LONGER CECUM INSERTION TIME AND MORE INADEQUATE COLONIC PREPARATION IN PATIENTS WITH ACROMEGALY: IS A DIFFERENT COLONOSCOPY PREPARATION NEEDED?

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Abstract

Purpose. To investigate whether there is a difference between acromegalic and non-acromegalic cases in terms of bowel preparation and colonoscopic intervention.

Methods. Patients with controlled and uncontrolled acromegaly and as a control group (CG) patients without acromegaly between January 2010 and March 2014 were included. Groups were compared regarding adequacy of bowel preparation, cecal insertion time (CIT) and colonoscopy results.

Results. Fifty-nine patients with acromegaly (controlled n=30, uncontrolled n=29) and 73 age and gender matched volunteers without acromegaly were evaluated. CIT in cases with controlled, uncontrolled acromegaly cases and in CG was 5.33 [4.00-6.00], 7.00 [4.91-11.31], and 3.10 [2.35-4.65] minutes, respectively ($p<0.001$). Cases in CG had shorter CIT compared to controlled and uncontrolled acromegaly cases ($p=0.014$ and $p<0.001$, respectively). There was no significant difference regarding CIT between controlled and uncontrolled acromegaly cases ($p=0.247$). Six (20%) of controlled acromegaly patients, 10 (35%) of uncontrolled acromegaly patients and three (4%) of CG had inadequate bowel cleansing ($p<0.001$). Although statistically insignificant, cases with inadequate bowel cleansing had tendency towards having prolonged CIT in comparison to cases with adequate bowel cleansing (6.00 [3.87-9.00] and 4.16 [2.95-5.70] minutes, respectively, $p=0.07$).

Conclusion. Inadequate bowel cleansing is one of the main problems encountered during colonoscopic investigation/surveillance in acromegalic patients. Therefore, a different protocol for colonoscopy preparation may be needed for these cases.

Key words: Acromegaly, colonoscopy, colon cleansing, colonoscopy preparation, cecal insertion time.

INTRODUCTION

Growth hormone (GH) and insulin like growth factor-1 (IGF-1) excess in acromegaly have impact on gastrointestinal system as well as various other organ systems. Dolichomegacolon, slow colonic transit, increased prevalence of colonic polyps, and adenoma are among well-known consequences of GH/IGF-1 excess in gastrointestinal system (1-4).

Because of increased risk of colorectal carcinoma, periodic screening is essential in cases with acromegaly (5-7). Based on the disease activity and findings of the first colonoscopy, repeat colonoscopies may be necessary, and total colonoscopy rather than sigmoidoscopy is recommended (7). However, structural changes in acromegaly cause concerns about safety and possible complications of total colonoscopy (4). Not only the risks but also reliability of the procedure is a concern. For a reliable and complete result, colonoscopy should be performed by experienced hands, and conditions necessary for a complete colonoscopy should be provided.

One of the major obstacles to perform a total colonoscopy is inadequate bowel cleansing. Inadequate bowel cleansing is also associated with prolonged cecal insertion time (CIT), which is also important for endoscopy staff, physician, and the patient (8, 9). In cases with acromegaly, although results of colonoscopy have been investigated in detail, preparation before colonoscopy and the procedure itself have not been widely evaluated. Herein, we aimed to investigate whether there is a difference between acromegalic and non-acromegalic cases in terms of bowel preparation and procedure of colonoscopy.

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PATIENTS AND METHODS

In this study we included 59 patients with acromegaly who were treated at the Endocrinology-Metabolism Outpatient Clinic of the Cerrahpasa Medical Faculty, Istanbul University between January 2010 and March 2014. The Control group (CG) was composed of patients to whom colonoscopy was performed for the first time, including 73 age and gender matched volunteers without acromegaly. The indication for majority of the procedures included colorectal cancer/polyp screening or irritable bowel syndrome. Patients who had a colon operation were excluded.

Patients stopped eating solid foods two days before the colonoscopy, and consumed liquid foods. One day before the procedure they consumed a total of 3 liters of water, and they were administered a total of 90 ml sodium phosphate solution (NaP) (Fleet Fosfo-Soda®; Kozmed, Turkey), with 45 mL of the amount at 14:00 and the other 45 mL at 18:00. All colonoscopies were performed with 160 cm standard colonoscope and by the same gastroenterologist (EC) with a ten-years of experience. All colonoscopies were performed under conscious sedation using a combination of midazolam (1-5 mg) and pethidine (20-50 mcg) intravenously. The time taken for insertion of the colonoscope to the cecum was defined as CIT. The adequacy of colon cleansing was evaluated by the endoscopist according to the Aronchick scale (Table 1) (10). Adequacy of bowel cleansing, CIT, and results of the colonoscopy were recorded for each patient.

Cases with acromegaly were stratified by the disease activity. Failure of random GH level suppression to less than 1 ng/dL, and high levels of IGF-1 adjusted for age and gender in a case, verified the presence of active acromegaly. Cases with controlled and uncontrolled acromegaly and cases without acromegaly were compared based on adequacy of bowel preparation, cecal insertion time, and colonoscopy results.

The study protocol was approved by the Ethics Committee of Cerrahpasa Medical School, Istanbul

University, Istanbul, Turkey. All the subjects read and signed the informed consent forms before being enrolled in the study.

Statistical analysis was performed using SPSS version 15.0 (Inc., Chicago, IL, USA). When the distribution was not normal, Kruskal-Wallis test was used to compare the groups. The origin of the difference between the groups was investigated by Mann-Whitney U test. The results were presented as median and interquartile range unless otherwise specified. Spearman correlation coefficient was used for the calculation of associations between variables. Chi-Square Test was also used when it was necessary. $P < 0.05$ was considered statistically significant.

RESULTS

The mean ($\pm$ SD) age of the patients with controlled acromegaly ($n=30$), uncontrolled acromegaly ($n=29$), and the CG ($n=73$) was 47.2 ± 11.2 , 42.9 ± 11.2 , and 43.9 ± 10.7 years, respectively ($p = 0.3$). The female/male ratio was 17/13, 15/14, and 46/27, in controlled acromegaly, uncontrolled acromegaly and CG, respectively ($p=0.6$).

The mean duration of the disease in controlled acromegaly patients was longer than the uncontrolled patients ($p < 0.001$). Two patients with controlled acromegaly and one patient with uncontrolled acromegaly had hypocortisolism, and five patients with controlled acromegaly had hypothyroidism. These patients were receiving appropriate hormone replacement therapy. During the study period, 21 cases with controlled and two cases with uncontrolled acromegaly were on medical therapy with a somatostatin analogue. Patient characteristics and GH/IGF-1 levels of the two groups with acromegaly are presented in Table 2.

Regarding adequacy of colon cleansing, six (20%) of controlled acromegaly patients, 10 (35%) of uncontrolled acromegaly patients, and three (4%) of CG patients were classified as fair or poor according to the Aronchick scale ($p < 0.001$). The adequacy of the colon cleansing of 24 (80%) patients with controlled

Table 1. Aronchick scale

Grade	Description
Excellent	Small volume of clear liquid or greater than 95% surface seen
Good	Large volume of clear liquid covering 5%-25% of the surface but greater than 90% of surface seen
Fair	Some semi-solid stool that could be suctioned or washed away but greater than 90% of surface seen
Poor	Semi-solid stool that could not be suctioned or washed away and less than 90% of surface seen
Inadequate	Re-preparation needed

Table 2. Characteristics and laboratory results of the patients with controlled and uncontrolled acromegaly

	Controlled acromegaly (n=30)	Uncontrolled acromegaly (n=29)	p
Duration of disease (month)	60 [IQR:33-144]	2 [IQR:1-8.5]	<0.001**
Treatment of acromegaly (n,%)			
Somatostatin analogue	21 (70%)	2 (7%)	<0.001
Previous surgery	27 (90%)	12 (41%)	0.7
Radiotherapy (RT)			0.07*
Conventional RT	1 (3%)	0 (0%)	
GKR	2 (7%)	3 (10%)	
None	27 (90%)	26 (90%)	
GH (ng/dl)	0.5 [0.22-1.64]	5.7 [2.2-28.3]	<0.001**
IGF-I (ng/dl)	202.5 [102.5-202.5]	681 [415.4-1069.]	<0.001**
Opioids using (%)	0(0%)	0(0%)	
Diabetes	3 (10%)	6(20.7%)	0.219

Data was expressed as median and IQR. GKR, Gammaknife radiosurgery; FBG, Fasting blood glucose.

acromegaly, 19 (65%) with uncontrolled acromegaly and 70 (96%) of CG patients were evaluated as excellent or good. There was no significant difference regarding adequacy of bowel cleansing between controlled and uncontrolled acromegaly cases ($p=0.2$). However, patients with controlled and uncontrolled acromegaly had increased frequency of inadequate bowel cleansing in comparison to CG ($p=0.009$ and $p<0.001$, respectively) (Fig. 1).

CIT in cases with controlled acromegaly, uncontrolled acromegaly and in CG was 5.33 [4.00-6.00], 7.00 [4.91-11.31], and 3.10 [2.35-4.65] min, respectively ($p<0.001$). Cases in CG had shorter CIT compared to controlled and uncontrolled acromegaly cases ($p=0.014$ and $p<0.001$, respectively) (Fig. 2). There was no significant difference with respect to CIT between uncontrolled and controlled acromegaly cases ($p=0.242$). CIT was not correlated with GH levels

($r=0.04$, $p=0.9$) or IGF-1 levels ($r=0.004$, $p=0.9$).

Although the difference was not statistically significant, cases who were on a somatostatin analogue tended to have shorter CIT compared to cases without medical treatment for acromegaly (4.16 [3.30-5.50] and 8.08 [5.91-11.15] min, respectively, $p=0.06$). In the whole cohort, cases with inadequate bowel cleansing had tendency towards having prolonged CIT in comparison to cases with adequate bowel cleansing (6.00 [3.87-9.00] and 4.16 [2.95-5.70] min, respectively, $p=0.07$). However, this difference was not statistically significant, either.

Colonoscopy detected hemorrhoids in eight (27%) of controlled acromegaly cases, one (3%) of uncontrolled acromegaly cases, and five (6%) of CG cases ($p=0.02$). Colonic diverticulum was present in none of the cases with controlled acromegaly, in one (3%) of cases with uncontrolled acromegaly, and in

Figure 1. Comparison of bowel cleansing between controlled acromegaly, uncontrolled acromegaly cases and control group. **Figure 2.** Comparison of CIT between controlled acromegaly, uncontrolled acromegaly cases and control group.

five (7%) of CG cases ($p=0.3$). Colonic polyps were detected in six (20%) controlled acromegaly patients, 11 (38%) uncontrolled acromegaly patients, and five (7%) CG patients ($p=0.001$). There was no complication during the colonoscopic procedures.

DISCUSSION

This study shows that inadequate bowel cleansing is more frequent in acromegaly cases compared to non-acromegalic cases, and CIT is prolonged in cases with acromegaly. Although insignificant, CIT tended to increase in cases with inadequate bowel cleansing and to decrease in acromegaly cases, which were on somatostatin analogue treatment.

In acromegaly patients, the risk of colorectal cancer is increased with a prevalence of 3.7 and relative risk of 7.4 and mortality from colon cancer is increased by 2.5 fold (3, 11). Due to its increased risk, previous patients with polyps seen on colonoscopy and/or patients with increased IGF-1 levels should be screened every five years with colonoscopic surveillance (12). Since colonoscopy is an invasive procedure, and requires expertise, technical difficulties and conditions which make it more challenging should be determined. Reasons for colonoscopic failure include inadequate cleansing, dolichocolon, diverticulosis, patient discomfort, previous abdominal surgery, strictures and obstructive tumors (13). Bowel cleansing has been regarded as the most important and only correctable factor affecting the colonoscopy success. Conditions affecting bowel cleansing are also important for ease of the procedure and patient comfort (9). In the presented study, patients with acromegaly had more inadequate bowel cleansing compared to the CG. Inadequate bowel preparation may decrease adenoma detection rate, resulting in increased colonoscopic failures and cost.

Factors predicting inadequate colon cleansing include previous failure in adequate bowel cleansing, debilitating diseases like diabetes mellitus and Parkinson's disease, polypharmacy (medications causing constipation), and prolonged colon transit time (14, 15). Veysey and colleagues reported that all patients with acromegaly had prolonged large bowel transit time; being more prominent in patients on long-lasting somatostatin analogues (16). Likewise, in another study with acromegalic patients, it was demonstrated that high serum GH/IGF-1 levels lead to prolonged intestinal transit time by increasing the serum somatostatin levels (14). Increased colonic

transit time in acromegaly may cause inadequacy of bowel cleansing.

Irreversible structural changes due to acromegaly, including increased left and total colon length, and pelvic loop complexity, which persist even after disease control, increase CIT, and cause technical difficulties for the endoscopist during colonoscopy (4, 7, 18). Prolonged CIT may theoretically expose patients to increased risk of complications (8). In the current study, cases with acromegaly had significantly increased CIT in comparison to CG. Although not statistically significant, patients with uncontrolled disease activity had more prolonged CIT than the patients with controlled acromegaly. Compliance of the controlled acromegaly patients to complex activities including colonoscopy preparation seems to be better than uncontrolled active acromegaly group. Impaired daily complex activities are reported in acromegalic patients (20). In the whole cohort, CIT had tendency towards prolongation in cases with inadequate bowel cleansing. This observation was in line with the literature since bowel cleansing was the most prominent factor affecting CIT (19). CIT was neither correlated with latest GH nor IGF-1 levels.

Polyethylene glycol-electrolyte (PEG) and NaP including laxatives are the most commonly used drugs for colon cleansing. Multiple randomized studies and meta-analyses comparing NaP and PEG demonstrated that, NaP solutions have a better compliance due to a better taste with lower volume, and are more cost effective, and provide an equal or better cleansing (21, 22). Due to these concerns, in this study we utilized NaP laxatives. Martel and colleagues published a meta-analysis, to compare bowel cleansing following split-dose regime and standard regime preparation. In that study, split-dose regimes were demonstrated to provide better cleansing and greater patient predilection (23). Due to reported nephrotoxic effects of NaP laxatives, its use in colonoscopy preparation is increasingly decreasing. Split-dose PEG, due to providing adequate bowel preparation, patient compliance and causing less electrolyte imbalance, could be an alternative in acromegaly patients.

The adequacy of the colon cleansing is evaluated naturally during the procedure. This subjective evaluation by the endoscopist sometimes leads to wrong or deficient results. For the evaluation of quality of bowel preparation, we utilized the Aronchick scale described previously (10). Aronchick scale, while being more subjective compared to other scales, is still the most utilized scale.

This study has two main limitations. First, we didn't collect any information about the adequacy of bowel cleansing of the patients' previous colonoscopic examinations. It is reported that, previous inadequate colon cleansing is related with increased risk for subsequent inadequate cleansing rate and these patients would need additional laxatives (24). Second, the daily complex activities that may affect the compliance for colonoscopy preparation of the acromegalic patients were not investigated (4). It should be noted that, performance of endoscopic examination and evaluation of the quality of bowel preparation by the same experienced endoscopist yields more accurate results.

In conclusion, higher suboptimal bowel preparation rates and prolonged CITs in acromegaly indicate the difficulties of colonoscopic examination in this patient group. Prolongation of the duration of colon preparation and intensified preparation regime with increased dose of the osmotic agents used for bowel cleansing may be helpful in this group of patients. Further studies are needed to determine the ideal preparation regime for better colonic cleansing in acromegaly patients.

Conflict of interest

There is no conflict of interest that would undermine the neutrality of this scientific work.

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