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Original Article

Pathological Evaluation of Ganglion Cells in Biopsies from Upper Side of the Dentate Line in Patients with Perianal Problems

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Abstract

Introduction:
Constipation is one of the most common complaints of individuals, which may present with complication like hemorrhoid and fissure. Hirschsprung is a disease presenting with chronic constipation and its diagnosis may be delayed until adulthood. It is diagnosed by biopsies from anorectal transitional zone. This study aimed to evaluate the association between Hirschsprung and anorectal problems.

Materials and Method:
Sixty three patients with anorectal problems who underwent surgery enrolled in this study. Some consecutive biopsies were obtained from anal canal at 2, 4 and 6 cm above the dentate line. Biopsies were assessed for ganglion cells changes. Patients' data and biopsies results were analyzed with SPSS version18.

Results:
Out of 63 patients 29 (46%) patients were female and 34 (54%) were male with the mean of 32.65±13.73 years. Fifty six (73%) patients complained from constipation with the mean time of 57.65±45.21 months. Aganglionic zones were reported in six patients with the mean length of 43.33 mm. There was not any relation between anal ganglion cells pathology and constipation (P=0.363), but there was a significant relation between duration of constipation and pathologic changes (P=0.001). The ratio of constipation duration to age was related to anal ganglion cell pathology (P=0.001). Hemorrhoid degree was also affected anal ganglion cells pathology (P=0.037).

Conclusion:
The relation between Hirschsprung's disease and anorectal problems in adults were significant. The pathologic findings were more presented in younger patients, and those with longer history of constipation and lower degree hemorrhoids.

Key words: Anal ganglion cells, Constipation, Hemorrhoids.

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Introduction

Constipation is one of the most common complaints of people, and if not treated, it may cause hemorrhoids and fissure (1). For many patients, constipation-associated symptoms are chronic and last for several weeks to several years (2). The exact prevalence of constipation depends on the chosen definition, which ranges from 2% to 28%. Previous studies reported stable or steady prevalence of constipation because of similar rates of the constipation's onset and disappearance; meanwhile they acknowledged the lack of accurate data on its incidence. Almost one third of those individuals with constipation demand for health care, though this is a very high proportion because of investigational and medication costs (3). Although non-steroidal anti-inflammatory drug use and the use of other constipation-inducing medications are important risk factors, there is weak evidence to support casual relationships between life style risk factors and constipation (4).

Hirschsprung's disease is a congenital disease usually diagnosed in childhood as congenital aganglionosis of the distal part of the colon. But its diagnosis sometimes is missed and sometimes is delayed in adulthood which demonstrates chronic constipation (5-7). Biopsies from upper side of anorectal transitional zone may confirm Hirschsprung's diagnosis. In adults with fissure and constipation, evaluation of ganglion cells may show pathological changes and confirm the diagnosis of Hirschsprung's disease (1,7). Therefore in this study we aimed to evaluate anorectal biopsy samples of patients for pathological ganglion cell changes. Patients were also evaluated for the history or length of constipation, and other complications including hemorrhoids and fissure.

Materials and Method

This was a cross sectional study. The research project was approved by the ethics committee of Mashhad University of Medical Sciences. The study population was patients older than 18 years old with perianal disorders (hemorrhoids and fissure) who underwent surgery during 2011 in Ghaem Hospital, Mashhad-Iran. A non-probability convenience sampling method was used, and the filed data collection was conducted through observation checklists.

Inclusion criteria were presence of hemorrhoids or fissure requiring surgical intervention, and age older than 18 years old. Exclusion criteria were having other colon or rectal diseases such as abscess, fistula, condyloma, bowel inflammatory diseases, angiodysplasia, and neoplasia.

Finally, 63 patients were enrolled in the study. An informed consent was obtained from all participants. During surgery some consecutive biopsies were obtained from the anal canal at 2, 4 and 6 cm above the dentate line. Biopsy samples were evaluated regarding ganglion cells condition. Pathologic biopsies were evaluated and compared with normal tissues. Ganglion cells changes were assessed with regard to patients' history of constipation and perianal disorders (hemorrhoids and fissure).

The data was entered into SPSS version18 for analysis. Quantitative data were analyzed by computing indices of central tendency and dispersion as well as frequency distributions. Study goals were evaluated by probability analysis including Chi square test, test for comparing two or more than two independent groups in parametric and non parametric data, statistical tests such as the student's t-test, one way ANOVA, Mann–Whitney test, and Kruskal–Wallis. The quantitative data were tested for normality by Kolmogorov-Smirnov test. The distribution of all the study variables were normal, therefore to analyze the data parametric statistical tests were employed.

Results

The patients' age ranged between 18 and 74 years (32.65±13.73); out of 63 patients

29 were female and 34 were male. Twenty one (34%) patients had low-activity occupations, 31 (49%) patients had medium-activity occupations and 11 (17%) patients had high activity occupations. Seventeen (30%) patients had anal fissure. Only seven (11%) patients did not have any history of constipation, 56 (89%) patients complained from constipation with average length of (57.65±45.21) months. The hemorrhoids involvement of patients are shown in Table1.

Table1: Distribution in patients of hemorrhoid involvement

Characteristics	Frequency
Any sign of involement	1(0.02%)
First degree hemorrhoids	1(0.02%)
Second degree hemorrhoids	21(33%)
Third degree hemorrhoids	29(46%)
Forth degree hemorrhoids	11(17%)

Pathologic findings in biopsies (aganglionic zones) were reported in six patients (3 males and 3 females) with average length of 43.33 mm. The other 57 patients (31 males and 26 females) did not show any sign of pathology in their biopsies, so the pathologic changes in ganglion cells of anal area were not related to gender (P= 0.838).

All the patients with anal pathologic findings reported constipation, and in general only seven (11%) patients did not complain from constipation. The mean age of patients with pathologic changes in anal ganglion cells was (18.17±0.41) years; the mean age of other patients was (34.18±13.56) years. The results of this study showed that age was an effective factor in determining pathologic changes in anal ganglion cells (P=0.006). Younger patients had more anal pathological ganglionic findings (P=0.006).

This study demonstrated that patients with average activity had more pathologic changes (P=0.033). Patients with pathologic changes in anal ganglion cells all had medium-activity occupations , while out of the remaining 57 patients without pathologic findings, 21, 25 and 11 patients had respectively low-, medium-, and high-activity occupations. This suggested that level of activity had significant effect on pathologic changes of anal ganglion cells.

Patients with pathologic findings all had history of constipation, in patients without pathologic changes, 50 (88 %) had history of constipation and the remaining 7 reported no history of constipation. This indicated that constipation was not a significant effective factor for the presence of pathological changes (P=0.363). The mean duration of constipation in patients with pathologic changes was (200. 00± 9.80) months and in other patients it was (28.92±28.87) months. The duration of constipation had significant effect on pathologic changes in anal ganglion cells (P=0.001). The ratio of constipation duration to patient age in the group with pathologic changes was (91.71 ±3.1); this ratio in other patients was (8.00±9.77). It showed that the ratio of constipation duration to patient age was a significant effective factor in determining or detecting pathologic changes in anal ganglion cells (P=0.001) (Fig.1).

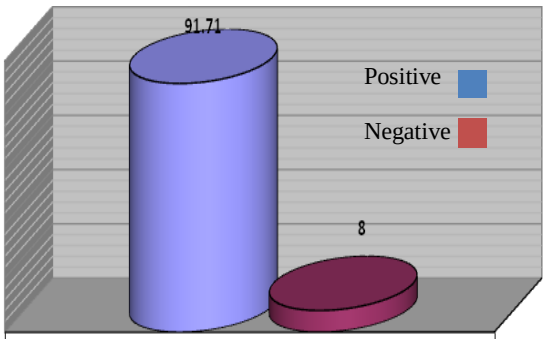

Fig 1: The effect of ratio of constipation duration to age on pathologic changes in ganglion cell

The severity of hemorrhoids was also effective in pathologic changes of anal

ganglion cells (P= 0.037). Among patients who had pathologic changes (n=6), only one had anal fissure; in other 57 patients 16 (25.3%) had anal fissure. Presence of anal fissure did not show any significant relation with pathologic changes in anal ganglion cells (P=0.20).

Discussion

Vorobyov et al in his study showed that a 60 mm full-thickness strip biopsy is able to confirm aganglionosis in 100 patients (12%). So in adults with constipation symptoms and bowel disorders a biopsy as explained above may confirm aganglio-nosis and Hirschsprung diagnosis. In Kapuller study the length of physiologic hypoganglionic area in people was determined as 7.5 -50 mm (13), for this reason we took our full-thickness biopcies at 2,4, and 6 cm interval from dentate line.
The percentage of aganglionosis in our study among adults with constipation was (10.53%). In Koszutski et al (14) study this percentage among children with constipation was (30%), and in Khan et al study was (14%) (15).

In Monajemzadeh study (16) the rate of Hirschsprung among patients with constipation was (75%), and in Ghosh study (17) it was (13%), both of these studies were conducted on children.

Howard (18) in his study on 60 patients with chronic constipation showed that 15 patients had normal biopsy, 7 patients minimal pathologic changes, 15 patients aganglionosis (Hirschsprung), 20 patients hypoganglionosis and 3 patients hyper-ganglionosis. His result indicated that (25%) of patients with chronic constipation had Hirschsprung disease. Regarding colon aganglionosis in patients with anorectal disorders, Jimenez-Urueta PS et al in his 2005 retrospective study in Spain found prevalence of (3.2%) between his study popluation. In our study the prevalence of agangliosis among pathiemts with hemorrhoid and fissure was (9.52%).

Conclusion

Our results showed that gender, constipation and fissure were not significantly related to pathologic changes in anal ganglion cells. The pathologic changes in anal ganglion cells were more common among younger patients, those with medium level activity, patients with longer history of constipation, and patients who have lower degree of hemorrhoid.

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