Comparison of New Onset Constipation Response to Lactolose, Bisacodyl in Acute Stroke Patients

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Abstract

Background: Constipation is one of the most common medical complications of acute stroke and new onset constipation is associated with poor stroke outcomes. Purpose: The present study designated to investigate and compare new onset constipation response to Lactulose, Bisacodyl treatment in acute stroke patients. Methods: This is an interventional study of 45 patients admitted with acute stroke. Patients were examined by the defecation in second day and constipated patients were treated by lactulose or Bisacodyl readomly. Severity of stroke was assessed by means of NIHSS. Finally, response to treatment in both lactulose and Bisacodyl treated groups and correlation between stroke severity and response to treatment was measured. Results: Our finding showed that average response to treatment in Bisacodyl group was weaker than lactulose group. Nonetheless, there was positive significant correlation between severity of stroke and response to treatment. Other correlations were insignificant. Conclusions: This study showed that in acute stroke patients with acute constipation, Bisacodyl prescription might be associated with better neurologic outcome.

Key words: Acute Constipation, Acute Stroke, NIHSS.

Introduction

Cerebrovascular accident or stroke is a neurological deficit of abrupt onset attributable to a focal vascular cause. (Smith et al., 2012) Each year near to 17 million new strokes occur worldwide, representing an important public health burden, with the majority of event causing permanent disability or death. (Feigin et al., 2014; Kung et al., 2008) Recent studies suggest that GI complication can also contribute to protracted hospitalization, dependency, poor neurological outcome and even demise. (Su et al., 2009) Constipation is often overlooked as a trivial medical concern, nonetheless, it can be associated with mild to extreme distress and potentially precarious complications. (Tariq, 2007) Constipation is a rife symptom among patients with central nervous system disease, including ischemic stroke, and can exacerbate social functioning and quality of life. (Krogh et al., 2001; Krogh and Christensen, 2009) Constipation is one of the most common medical complication of acute stroke. (Doshi et al., 2003; Ingeman et al., 2011) It affects a person's physical health as well as psychological wellbeing and quality of life. (Dennison et al., 2005; Su et al., 2009) Despite its high prevalence, it is considered a non-life-threatening condition. Constipation has been linked to many neurological diseases including stroke. (Ullman et al., 1996; Winge et al., 2003) In the present study, we adopted the symptom-based Rome 3 criteria (Thompson et al., 1999) to exclude preexisting constipation before stroke and diagnose new-onset constipation at acute stage after stroke because this is widely used in research and clinical practice, retrospectively to make a better discrimination in constipation resulting from new onset of stroke and its treatments. (Pare et al., 2001; Bassotti et al., 2004; Bradley et al., 2007; Ponce et al., 2008; Marfil et al., 2005)

Constipation is affecting 60% of stroke patients in rehabilitation wards. (Robain et al., 2002) We identified only 2 published clinical studies of constipation in stroke which didn't include medicinal intervention. Munchiando found that daily versus alternate day digital bowel stimulation lead to regular evacuation sooner after acute stroke in an uncontrolled trial study, (Munchiando and Kendall, 1993) whereas Venn found no difference in efficacy between morning versus evening inpatient bowel care, with or without a suppository. (Venn et al., 1992)

Contemplating aforementioned lack of comprehensive research literature and the need for more investigation in after-stroke constipation as determining critical factor for patient's both physical and mental well-being, the current study aimed to assess the responsiveness to

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two type of laxatives in new onset constipation among patients after their stroke and the association with type of stroke to determine if it is beneficial for treatment of new onset constipation in stroke patients as a clinical routine. Consequently, we evaluated the effects of lactulose and Bisacodyl on new onset constipation of acute stroke patients, to see more common prescription of these two drugs in clinical practice.

Material and methods

Study design:

This study was confirmed by Iranian Randomized Clinical Trials center (IRCT20181009041286N1). We recruited participants from neurology section of Shahid-Beheshti Hospital in Kashan, Iran who had experienced acute stroke from January 2014 to June 2015. Patients were screened by researcher made Checklist to identify constipation according to standardized definitions. (Harari, 2002; Potter et al., 2002; Talley et al., 1993):

Constipation (≤ 2 bowel movement per week or ≥ 2 of the following on more than 1 in 4 occasions: straining, hard stool, feeling of incomplete evacuation).

Patients with confirmed stroke diagnosis by brain imaging and hospitalized within 48 hours of symptoms beginning and with the above mentioned constipation met the inclusion criteria. individuals reporting preexisting constipation or fecal incontinence, history of colon or rectum cancer, constipation producing metabolic disturbance such as hypokalemia, taking drug induced constipation such as anticholinergic, calcium channel blocker and so on were excluded. Random selection was done by external process using computer-generated numbers and closed envelopes.

Intervention:

Patients were inquired at ward setting. The intervention consisted of administering 30 cc lactulose syrup (20 g) or 10 mg Bisacodyl tablet in two groups of patients (the above-mentioned doses of drugs were in association with their maximum dosage in pharmacologic references). During and after the administration of the drug, the patients were regularly visited for evaluating if defecation had occurred. After that, we started to measure and record the treatment period of the medications used. Group A (the Bisacodyl group) were treated by Bisacodyl (with the dose of 10 mg) and Group B (the lactulose group) were treated by lactulose (with the dose of 20 gr). For the patients who had discharged sooner Were Followed-up via phone call

Statistical analysis:

SPSS 18 were used for data analysis. Chi-square test or Fisher's exact test were utilized to compare qualitative variables between two groups, and Independent t test and Mann Whitney U test for quantitative variables between two groups. P-value<0.05 was considered statistically significant.

Result

During the study, stroke patients were admitted to the department of neurology and stroke center of the hospital. Of all stroke patients 50 met the inclusion criteria on admission procedure. Five patients were excluded because of the change in type and amount of laxative prescribed and confirmed by other neurologists. We studied 45 stroke patients, the mean time for admission was 2 hours and mean length of stay in hospital was 7 days. The mean age was 72 (range: 32 to 93). The majority of them were female (56.5%). There were 40 (88.9%) ischemic stroke patients and 5 intracerebral hemorrhage (11.1%).

The mean and SD for response to treatment was 1.96±1.98 in Bisacodyl group and 2.73±1.72 in lactulose group.

The mean of rating was 19.26 in Bisacodyl group and 26.91 in lactulose group. In Mann Whitney U nonparametric test, there was no significant statistical difference between two groups (p=0.04). Also, there was 3 Perth value in Bisacodyl group and 1 in lactulose group.

We omitted Perth data and used parametric independent T-test, consequently and the mean of response to treatment was 1.55 ± 0.99 in Bisacodyl group and 2.76 ± 1.76 in lactulose group and the statistical deference was significant. There was significant and positive correlation between the severity of stroke and response to treatment (p=0.001, r=0.44) as well as severity of stroke and duration of hospitalization. The respective variables are presented in table 1 and 2.

Discussion

It seems momentous to have a clear and reliable definition of constipation. (Robain et al., 2002; Winge et al., 2003) In this study we used Rome III criteria to diagnose the new onset constipation after stroke and exclude preexisting constipation before stroke. There has been few studies to compare medical treatment in new onset constipation after stroke. In the general population, constipation is more common in female and elderly patients (Stewart et al., 1999) and in our study majority of the patients were female, however, our sample size was inadequate to find out this association. Constipation has been found to be associated with poor stroke outcome in rehabilitation unit. (Otegbayo et al., 2006) In Yongjing Su study, new onset constipation is associated with poor stroke outcome among patients with strokes of moderate severity at baseline (NIHSS 4 to 11). Nevertheless, such association cannot be shown in patients with mild or severe stroke. We speculate that there was positive and significant correlation between response to treatment and duration of hospitalization, and response to treatment and duration of hospitalization was longer in patients with moderate to severe stroke (NIHSS ≥ 11), however this association was absent in the mild stroke.

Poor response to treatment in moderate to severe stroke maybe is related to use of nasogastric tube and dysphagia because of insufficient fiber diet in them. Of course our sample size was not adequate to confirm the association between nasogastric tube and constipation. On Otegbbayo et al. study, (Otegbayo et al., 2006) there was no significant difference in GI symptoms in site or type of stroke, except that constipation was more common in ischemic stroke. In our study the number of ischemic stroke patients who had constipation were much more, but we couldn't conclude that constipation is more common in these patients because of low sample size.

In summary, response to both drugs (Bisacodyl and lactulose) in stroke patients was as same as its effects on general population and this looks that there is no difference in pathophysiology.

Conclusion

Our data showed that acute stroke patients with new onset constipation respond better to Bisacodyl than lactulose as in general population and also there is meaningful and positive correlation between severity of stroke and response to treatment and duration of hospitalization.

Authors Contributions

Elina Rafiee: Data curation

Reza Daneshvar: Conceptualization, Methodology

Conflict of Interest

The authors have no potential conflicts of interest to disclose.

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References

- Bassotti, G., Bellini, M., Pucciani, F., Bocchini, R., Bove, A., Alduini, P., ... & Italian Constipation Study Group. (2004). An extended assessment of bowel habits in a general population. *World journal of gastroenterology*, 10(5), 713.
- Bradley, C. S., Kennedy, C. M., Turcea, A. M., Rao, S. S., & Nygaard, I. E. (2007). Constipation in pregnancy: prevalence, symptoms, and risk factors. *Obstetrics & Gynecology*, 110(6), 1351-1357.
- Dennison, C., Prasad, M., Lloyd, A., Bhattacharyya, S. K., Dhawan, R., & Coyne, K. (2005). The health-related quality of life and economic burden of constipation. *Pharmacoeconomics*, 23(5), 461-476.
- Doshi, V. S., Say, J. H., Young, S. H., & Doraisamy, P. (2003). Complications in stroke patients: a study carried out at the Rehabilitation Medicine Service, Changi General Hospital. Singapore Med J, 44(12), 643-52.

- Feigin, V. L., Forouzanfar, M. H., Krishnamurthi, R., Mensah, G. A., Connor, M., Bennett, D. A., ... & O'Donnell, M. (2014). Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. *The Lancet*, 383(9913), 245-255.
- Harari D. (2002). Constipation and faecal incontinence in old age. In: Tallis RC, Fillit SH, Brocklehurst's Textbook of Geriatric Medicine and Gerontology.6th ed. London: Churchill Livingstone.
- Ingeman, A., Andersen, G., Hundborg, H. H., Svendsen, M. L., & Johnsen, S. P. (2011). Processes of care and medical complications in patients with stroke. *Stroke*, 42(1), 167-172.
- Krogh, K., & Christensen, P. (2009). Neurogenic colorectal and pelvic floor dysfunction. Best Practice & Research Clinical Gastroenterology, 23(4), 531-543.
- Krogh, K., Christensen, P., & Laurberg, S. (2001). Colorectal symptoms in patients with neurological diseases. ACTA Neurologica scandinavica, 103(6), 335-343.
- Kung, H. C., Hoyert, D. L., Xu, J., & Murphy, S. L. (2008). Deaths: final data for 2005. Natl Vital Stat Rep, 56(10), 1-120.
- Marfil, C., Davies, G. J., & Dettmar, P. W. (2005). Straining at stool and stool frequency in free-living and institutionalised older adults. *The journal of nutrition, health & aging*, 9(4), 277-280.
- Munchiando, J. F., & Kendall, K. (1993). Comparison of the effectiveness of two bowel programs for CVA patients. *Rehabilitation Nursing*, 18(3), 168-172.
- Otegbayo, J. A., Talabi, O. A., Akere, A., Owolabi, M. O., Owolabi, L. F., & Oguntoye, O. O. (2006). Gastrointestinal complications in stroke survivors. *Tropical gastroenterology: official journal of the Digestive Diseases Foundation*, 27(3), 127-130.
- Pare, P., Ferrazzi, S., Thompson, W. G., Irvine, E. J., & Rance, L. (2001). An epidemiological survey of constipation in Canada: definitions, rates, demographics, and predictors of health care seeking. *The American journal of gastroenterology*, 96(11), 3130-3137.
- Ponce, J., Martínez, B., Fernández, A., Ponce, M., Bastida, G., Plá, E., ... & Ortiz, V. (2008). Constipation during pregnancy: a longitudinal survey based on self-reported symptoms and the Rome II criteria. *European journal of gastroenterology & hepatology*, 20(1), 56-61.
- Potter, J., Norton, C., & Cottenden, A. (Eds.). (2002). Bowel care in older people: research and practice. Royal College of Physicians.
- Robain, G., Chennevelle, J. M., Petit, F., & Piera, J. B. (2002). Incidence of constipation after recent vascular hemiplegia: a prospective cohort of 152 patients. *Revue neurologique*, 158(5 Pt 1), 589-592.
- Smith, W.S., English, J.D. & Johnson, S.C. (2012). Harrison's principles of internal medicine. McGraw-Hill, NewYork.
- Stewart, W. F., Liberman, J. N., Sandler, R. S., Woods, M. S., Stemhagen, A., Chee, E., ... & Farup, C. E. (1999). Epidemiology of constipation (EPOC) study in the United States: relation of clinical subtypes to sociodemographic features. *The American journal of* gastroenterology, 94(12), 3530-3540.
- Su, Y., Zhang, X., Zeng, J., Pei, Z., Cheung, R. T. F., Zhou, Q., ... & Zhang, Z. (2009). New-onset constipation at acute stage after first stroke: incidence, risk factors, and impact on the stroke outcome. *Stroke*, 40(4), 1304-1309.
- Talley, N. J., Weaver, A. L., Zinsmeister, A. R., & Melton III, L. J. (1993). Functional constipation and outlet delay: a population-based study. *Gastroenterology*, 105(3), 781-790.
- Tariq, S. H. (2007). Constipation in long-term care. Journal of the American Medical Directors Association, 8(4), 209-218.
- Thompson, W. G., Longstreth, G. F., Drossman, D. A., Heaton, K. W., Irvine, E. J., & Müller-Lissner, S. A. (1999). Functional bowel disorders and functional abdominal pain. *Gut*, 45(suppl 2), II43-II47.
- Ullman, T., & Reding, M. (1996, September). Gastrointestinal dysfunction in stroke. In *Seminars in neurology* (Vol. 16, No. 03, pp. 269-275). © 1996 by Thieme Medical Publishers, Inc.
- Venn, M. R., Taft, L., Carpentier, B., & Applebaugh, G. (1992). The influence of timing and suppository use on efficiency and effectiveness of bowel training after a stroke. *Rehabilitation Nursing*, 17(3), 116-121.
- Winge, K., Rasmussen, D., & Werdelin, L. (2003). Constipation in neurological diseases. Journal of neurology, neurosurgery, and psychiatry, 74(1), 13.

Variable	Areas	Bisacodyl Group	Lactulose Group	P-value
Age		70.09±11.84	74.18±16.76	0.35
Sex	Female	13(56.5%)	9(40.9%)	0.29
	Male	10(43.5%)	13(59.1%)	
Type Of Stroke	Ischemic	19(82.6%)	21(95.5%)	0.19
	Hemorrhagic	4(17.4%)	1(11.1%)	
Severity of Stroke	Mild	12(52.2%)	10(45.5%)	0.65
	Moderate To Severe	11(47.8%)	12(54.5%)	
Side of Stroke	Left	11(50%)	14(63.6%)	0.36
	Right	11(50%)	8(36.4%)	
Cerebral Location of Stroke	Cortical	10(43.4%)	17(77.3%)	0.3
	Subcortical	12(52.1%)	4(18.1%)	1
	Infratentorial	1(4.3%)	1(4.5%)	1

Table 1. Univariate Analysis on the association between New-onset constipation and Demographics

There was no meaningful difference between two groups with respect to all of the variables.

Table 2. Univariate Analysis results

Variable	Bisacodyl Group Mean±SD	Lactulose Group Mean±SD	p-value				
Duration of response	1.96	1.98	0.04^{*}				
NIHSS	10.96±8.34	11.09±5.23	0.95*				
*Mann Whitney U test							

There was meaningful, borderline statistical difference between two groups with respect to duration of response. There was no meaningful difference between two groups with respect to NIHSS (National Institute of Health Stroke Scale).

Model	Unstandardized coefficients		Standardized coefficients	Т	P-value
Constant	1	1.384	-	0.723	0.474
Group	-0.007	0.435	-0.341	-2.315	0.026
Sex	0.347	0.431	0.118	0.805	0.426
ages	0.016	0.015	0.155	1.067	0.292

 Table 3. Multivariate Analysis results

We used Linear regression test for multivariate analysis. Meaningful variable at univariate analysis and borderline variables were included by Enter model. By elimination of confounding effect of age and sex, group variable was meaningful likewise. The results are presented on table 3.