

Prognosis in Patients with Melanosis Coli; A Prospective Study

Melanozis Kolili Hastalarda Prognoz; Prospektif Bir Çalışma

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ABSTRACT

Introduction: Melanosis coli is a benign lesion associated with the overuse of laxatives containing anthraquinone. The aim of this study is to determine whether melanosis recovers after the discontinuation of laxatives and whether this condition is associated with a higher incidence of colon polyps or cancer compared to the general population.

Methods: Patients with confirmed melanosis coli were performed a repeat colonoscopy and biopsy 2 years later and their histopathological examination results were compared. Data on age, sex, the use of any medicinal laxative or herbals, the presence of findings after the discontinuation of laxatives, constipation, colon polyp, and the relationship with colon cancer were examined. The similarity of segments and their relationships in the first and control colonoscopies were investigated in cases detected to have melanosis coli.

Results: All 104 patients included in the study were suffering from constipation. While the number of patients using laxatives or herbal tea was initially 96, it was 24 at the time of follow-up colonoscopy. Although the majority of subjects had discontinued laxatives, histological findings of melanosis coli persisted in 88 of 104 subjects. Mostly descending colon and rectum were involved.

Conclusion: It is thought that the findings of melanosis coli disappear in about 6 months following the discontinuation of laxative drugs and herbal teas. However, it was detected in our series that while the macroscopic findings were mostly healed even in the follow-up after two years, microscopic findings of melanosis coli continued to remain. No relationship was found between melanosis coli and the development of colon cancer and polyp. In the present study, it was aimed to emphasize that melanosis coli's becoming chronic and its creating a predisposition to colon cancer should be investigated with longer follow-ups and some herbal teas may cause a long-term change in the colon mucosa.

Keywords: Melanosis coli, constipation, colonoscopy, hyperpigmentation

ÖZ

Amaç: Melanozis koli antrakinon içeren laksatiflerin fazla kullanımına bağlı olarak ortaya çıkan benign bir lezyon olarak düşünülmektedir. Çalışmanın amacı melanozis kolili hastaların laksatiflerle ilişkisi, laksatif bırakılınca iyileşip iyileşmediği, normal popülasyona göre kolon polipi ve kolon kanseri ile ilişkili olup olmadığını saptamaktır.

Yöntemler: Kolonoskopi ile melanozis koli saptanan olgulara 2 yıl sonra kontrol kolonoskopisi yapıldı ve histopatoloji sonuçları karşılaştırıldı. Olguların yaşları, cinsiyetleri, laksatif ilaç veya bitki çayı kullanıp kullanmadığı, laksatif kullananların bıraktıktan sonra bulgularının devam edip etmediği, konstipasyon, kolon polipi ve kolon kanseriyle ilişki olup olmadığı araştırıldı. Melanozis koli saptanan olguların ilk ve kontrol kolonoskopilerindeki segmentlerin benzerliği ve ilişkisi araştırıldı.

Bulgular: Çalışmaya alınan 104 olgunun hepsinde konstipasyon mevcuttu. Laksatif ilaç veya çay kullanan olgu sayısı ilk başta 96 idi, kontrolde ise 24 hasta laksatif ilaç veya çay kullanmaya devam ediyordu. Olguların büyük çoğunluğu laksatif kullanımını bıraktığı halde 104 olgunun 88'inde histopatolojik olarak melanozis koli bulguları devam etmekteydi. Çalışmamızda en sık sol kolon ve rektum tutulmuştu.

Sonuç: Melanozis koli bulgularının laksatif ilaç veya çayların kullanımını bırakıldıktan yaklaşık 6 ay sonra düzeldiği düşünülmektedir. Fakat bizim serimizde 2 yıl sonraki takipte bile büyük çoğunluğunda makroskopik bulgular düzeldiği halde mikroskopik olarak melanozis koli bulgularının devam ettiği saptandı. Çalışmada melanozis koluyle kolon kanseri ve kolon polipi arasında bir ilişki saptanmadı. Melanozis kolinin kronikleşmesinin ve kolon kanserine yatkınlık oluşturup oluşturumamasının daha uzun takiplerle araştırılması gerektiğini ve bazı bitki çaylarının kolon mukozasına uzun süreli değişikliğe yol açabileceğini vurgulamak istedik.

Anahtar Kelimeler: Melanozis koli, konstipasyon, kolonoskopi, hiperpigmentasyon



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Introduction

Melanosis coli is a condition characterized by the dark pigmentation of the mucosal lining of the large intestine, resulting from chronic use of laxatives containing anthraquinone. This condition may occur within a few months following the use of laxatives and may gradually disappear within a few months following the discontinuation of laxatives (1,2). Overuse of laxatives, notably the ones containing anthraquinone laxative, and overuse of herbal teas, including aloe vera, meadow saffron, cockspur-hawthorn, and buckthorn, have been implicated in the development of melanosis coli. The mechanism of action of this group of drugs and herbal teas is to increase the accumulation of fluid and electrolytes in the distal ileum. Herbal laxatives containing anthraquinone cause a damage in the epithelial cells and lead to changes in absorption, secretion and motility (3,4).

The pigment deposits in melanosis coli consist of hemosiderin, lipofuscin, lipofuscin-like pigment and ferrous sulfate rather than melanin (3,4). The diagnosis of melanosis coli is made based on the histological examination of biopsy specimens collected from suspicious segments during colonoscopy or biopsy specimens taken for any other reasons (Figure 1). Pigment deposits are observed in macrophages located in lamina propria of the large intestine while pigments are unequally distributed across different segments of the large intestine and melanosis affects more frequently the cecum and proximal colon (5,6).

Although melanosis coli has been considered as a benign condition, it remains unknown whether melanosis increases the risk for colorectal cancer. Melanosis begins 4 months after the initiation of anthraquinone laxatives. Melanosis has been usually reported to be a benign condition and resolves within one year after the discontinuation of laxatives (4,7). In this study, we aimed to assess follow-up clinical and colonoscopy findings in comparison with initial findings in patients diagnosed with melanosis coli.

Methods

This study was designed to prospectively assess patients diagnosed with melanosis coli following the histopathological examination of biopsy specimens taken from the areas of macroscopic hyperpigmentation which were detected during colonoscopy that was performed in our clinic. Ethics approval for this study was obtained from the Istanbul Training and Research Hospital Ethics Committee (KAEK-50-1267). All participants provided their informed consent. Patients who had bowel movements 3 times or less per week were considered as constipated. Data on the age and sex were collected and study subjects were asked if they were using any medicinal laxative or herbal teas and whether they had a history of constipation or colon polyps or colon cancer and they were screened for such lesions via colonoscopy. Colonoscopy findings of these patients were assessed to detect whether colon segments found to be involved in melanosis during the follow-up colonoscopy were similar or connected to those detected during the initial colonoscopy.

Statistical Analysis

Data were analyzed using w-2 test in SPSS version 16 software. Continuous variables were presented as mean \pm standard deviation,

whereas categorical variables were shown as percentages. A p value less than 0.05 indicated statistical significance.

Results

During the above-mentioned period, a total of 3416 colonoscopy procedures were performed and 112 patients were diagnosed with melanosis coli (Figures 1, 2). Eight of these patients died of unrelated causes during the follow-up, therefore, a follow-up colonoscopy procedure could not be performed. Seventy-two of these patients were female (64.3%), and 40 patients were male (35.7%). The age range of study patients varied from 29 to 82 years (the mean age 56.1 ± 17.8 years). All patients were experiencing constipation. Benign colon polyps were removed in 16 subjects (14.3%) during the initial colonoscopy. The descending colon was affected by melanosis in 64 patients (57.1%) while ascending colon involvement was detected in 16 patients (14.3%) and melanosis affected the colon in whole in 32 patients (28.6%) (Table 1).

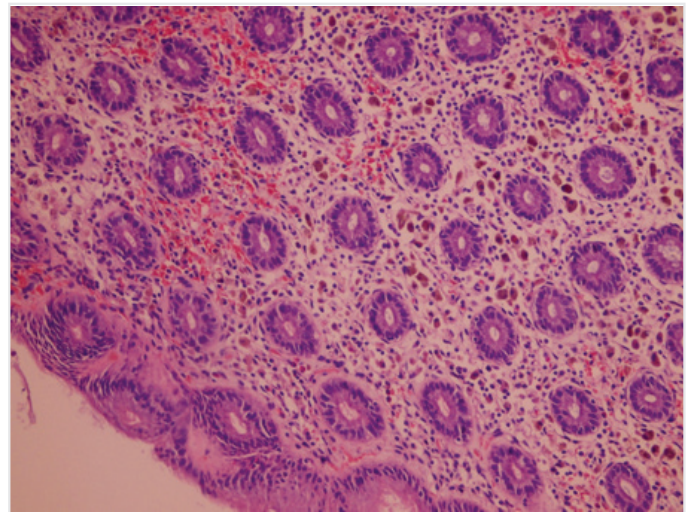


Figure 1. Microscopic appearance of melanosis coli with hematoxylin eosin enlargement of 100 dyes

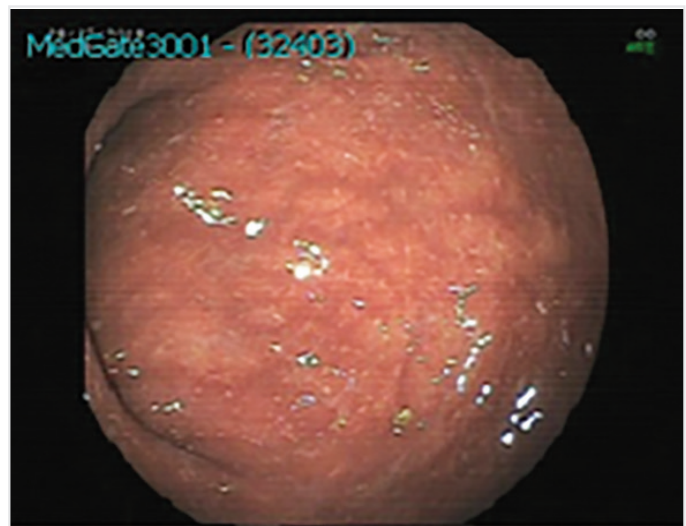


Figure 2. Macroscopic appearance of melanosis coli during colonoscopy

Table 1. Locations of melanosis coli in the initial colonoscopy and follow-up colonoscopy

	Location (at the diagnosis) n=112	Location (follow-up) n=104	p
None	0	16 (15.4%)	-
Ascending colon	16 (14.3%)	16 (15.4%)	$\chi^2=0.052$, p=0.82
Descending colon	64 (57.1%)	48 (46.1%)	$\chi^2=1.107$, p=0.293
Entire colon	32 (28.6%)	24 (23.1%)	$\chi^2=0.848$, p=0.357

Table 2. The use of laxatives and herbal teas at the diagnosis and during the follow-up

	At the diagnosis, n=112	During the follow-up, n=104
None	8 (7.1%)	80 (76.9%)
Use of laxatives	24 (21.4%)	16 (15.4%)
Herbal tea consumption	80 (71.4%)	8 (7.7%)

Eighty of the patients diagnosed with melanosis coli were drinking herbal teas (71.4%) and 24 patients were receiving laxatives (21.4%). Only eight patients (7.1%) had received neither laxatives nor herbal tea (Table 2).

Patients with melanosis coli were advised not to receive laxatives or herbal teas. These 104 patients underwent a follow-up colonoscopy within two years after the initial colonoscopy. Follow-up colonoscopy procedures did not reveal any polyps or malignancy in these patients. At the time of follow-up colonoscopy, the age of study subjects varied from 30 to 83 years (the mean age: 56.1 ± 17.1 years). All study subjects except eight (7.7%) were experiencing constipation at the time of follow-up colonoscopy. Eighty study subjects (76.9%) had stopped using laxatives and herbal teas while 16 study subjects (15.4%) were still using laxatives and eight subject (7.7%) had not stopped drinking herbal tea. Follow-up colonoscopy revealed melanosis in the descending colon in 48 patients (46.1%), in the entire colon in 24 subjects (23.1%) and in the ascending colon in 16 subjects (15.4%) while melanosis coli disappeared only in 16 subjects (15.4%). The last 16 study subjects were the ones who had discontinued laxatives and herbal teas and had ascending colon involvement at the time of the initial colonoscopy. No statistically significant differences were found between the initial colonoscopy and follow-up colonoscopy in terms of the location of melanosis.

Discussion

Melanosis coli was first defined by Andral and Cruveilhier in 1830 as black discoloration of the mucosal lining of the colon detected during the autopsy of a patient with chronic diarrhea. In 1858, Virchow used the term "melanosis" to describe this finding.

The association between melanosis coli and constipation and the use of laxatives was first reported by Freeman (8) in 1829. Our study provided further evidence for the presence of such association as all subjects were constipated and 104 of 112 subjects were receiving laxatives or herbal teas. The cecum and ascending colon have been reported as the most common locations of melanosis in several publications (9,10). In our

study, the descending colon and rectum were predominantly involved in melanosis.

In a study conducted by Liu et al. (11), any association was not found between colon polyps and melanosis coli. In our study, benign colon polyps were detected only in 16 patients (14.3%) with melanosis coli during the initial colonoscopy. Melanosis persisted in most of the subjects (84.6%) in this study, as detected by follow-up colonoscopy procedures performed 2 years later, while none of the subjects developed colon polyps during the follow-up period. The prevalence of colon polyps in our study patients was found to be similar to the prevalence in age-matched general population.

In a prospective study, Siegers et al. (12) found associations between colon cancer and melanosis coli in patients who were suffering from constipation and using anthraquinone laxatives. In another study, a retrospective analysis revealed preexisting melanosis coli in 11.9% of those with colon cancer (13). That study reported an association between melanosis coli and colon cancer. In another study presented by Speare, no association was found between melanosis coli and colon cancer and the author declared that melanosis coli might be reversible upon the discontinuation of laxatives (14). In line with this study, neither initial nor follow-up colonoscopy procedures revealed any evidence of colon cancer.

There are several publications reporting that the incidence of melanosis coli increases with age and this condition has been detected only in constipated patients over the age of 50 years and using anthraquinone laxatives (12,15). Although the mean age of study subjects was 56.1 years, the youngest study subject was a 29-year-old patient in our study. We would like to emphasize that melanosis coli may also be seen in young people although it is usually diagnosed in the elderly.

Higher incidence rates have been reported among women in the study conducted by Siegers (12) as well as in studies conducted in Mayo Clinic (15). This difference has been explained by higher prevalence of constipation among women, which is associated with an increased use of anthraquinone laxatives compared to a male population. However, any significant gender difference was not detected in the incidence of melanosis coli in the studies conducted by Speare (16). A female dominance (64.3%) was observed in this study.

Conclusion

While melanosis coli has been reported to be a reversible condition by several studies, clinical and histological findings have persisted in our study subjects. Considering studies reporting a potential association between colon cancer and melanosis coli, the presence of melanosis coli may be underestimated, and we believe that these patients should be monitored. Although constipation underlies melanosis coli and anthraquinone laxatives used in the treatment of constipation have been implicated in the development of melanosis coli, one should keep in mind that herbal tea consumption is another etiological factor. Many publications reported anthraquinone-related melanosis while our literature search did not reveal any studies on a possible association between melanosis coli and herbal teas containing anthraquinone. We would like to emphasize that increased herbal tea consumption

in the society may increase the prevalence of melanosis coli and even macroscopic evidence of melanosis coli may disappear and histopathological findings may persist after stopping drinking herbal teas. Considering reports on potential associations between melanosis coli and colon cancer, we believe that consideration should be given on the consumption of herbal teas and drugs containing anthraquinone hence public awareness and even awareness among healthcare professionals about melanosis coli should be raised.

Ethics Committee Approval: Ethics approval for this study was obtained from the İstanbul Training and Research Hospital Ethics Committee (KAEK-50-1267).

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