEASE

TÜRK İNFLAMATUVAR BARSAK HASTALIKLARI DERNEĞİNİN CROHN HASTALIĞI İLE İLGİLİ SEÇİLMİŞ KONULARDA ÖNERİLERİ

How should we follow the Crohn's disease patients in remission?

Remisyondaki Crohn hastaları nasıl takip edilmelidir?

Key words: Crohn's disease, remission, follow up

Anahtar kelimeler: Crohn hastalığı, remisyon, takip

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INTRODUCTION

Crohn's disease is a chronic inflammatory disease, characterized by remissions and exacerbations. One of the major problems in the follow up of the patients in remission is detecting its early relapse. There is not a single parameter in determining the early relapses in the patients in remission. The physical examination, laboratory, radiology, endoscopy and histology findings provide information on the prognosis of the disease during the follow up of the patients. The complications may be prevented by timely treatment, when early relapse is detected.

The follow up frequency of the drug using patients in the remission depends on the types of drugs used, the duration of the disease and the existence of poor prognostic indicators. Poor prognostic indicators are correlated with parameters such as young age, ileal involvement, fistulising disease, previous surgical operation and active smoking.

METHODS

Using the systematic literature search to perform a systematic review of the literature, the following keywords have been scanned in Medline: "Crohn's disease, remission, laboratory tests", "Crohn's disease, recurrence, laboratory tests", "Crohn's disease, relapse, laboratory tests", " Crohn's disease, relapse, CRP", "Crohn's disease, remission, CRP", "Crohn's disease, remission, erythrocyte sedimentation rate", "Crohn's disease, relapse, abdominal pain", "Crohn's disease, remission, abdominal pain", "Crohn's disease, remission, endoscopic findings", "Crohn's disease, relapse, endoscopic monitoring", "Crohn's disease, biopsy sample". All the studies conducted in the adult age group have been included in the assessment. Other studies have also been found by scanning the literature references. Eleven studies have been retrieved after 3e literature scanning of 932 studies in order to specify the sensitivity and specificity of the clinical findings, laboratory tests and endoscopic findings in the detection of remission and relapse in Crohn's disease. The types of 11 studies analyzed are provided in Table 1, whereas the distribution of the follow up and the methodologies considered in the studies are provided in Table 2.

Table 1. Types of the studies analyzed

Types of studies	Number of studies
Prospective study	6
Retrospective study	3
Review	2

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Table 2. The distribution of diagnostic methods in the studies analyzed

Follow up methods	Number of studies
Laboratory	10
Clinical	1
Endoscopic	2

RESULTS

Clinical relapse occurs within one year among 30-60% of the patients in remission. High CRP, fistulising disease, colon localized disease and stress have been identified as the independent predictors in Crohn's disease at remission (1). The relapse risk within 6 months after having an exacerbation was found to be related with the parameters like age <25, a period of less than 6 months after the attack, a period of >5 years since observation of the first symptoms and colonic involvement (2). Smoking is a risk factor for relapse. Smoking even a few cigarettes is effective on disease activity (3, 4). The sensitivity of CRP is 54-75% and the specificity is 45-70% in determining endoscopic and clinical relapse (5, 6,7). Identifying the CRP cutoff level as 15 mg/L, more frequent and more serious relapse is observed in patients a with CRP level >15 mg/L (8). In 2 years time, the relapse risk for the patients who attained clinical remission is higher in the group having a constantly high CRP value, than in the group with a constantly normal CRP (9). The 71 patients with Crohn's disease were checked for the erythrocyte sedimentation rate and CRP every 6 weeks, and the relapse risk in the short term has been found to be 8 times higher in those with a sedimentation rate >15 mm and CRP >20 mg/L. The sensitivity of the fecal calprotectin is 68% to 100% and the specificity is 30% to 67% in determining the relapse for patients with clinical and endoscopic remission (6, 11,12). The colonoscopy should be performed every 1 – 2 years for surveillance against tumor development in patients having Crohn's colitis in 8-10 years after the diagnosis of the disease for the patients with complete colonic

Table 3. Analysis of CRP

Author, year, journal	Number of patients	Relapse according to	Sensitivity	Specificity
Craig A.Solem, 2005 Inflamm Bowel Dis	104 Crohn	Endoscopic	54%	45%
Jost Langhorst, 2008 American Journal of Gastroenterology	43 Crohn 33 active	Endoscopic	CRP: 69.8% Lf: 81.8% Calp: 100% PMN: 81.8% CDAI: 24.2%	CRP: 50% Lf: 60% Calp: 30% PMN: 70% CDAI: 100%
B. Simonis, 1998 Scand J of Gastroenterology	36 Crohn 16 active	Endoscopic CDAI	CRP: 75% α-1 antitripsin: 94% α-1 acid glycoprotein: 75% Sialic acid: 88% Prealb: 94% Alb: 69% CDAI: 81% Van Hees: 75% (Endoscopic evaluation)	CRP: 70% α-1 antitripsin: 85% α-1 acid glycoprotein: 70% Sialic acid: 80% Prealb: 85% Alb: 60% CDAI: 75% Van Hees: 70% (Endoscopic evaluation)

Lf: lactoferrin, Cal: calpoprotectin,PMN-e: polymprphonuclear-elastase (fecal)

Table 4. Analysis of Calprotectin

Author, year, journal	Number of patients	Relapse according to	Sensitivity	Specificity
Renata D Inca, 2008 American Journal of Gastroenterology	65		Calp: 68% (calp cut-off: 130mg/kg) Sed: 72% Determination of relapsed colonic Crohn in remission	Calp: 67% (calp cut-off: 130mg/kg) Sed: 85% Determination of relapsed colonic Crohn in remission
Jost Langhorst, 2008 American Journal of Gastroenterology	43 Crohn (33 active)	Endoscopic	Calp: 100%	Calp: 30%
Costa F, 2005 Gut	30 Crohn		87% (calp cut-off: 150ug/g)	43% (calp cut-off: 150ug/g)

involvement and after 15 years for the patients with left colonic involvement. It is recommended to take 4 biopsies in every 10 cm and from the lesion if exists (13). The studies analyzing CRP and the sensitivity and specificity of the calprotectin in determining relapse are shown in the tables below (Table 3-4).

CONCLUSION

The follow up frequency of patient in remission is important in order to detect the relapse, to determine the side effects of the drug and for the surveillance. Fistulising disease, high CRP and sedimentation rate, cigarette smoking, young age and colonic involvement are the risk factors for relapse.

It is suggested that the patient in remission is followed up with the physical examination findings, with laboratory tests (sedimentation rate, CRP, hemogram, creatinin, ALT, AST, GGT and ALP) and with endoscopy (when activation is considered or for surveillance). Based on these findings, national recommendations for the follow up of Crohn's Disease patients in remission are seen in the box.

Recommendation:

It is suggested that the patient is followed up once a month in the first 3 months and then once in 3 to 6 months after remission has been maintained. During follow up apart from the inspections to be performed for the drug side effects erythrocyte sedimentation rate, CRP, haemogram, creatinine, ALT, AST, GGT, and ALP can be required in order to monitor disease activity and development of complications.

In the patient in remission endoscopy can be performed when it is considered that the disease is activated or complications have developed. It is repeated according to the age of the disease and in compliance with the surveillance criteria. ***[EL 5, RG D]***

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