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World J Gastroenterol 2007 August 7; 13(29): 3967-3972
World Journal of Gastroenterology ISSN 1007-9327
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RAPID COMMUNICATION

Chronic constipation in hemiplegic patients

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Received: 2007-04-05 Accepted: 2007-04-26

Abstract

AIM: To assess the prevalence of bowel dysfunction in hemiplegic patients, and its relationship with the site of neurological lesion, physical immobilization and pharmacotherapy.

METHODS: Ninety consecutive hemiplegic patients and 81 consecutive orthopedic patients were investigated during physical motor rehabilitation in the same period, in the same center and on the same diet. All subjects were interviewed ⩾ 3 mo after injury using a questionnaire inquiring about bowel habits before injury and at the time of the interview. Patients' mobility was evaluated by the Adapted Patient Evaluation Conference System. Drugs considered for the analysis were nitrates, angiogenic converting enzyme (ACE) inhibitors, calcium antagonists, anticoagulants, antithrombotics, antidepressants, anti-epileptics.

RESULTS: Mobility scores were similar in the two groups. *De novo* constipation (OR = 5.36) was a frequent outcome of the neurological accident. Hemiplegics showed an increased risk of straining at stool (OR: 4.33), reduced call to evacuate (OR: 4.13), sensation of incomplete evacuation (OR: 3.69), use of laxatives (OR: 3.75). Logistic regression model showed that constipation was significantly and independently associated with hemiplegia. A positive association was found between constipation and use of nitrates and antithrombotics in both groups. Constipation was not related to the site of brain injury.

CONCLUSION: Chronic constipation is a possible outcome of cerebrovascular accidents occurring in 30% of neurologically stabilized hemiplegic patients. Its onset after a cerebrovascular accident appears to be independent from the injured brain hemisphere, and unrelated to physical inactivity. Pharmacological treatment with nitrates and antithrombotics may represent an independent risk factor for developing chronic constipation.

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Key words: Constipation; Disphagia; Stroke; Pharmacotherapy

Bracci F, Badiali D, Pezzotti P, Scivoletto G, Fuoco U, Di Lucente L, Petrelli A, Corazziari E. Chronic constipation in hemiplegic patients. *World J Gastroenterol* 2007; 13(29): 3967-3972

http://www.wjgnet.com/1007-9327/13/3967.asp

INTRODUCTION

Involvement of the gastrointestinal tract after cerebrovascular accidents (CVA) manifests as dysphagia and altered bowel function. Lesions of the brain centers controlling the swallowing act, when located in the dominant hemisphere for swallowing, are sufficient to explain the onset of dysphagia[1]. Several causes, other than neurological damage itself, have been advocated to explain the altered bowel function.

Fecal incontinence[2] and constipation have been reported[3] in hemiplegic institutionalized patients or after recent CVA[4], but their onset and prevalence after cerebral stroke and their relationship, if any, with neurological lesion and its hemispheric side or site, physical immobilization, drug consumption and mental disability, are unknown.

The aim of this study was to assess in patients with hemiplegia (1) the prevalence of bowel dysfunctions after stroke in patients with hemiplegia, and (2) the role of the site of neurological lesion, physical immobilization and pharmacotherapy in bowel dysfunction.

MATERIALS AND METHODS

Subjects

Consecutive hemiplegic patients with stabilized neurological lesions following a CVA were compared with consecutive orthopedic patients, following a fracture or surgery of pelvis or femur. Neurological and orthopedic patients presenting a normal cognitive status were investigated, after a period of physical immobilization of at least three months, with stabilized orthopedic or neurological lesions, while undergoing motor rehabilitation in the same period,

in the same rehabilitative center. All patients were on a similar diet for fiber and caloric intake.

Exclusion criteria were presence of fecal incontinence or constipation and chronic use of laxatives before the neurological or orthopedic event, presence of multiple vascular lesions of the brain, other neurological lesions, gastrointestinal or systemic diseases, impairment of cognitive status and previous abdominal surgery (except appendectomy and cholecystectomy).

Assessment

The diagnosis of CVA and the site of brain injury were ascertained, soon after the stroke, by computerized tomography or magnetic resonance imaging. Severity of the stroke was evaluated by the Canadian Neurological Scale[5] ranging from 1.5 to 11.5. Score 1.5 corresponds to patients sleepy with complete hemiplegia and severe speech deficit, score 11.5 corresponds to patients with less severe stroke (good consciousness and absence of speech and strength deficit). Cognitive status was assessed by the Mini-Mental State[6]. Patients with a score < 26, corrected for age and scholarity, were excluded from the study.

Physical mobility of the patients was assessed using the Adapted Patient Evaluation Conference System (APECS), a standardized 0-7 score point system[7]. The score value of 7 indicates the maximal mobility, i.e. autonomy to walk.

The same operator (FB) used a standardized questionnaire to inquire about diet and weekly bowel frequency and the following bowel characteristics, including difficulty of evacuation, feeling of incomplete evacuation, stool consistency, use of laxatives and/or digital maneuvers to defecate, loss of the call to defecate, and uncontrolled loss of feces before stroke or the orthopedic event and at the time of the study.

In addition, the questionnaire inquired about socio-demographic conditions such as social and smoking habits and alcohol intake. All patients were carefully investigated about medicine consumption. Drugs specifically considered for the analysis in both groups were nitrates, ACE-inhibitors, calcium antagonists, anti-depressants, anti-convulsivants, anti-thrombotics, anticoagulants, cardiac glycosides.

Constipation was defined as less than two bowel movements (bm) per week or presence of two or more of the following complaints (when laxatives and/or enemas were not used), less than three bowel movements per week, straining at defecation, feeling of incomplete evacuation and hard stools on at least 25% of occasions (Rome Ⅱ Diagnostic Criteria)[8], or continuous use of laxatives. Fecal incontinence was defined as recurrent uncontrolled passage of rectal contents through the anal canal[9].

The protocol was approved by the Local Ethics Committee.

Statistical analysis

Descriptive statistical techniques were used to compare the two groups of patients. Chi-square test and Fisher's exact test were used to compare frequency of symptoms in the different study groups and Student's *t*-test was used to compare the two groups for continuous variables.

Table 1 Characteristics of the study groups *n* (%)

	Hemiplegic (*n* = 90)	Orthopedic (*n* = 81)	*P*-value
Past/current smokers	25 (27.7)	11 (13.6)	0.03
Wine	40 (44.4)	42 (51.8)	0.29
Liqueurs	9 (10.0)	10 (12.3)	0.63
Secondary school	23 (25.5)	25 (30.8)	0.44
Employed	17 (18.8)	11 (13.6)	0.35
Sedentary activity	25 (27.7)	13 (16.0)	0.06

Univariate and multivariate logistic regression analysis[10] was performed to evaluate the relationship between constipation and stroke by odds-ratio (OR) calculation, with the orthopedic group used as reference. In multivariate analysis, these ORs were adjusted for socio-demographic factors, mobility degree, drug consumption without interference of each of these factors. Model-building strategy used to select the variables reported in the final multivariate analysis, was started from a multivariate model including all the variables analyzed at the univariate level, and then excluding one variable with the highest *P* value (resulting from the log-likelihood test). This procedure was repeated until the model included only the variables with a *P* value < 0.20. The association of *de novo* constipation with the site of brain injury was analyzed in hemiplegic patients using OR as an epidemiological measure.

RESULTS

Study population

Ninety hemiplegic patients (47 females and 43 males; mean age 68 years, range 27-95 years) and 81 orthopedic patients (63 females and 18 males; mean age 74 years, range: 22-94 years) were included in the study. The number of female and older subjects was greater in the control orthopedic group than in the hemiplegic population ($P < 0.01$ and $P = 0.04$, respectively).

The median time from the day of stroke/fracture and interview was about 36 wk (median: 254 d; interquartile range 138-565) and did not differ between the two groups. The Median Canadian Scale value was 7.59 ± 1.63 with no statistical difference between hemiplegics with and without onset of constipation (7.39 ± 1.35 and 7.48 ± 1.40, respectively).

The two groups did not differ either in diet, alcohol consumption, scholarity and occupational status. The number of smokers was greater in the hemiplegic group than in the orthopedic group ($P = 0.03$, Table 1). At the time of investigation, mobility evaluated by the APECS score, did not significantly differ between hemiplegic patients (mean 3, range 0-7) and orthopedic patients (mean 3, range 0-7). Brain injury was found in the right hemisphere of 51 hemiplegic patients (57%) and in the left hemisphere of 39 hemiplegic patients (43%).

Bowel variation

After stroke, bowel function varied in 55 patients (61%): 33 patients (37%) referred a decrease in weekly bowel

Table 2 Univariate analysis evaluating the association between social-demographic variables, mobility and drugs with onset of *de novo* constipation after cerebrovascular accidents of orthopedic trauma *n* (%)

All subjects	*De novo* constipation				
	Yes *n* = 33 (19.30%)	No *n* = 138 (80.70%)	OR	95% CI	*P* value
Age[1] mean (range)	68.4 (27-95)	71.4 (22-94)	0.94	0.74-1.21	0.64
APECS[2] mean (range)	3.29 (0-7)	3.68 (0-7)	0.88	0.71-1.09	0.27
Hemiplegics	27 (30.0)	63 (70.0)	5.36	2.08-13.8	0.01
Orthopedics	6 (7.4)	75 (92.6)	1		
Males	13 (21.3)	48 (78.7)	0.82	0.38-1.79	0.62
Females	20 (18.2)	90 (81.8)	1		
Smoking	11 (30.6)	25 (69.4)	2.26	0.97-5.25	0.06
Wine	12 (14.6)	70 (85.4)	0.56	0.25-1.22	0.14
Liqueur	2 (10.5)	17 (89.5)	0.46	0.10-2.09	0.32
Secondary school	9 (18.7)	39 (81.3)	0.95	0.41-2.23	0.91
Employed	6 (21.4)	22 (78.6)	1.17	0.43-3.17	0.31
Sedentary activity	8 (21.0)	30 (79.0)	1.15	0.47-2.81	0.76
Drugs					
Nitrates	12 (37.5)	20 (62.5)	3.37	1.43-7.91	0.005
Ace	12 (27.3)	32 (72.7)	1.89	0.84-4.26	0.12
Calcium antagonists	16 (27.1)	43 (72.9)	2.08	0.96-4.50	0.06
Antithrombotics	20 (35.07)	36 (64.3)	4.36	1.97-9.66	< 0.001
Anticoagulants	4 (22.2)	14 (77.8)	1.22	0.37-3.99	0.74
Anticonvulsivants	3 (27.3)	8 (72.7)	1.63	0.41-6.49	0.49
Antidepressants	4 (22.2)	14 (77.8)	1.22	0.37-3.99	0.74
Cardiac glycoside	9 (39.1)	14 (60.9)	3.32	1.29-8.54	0.01
Diet					
Vegetables ⩾ 1 time/d	22 (19.3)	92 (80.7	1.00	0.45-2.24	1.00
Fruits ⩾ 1 time/d	26 (18.1)	118 (81.9)	0.63	0.24-1.64	0.34
Brown ⩾ 1 time/d	3 (25.0)	9 (75.0)	1.43	0.37-5.72	0.61
Liquid intakes ⩾ 1500/d	2 (10.5)	17 (89.5)	0.46	0.10-2.09	0.31

Percentages are calculated referring to the total patients for considered variable. OR: Odds-ratio; CI: Confidence interval; [1]The OR for age refers to an increase of ten-year step. [2]The OR for APECS refers to one point increase in the score. APECS: Adapted Patient Evaluation Conference System.

frequency, 30 patients (33%) straining or pain at defecation, 29 patients (32.2%) hard stools, 21 patients (23.3%) feeling of incomplete evacuation, 22 patients (24.4%) continuous use of laxatives, 3 patients (3.3%) digital maneuvers to evacuate, 4 patients (4.4%) loss of the urge to defecate, and 5 patients (5.6%) fecal incontinence.

After orthopedic trauma, bowel function varied in 20 patients (24.7%) ($P < 0.005$ *vs* hemiplegic patients), 9 patients (11%) referred a decrease in weekly bowel frequency, 8 patients (9.9%) straining or pain at defecation, 12 patients (14.8) hard stools, 6 patients (7.4%) sensation of incomplete evacuation, 7 patients (8.6%) continuous use of laxatives, 1 patient (1.2%) loss of the urge to defecate, and 3 patients (3.7%) fecal incontinence.

De novo constipation according to Rome Ⅱ criteria

Twenty-seven (30.0%) hemiplegic patients presented constipation as compared to 6 (7.4%) orthopedic patients (OR = 5.36, $P < 0.01$).

Statistically significant association was found at the univariate analysis, between *de novo* constipation, hemiplegia, use of antithrombotics, nitrates and cardiac glycosides (Table 2).

No statistically significant association was observed between *de novo* constipation and gender, age, mobility and use of ACE-inhibitors, calcium antagonists, anticoagulants, anticonvulsivants and antidepressants (Table 2).

The effects of nitrates, antithrombotics and cardiac glycosides on *de novo* constipation did not differ in hemiplegics and orthopedics.

Multivariate analysis (Table 3) confirmed that constipation was significantly and independently associated with ischemic or hemorrhagic hemiplegia, use of antithrombotics, nitrates and glycosides.

Table 3 Multivariate analysis

	AOR	95% CI
Hemiplegics *vs* orthopedics	3.28	1.18-9.09
Ischemic hemiplegics patients *vs* orthopedic patients	3.11	1.04-9.29
Hemorrhagic hemiplegics patients *vs* orthopedic patients	3.64	0.92-14.44
Use of antithrombotics	2.72	1.05-7.11
Use of nitrates	2.48	0.98-6.27
Use of cardiac glycosides	2.77	0.99-7.79

AOR: Adjusted OR.

Table 4 Patients referring *de novo* gastrointestinal smptoms after cerebrovascular accident or orthopedic trauma *n* (%)

Gastrointestinal symptoms	Hemiplegics *n* = 90	Orthopedics *n* = 81	OR	95% CI	*P* value
Dysphagia	14 (15.5)	0 (0)	∞	3.36-∞	0.0001
Heartburn	2 (2.2)	0 (0)	∞	0.27-∞	0.51
Abdominal pain	6 (6.7)	2 (2.5)	2.82	0.48-29.22	0.28
Fecal incontinence	5 (5.5)	3 (3.7)	1.53	0.29-10.15	0.72

Other gastrointestinal symptoms

Gastrointestinal symptoms other than constipation occurred after stroke or orthopedic trauma, are reported in Table 4. Although the risk of onset of other GI symptoms was higher after stroke than that of orthopedic injury, the difference did not reach statistical significance in any of them but dysphagia.

After stroke, constipation was associated with dysphagia in 7/14, and incontinence in 2/14 of the patients.

Characteristics of neurological lesions and GI symptoms

Chronic constipation was reported in 63% (17/27) of hemiplegic patients after right brain hemispheric injury and in 37% (10/27) hemiplegic patients after left brain hemispheric lesions (n.s.). Injured brain sites in *de novo* constipated patients were thalamo-capsular area (11/25, 41% patients, OR = 2.83 *vs* parietal area: 5/18 patients 18.5%, reference group), temporal area (1/6 patients, OR = 0.6 *vs* parietal area), multisited lesions including frontal, temporal and parietal (8/11 patients, OR = 2.62 *vs* parietal area), other sites (2/8 patients, OR = 0.9 *vs* parietal area). Dysphagia, constipation, as well as concomitant occurrence of constipation with dysphagia or with fecal incontinence, did not significantly differ between patients with right or left brain hemispheric lesion, or with different sites of lesion.

DISCUSSION

It is known that the central nervous system (CNS) takes part in the control of visceral functions and its damage can lead to gastrointestinal impairment as demonstrated in spinal cord lesions[11,12] and in many other neurological diseases, such as Parkinson's disease[13], multi system atrophy[14], multiple sclerosis[15], and Altzheimer disease[3].

Dysphagia[16] and bowel dysfunction are the most frequent gastrointestinal complaints reported after stroke. Previous studies have attempted to evaluate the prevalence and pathogenesis of chronic constipation after stroke[3,17]. A statistical association between constipation and stroke both in institutionalized subjects[3] and in independently-living elderly subjects[17], has been reported.

However, neither prevalence of after stroke constipation nor the pathogenic role of neurological lesions per se in causing bowel dysfunction has never been convincingly proven for the concomitance of confounding factors such as old age, pharmacological treatment, and mental disability.

In addition, previous studies[3-4] did not attempt to differentiate constipation presenting *de novo* after stroke from that already presented prior to CVA. Furthermore, these studies did not use a standardized definition of chronic constipation and relied on the patient's self definition.

The degree of physical inactivity is related with the risk of constipation[18,19]. No previous investigation has assessed the relationship between stroke and the degree of body mobility, with the exception of Robain and coworkers[4]. However, their observation, indicating a possible association between stroke and body immobility, refers to the immediately after-stroke period of two weeks. Moreover, it lacked a comparative group, and did not differentiate between *de novo* and pre-existing constipation.

In our study, to assess the role of CVA in bowel dysfunction, the neurological patients were examined after stabilization of the lesion, at the end of motor rehabilitation. They were compared with non neurological ones who presented the same mobility, and other risk co-factors for constipation, such as diet and drug consumption[20]. The orthopedic control group had an older age and comprised more females than the neurological group. These differences, however, did not appear to influence the results of this study. Old age and female gender that are considered predisposing factors for constipation[21], prevailed in the orthopedic control group that referred less constipation than the neurological one. In addition, a gender-related risk of constipation was probably balanced because it was reported that in elderly people, as those investigated, the risk for constipation is comparable in males and females[21]. In this study group, constipation was not associated with age or physical mobility, but most of the enrolled patients were elderly. Moreover, all patients and controls were affected by reduced mobility to avoid these confounding factors. Furthermore, a significant association between constipation and hemiplegia has been confirmed by multivariate analysis after adjustment for age, sex and mobility degree.

Different from previous studies, only *de novo* constipation is used as an international standardized definition of chronic constipation with both bowel frequency and dysfunction of evacuation taken into account[8]. In our study, only subjects with a normal cognitive status were enrolled to exclude patients who were unreliable or had reduced awareness and insufficient cognitive status.

De novo constipation was significantly more frequent after CVA than orthopedic trauma, indicating that CVA represents an independent risk factor for constipation. The association between *de novo* constipation and hemiplegia was higher after hemorrhagic event than after ischemia. This observation demonstrates a trend associating constipation and increased severity of stroke. The risk of constipation due to CVA may be underestimated in this study group, because it excluded patients with impaired cognitive status, usually consequent to more severe ictus.

No significant association was found in this study population between *de novo* chronic constipation and use of ACE inhibitors, anticoagulants and calcium antagonists. Constipation was otherwise significantly associated with assumption of nitrates, antithrombotics and cardiac glycosides. The effect of nitrates, antithrombotics and cardiac glycosides on *de novo* constipation did not differ between neurological and orthopedic patients.

Nitroglycerin[17] has been associated with constipation in elderly subjects. Although not fully clarified, nitrates may cause constipation due to the inhibitory role in gut motility secondary to the release of nitric oxide[22,23]. Antithrombotic drugs used by the patients investigated in the present study were acetyl salicylic acid (ASA), indobufen, and ticlopidine. All of them have been reported to be associated with bowel alterations[24-27]. ASA and NSAID appear to be more frequently associated with constipation[24] probably via inhibition of the propulsive activity by preventing the release of prostaglandins[25]. Indobufen and ticlopidine are usually associated with diarrhea[26,27] and the apparent relationship with constipation is not easily explained by their known pharmacological mechanism of action[28]. Although the association between calcium antagonists and constipation did not reach the level of statistical significance, it is consistent with the notion that constipation is a possible adverse event of these drugs[29]. No data are available in literature assessing relationship between digoxine and constipation. However, contribution of each of the above mentioned drugs in inducing constipation could not be properly assessed since 70% and 35% of the patients received combination therapy, with at least two and three drugs respectively.

De novo constipation occurred in 30% of the hemiplegic patients and did not have any consistent relationship with anyone of the hemispheric sides, or with the severity of stroke even if a trend of reduced risk of constipation was noted in patients with a less widespread lesion.

It can be hypothesized that, not different from the act of swallowing, cortical control of the defecatory function derives from centers located in both hemispheres[30] being only one of the two physiologically dominant. Topographic cortical mapping performed with transcranial magnetic stimulation has shown that anal and rectal responses are in fact bilaterally represented on the superior motor cortex of both cerebral hemispheres[31]. In analogy with after stroke dysphagia, constipation too may become a clinically manifestion only when CVA damages the

defecatory dominant center, and controlateral center is unable to maintain the control of anorectal function.

Patients, who become dysphagic immediately after CVA, might recover with time when the controlateral non-injured center acquires the control of the complex act of swallowing[16]. In the present study, patients were investigated after stabilization of neurological lesions following a program of motor rehabilitation. Future investigations should evaluate the entity of post CVA recovery of constipation, if any, comparing bowel dysfunction immediately after CVA and after stabilization of the lesion and during a rehabilitative treatment.

Only 50% of the dysphagic patients complained of *de novo* constipation and the concomitant presence of both dysfunctions had no relationship with the site of neurological lesions. This finding is consistent with previous studies that identified distinct centers controlling the pharyngo-esophageal and anorectal function[31,32].

Data of this study did not show any association between *de novo* constipation and lesions of specific brain sites, but this relationship could not be properly addressed in the present investigation because brain injuries were widespread involving several centers and damaging many nervous loops.

Fecal incontinence has been reported to occur in about 30% of patients in the first few weeks immediately after stroke and between 3%-11% at 3 months and thereafter[33,34]. The 5.5% prevalence of *de novo* fecal incontinence at least 3 months after a CVA in patients of this study, is consistent with previous reports[33]. The largely transient and early manifestation of fecal incontinence after stroke appears to be related more to impaired consciousness, immobility and inadequate nurse assistance than to the neurological damage per se. The similar occurrence of fecal incontinence in hemiplegic and orthopedic patients suggests that this phenomenon can be secondary to other factors than the neurological damage.

This study shows that chronic constipation is a frequent outcome secondary to cerebrovascular accident. Constipation is due to neurological lesions independently from the injured brain hemisphere, and is unrelated to age, gender and physical inactivity.

The risk of developing chronic constipation with CVA in either one of the cerebral hemispheres suggests that defecatory centers are located in both hemispheres being only one of the two physiologically dominants. The role of drugs as a co-factor in constipation after stroke must be better evaluated and interpreted.

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