Bulletin of Environment, Pharmacology and Life Sciences Bull. Env. Pharmacol. Life Sci., Vol 3 (4) March 2014: 01-06 ©2014 Academy for Environment and Life Sciences, India Online ISSN 2277-1808 Journal's URL:http://www.bepls.com CODEN: BEPLAD Global Impact Factor 0.533 Universal Impact Factor 0.9804



## **ORIGINAL ARTICLE**

# The Comparison of the Effects of Two Herbal Medicines, Namely Senna and Lactulose, on Induced Acute Constipation in Rabbits

## Saam Torkan<sup>1\*</sup> and Faham Khamesipour<sup>2</sup>

<sup>1\*</sup>Department of Small Animal Internal Medicine, Faculty of Veterinary Medicine, Islamic Azad University, Shahrekord Branch, Shahrekord, Iran

<sup>2</sup> Young Researchers and Elite Club, Islamic Azad University, Shahrekord Branch, Shahrekord, Iran

#### ABSTRACT

Constipation is a disease caused by various factors and results in the remaining of stools in colons, excessive water absorption by stools, hardening of stools and in case not treated degeneration of neural network inside colons and mega colons and is a common disease in small animals. The purposes of this study after the constipation was induced, it was treated by Senna in one group, Lactulose in another group and placebo in the third one. After a specified period of time, the information was analyzed and the treatment effects of Senna and Lactulose were compared. This Study is a clinical and semi blind trial and was performed on 30 rabbits with the same sex, breed, age and weight. These statistical studies states that lactulose with dose 0.2 ml in respect of per kg body weight was more effective than lactulose (p<0.01). Whereas there were not significant statically differences between more or less dose of Senna in respect of treatment duration. These statistical analyses on vital factors showed that dose 18-22 mg of Senna could make significant changes in respiratory rate and blood factors such as PCV, RBC rate, WBC density, full and subtracted count of WBC, Neutrophil and Lymphocytes, in this group as compared with other group.

Keywords: Herbal Medicines, Senna, Lactulose, Acute Constipation, Rabbits

Received 12/02/2014 Accepted 06/03/2014

©2014 AELS, INDIA

## INTRODUCTION

Constipation is a disease caused by various factors such as food, drugs, neuro-muscular diseases, inguinalrectal pains, trauma, large intestine, rectum and anus obstructions, and results in the remaining of stools in colons, excessive water absorption by stools, hardening of stools and in case not treated degeneration of neural network inside colons and megacolons [1, 2].

Constipation which is divided into two types: acute and chronic, is a common disease in small animals [3]. In order to cure constipation, first the primary symptoms should be diagnosed and treated. Herbal medicines and other methods like enema, etc. should be used simultaneously as well [3].

The continuity of the disease can cause loss of appetite, vomiting and if not treated degeneration of neural network inside colons and mega colons [1, 2]. Senna is a laxative and purgative medicine in the form of Senna lax tablets (a product of Iran Daroo Company) produced from the leaves of Senna plants scientifically known as Cassia angustifol. This tablet contains 9-11 mg of A and B sennosides [1, 2, 4-6].

Lactulose is also a laxative and purgative medicine used orally (that works like an osmotic laxative). However, this medicine causes dehydration and an increase in Sodium extraction [2, 6-8].

In this study after the constipation was induced, it was treated by Senna in one group, Lactulose in another group and placebo in the third one. After a specified period of time, the information was analyzed and the treatment effects of Senna and Lactulose were compared.

## **MATERIALS AND METHODS**

## Samples collection

All experiments were carried out under ethical guidelines of the Islamic Azad University of Shahrekord Branch, for the care and use of animals. This research was performed on 30 rabbits with the same sex,

breed, age and weight. All the rabbits were from Angora breed and were numbered with special labels. Senna is a laxative and purgative medicine in the form of Senna lax tablets (a product of Iran Daroo Company) produced from the leaves of Senna plants scientifically known as Cassia angustifol. This tablet contains 9-11 mg of A and B sennosides. After being treated with anthelminthes to assure their physical health, they were prepared for the test and divided into 5 groups of 6 rabbits: groups A, B, C, D and E (the average weight of each group was 1.5kg.). All the rabbits in each 5 groups were females and were kept under similar conditions with the same diet. They were provided with food and water with no limitations. The first day of the study was considered day zero, the criteria of which was the administration of 0.1 mg of Loperamide for each kg of body weight for all rabbits (to induce constipation). Before the administration of Loperamide on day zero, the rabbits were clinically examined, their vital signs were recorded and their blood samples were collected for hematology tests. In addition, to examine the digestive systems of the rabbits latrolateral and ventrodorsal graphies were taken ,and their stools were checked to make sure they are in normal condition. On day zero of the study, Loperamide (in the form of a syrup produced by Pakdaroo Company) was used with the dose of 0.1 mg per kg of body weight every 8 hours. During the administration of the drug, the rabbits were regularly examined for clinical signs, stool, the quantity of the stool and its density and the ease of defecation. After 5 days, on day 4 of the study when 15 doses of Loperamide was already given to each rabbit, their stools were completely dry, hard and very little in amount. Latrolateral and ventrodorsal graphies taken from each rabbit at this time confirmed constipation in all of the rabbits. After hematology tests, we started to treat each group, measuring and recording the treatment period of the medications used. Group A (the control group) were treated by physiological serum as placebo, the quantity of which for each dog was equal to the quantity of Lactulose used (0.1 mg per kg). In this group the treatment of constipation was decided according to the clinical signs proved by radiography. Group B were treated by Lactulose(with the dose of 0.1 ml per kg of body weight) every 8 hours. Group D were treated by one Senna Lax tablet produced by Iran Daroo Pharmaceutical Company (containing 9-11 mg of A and B sennosides) every 24 hours.

## Statistical analysis

Data were transferred to a Microsoft Excel spreadsheet (Microsoft Corp., Redmond, WA, USA) for analysis. Using the Statistical Package for the Social Sciences (SPSS) 18.0 statistical software (SPSS Inc., Chicago, IL, USA).

## **RESULTS AND DISCUSSION**

In this study to compare the treatment effects of Senna and Lactulose on induced constipation by Loperamide in rabbits, the treatment periods of the prescribed medicines with various concentrations in all groups were statistically analyzed. The mean and the standard deviations of vital signs and hematology tests prior and after induced constipation are presented in tables 1 to 3.

It should be mentioned that number 1 is added to the name of the groups before induced constipation, number 2 is added to their names after induced constipation, and number 3 is added when constipation is cured.

The mean of treatment period in group A3 was 120 hours. The statistical analysis of the results showed no significant differences regarding the treatment period between group B3 and the groups treated with placebo (A3). However ,there was a significant difference between groups C3 and B3 with the groups treated by placebo (p<0.01).

These results indicated that Lactulose with the dose of 0.2 ml per kg body weight is more effective than Lactulose with the dose of 0.1 ml per kg body weight or placebo on the treatment of induced constipation by Loperamide in rabbits. In addition, there was a significant difference regarding the treatment period between the groups treated by 9-11 mg (one tablet of Senna Lax) with the groups cured with placebo (A3), the group treated by 0.1 dose of Lactulose (B3) and group C3.

According to the clinical examinations and vital signs records, the respiration rate in group C3 was 43 breaths per minute, and in group E3, 53 breaths per minute (Table 3) which was statistically significant. Apparently, the dose used to treat induced constipation by Loperamide in rabbits in group E3 exceeds the required amount and the dose used in group D3 is more appropriate regarding the fewer effects it had on blood factors.

The advantages of Senna Lax such as fewer side-effects, stronger effects than Lactulose and many other laxative-purgatives, easier usage compared with vegetable and mineral oils, no respiratory pneumonia, easier administration along with the food compared with enema (thus causing less annoyance for the animal) together with availability turn it into a good option for treating sever constipation that does not require enema in rabbits and other species.

Groups	Respiratory Rate per minute	Heart Rate per minute	body temperature	PCV %	RBC* 106	Hb gr/dl	WBC/M lit	Nut %	Lym %	Mon %	Eos %	Baso %	Band %
A1	46±3.8	232±32.4	38.1±0.42	38.8±2.6	6.3±0.4	12.5±0.8	8916±2596	42.6±9.5	50.5±6.4	3.1±0.7	3±1.6	0.8±0.7	2.1±1.9
B1	45±3	204±7.8	38.1±0.27	42±3.6	7±0.7	14±1.4	$11666 \pm 2483$	$51.8 \pm 10.1$	37.1±10.1	3.8±2.1	3.5±2.1	8.0∓9.0	2±1
C1	42±4.8	219±23.9	38.4±0.38	40.8±1.7	6.6±0.4	13.3±0.8	$11500\pm632$	45.6±8.6	45.1±8.1	3.3±2	3.3±2.4	6.0∓8.0	1.6±0.5
D1	45±4.3	209±9.4	37.9±0.17	43.5±4.8	7.4±0.8	14.9±0.7	$12416 \pm 1319$	58.1±16.4	35.3±17.7	$1.6 \pm 0.8$	1±1.2	0.3±0.5	1.6±1
E1	47±2.9	209±9.4	38±0.21	39.1±2.1	6.7±0.69	12.5±0.8	$1025\pm821$	40.3±7.7	50.8±6.8	3.1±0.7	3±1.6	0.6±0.8	1.8±1.7

Table 1. The mean and the standard deviations of vital signs and hematology tests prior induced constipation.

Senna is a laxative purgative anthraquinone that has been used as a safe herbal medicine to treat constipation in human beings and is grouped as a none-oil purgative (1,2, 4-6). This plant, whether used alone or together with other laxatives, treats constipation caused by unknown factors and is more effective than other laxatives [9].

Senna contains H.glycoside, also known as Sensodine, which stimulates the function of colons and increases the discharge of liquids by them, through which it applies the purgative effects (1, 2, 4- 6). Combinations like Loperamide increase intestinal segmental movements and decrease the speed by which materials move through the intestines [6]. All of the three drugs (senna, fibre, and fibre + senna) increased stool weight significantly in Ewe et al (1993) study [10].

the results by Ramesh et al study (1998) indicate that the small volume of the drug required for effective laxative action, the tolerable taste, the once-daily dose, the acceptable side effect profile, and the low cost make Misrakasneham a good choice for prophylaxis in opioid-induced constipation [11].

In a double-blind crossover study the efficacies of Agiolax, a combination of fibre and senna pod, and lactulose were compared in 77 long-stay elderly patients with chronic constipation. Mean daily bowel frequency, stool consistency and ease of evacuation were significantly greater with Agiolax than lactulose. The recommended dose was exceeded more frequently with lactulose than Agiolax (chi 2 = 8.38, p < 0.01). Adverse effects were not different for the 2 treatments. In long-stay elderly patients with chronic constipation Agiolax and lactulose were well tolerated, but Agiolax proved a more effective treatment (9).

Thirty geriatric long-stay patients aged 65-94 years (mean 81.8) participated in the trial the aim of which was to examine bulk laxative plus senna (Agiolax) in the treatment of chronic constipation using lactulose (Levolac) as a reference medicine. Bulk laxative plus senna (daily doses 14.8 g) produced more frequent (p < 0.05) bowel habits (4.5 vs. 2.2-1.9/week) than lactulose (daily doses 20.1 g). Both laxatives proved to be safe to use. In this study indicated bulk laxative plus senna to be more efficient in treating constipation in geriatric long-stay patients [12].

E2	D2	C2	B2	A2	Groups
47±3.5	45±4.3	41±4.4	45±2.4	45±3.6	Respiratory Rate per
208±5	209±7	213±18	206±7	231±25	Heart Rate per minute
37±0.1	38±0.1	38.2±0.4	38±0.2	38.5±0.8	body temperature
39±2.1	41±6.5	39.8±3.4	40.6±2.3	36.6±3.4	PCV %
6.3±0.4	7±1.2	6.7±0.5	6.7±0.5	6±0.3	RBC* 106
12.5±0.8	14.3±2.4	13.4±1.4	13.4±1.4	12.5±0.8	Hb gr/dl
10333±60	11583±1393	10250±1864	1075±758	9666±3027	WBC/M lit
41±7.5	53.6±9.3	43.6±9.5	39.5±6.8	54.3±10.6	Nut %
52.1±6.3	36.3±9.3	49.6±9.8	54.3±6.2	37.6±10.8	Lym %
2.8±0.7	2.5±0.8	3.5±0.8	3.5±0.8	3.1±0.7	Mon %
2.5±2.2	1.8±0.7	2.3±1.8	2±2	2.3±1.5	Eos %
0.6±0.8	$0.5 \pm 0.5$	0.1±0.4	0.3±0.5	0.6±0.5	Baso %
0.2±0.4	ı	ı	'	'	Band %

 Table 2. The mean and the standard deviations of vital signs and hematology tests after induced constipation.

The aim of the study by Quah et al., (2006) was to compare the clinical efficacy and tolerability of fibre versus lactulose in outpatients with chronic constipation. In a prospective randomized crossover trial, patients were randomized to receive fibre or lactulose for four weeks. Between treatments, patients had at least one week free of laxatives. From 50 patients, of median age 50 years (range, 18-85) were recruited and 39 patients completed the trial. Compared to fibre, lactulose resulted in significantly higher mean bowel frequency (7.3, 95% CI 5.7 to 8.9 vs. 5.5, 95% CI 4.4 to 6.5; p=0.001) and stool consistency score (3.4, 95% CI 3.1 to 3.7 vs. 2.9, 95% CI 2.5 to 3.3; p=0.018). Scores for ease of evacuation were similar. The frequencies of adverse effects were not significantly different, but greater in the lactulose group. Mean patients' recorded improvement score was significantly higher after taking lactulose than fibre (6.2, 95% CI 5.5 to 7.0 vs. 4.8, 95% CI 4.0 to 5.9; p=0.017). Of the 39 patients who completed the trial, 24 (61.5%) preferred lactulose and 14 (35.9%) preferred fibre. Also, Lactulose had better efficacy than fibre for chronic constipation in ambulant patients, although both treatments were equally well tolerated in terms of adverse effects [13].

This Study, these statistical studies states that lactulose with dose 0.2 ml in respect of per kg body weight was more effective than lactulose with dose 0.1 ml in respect of per kg body weight and placebo, and also state that Senna was more effective than lactulose (p<0.01). Whereas there were not significant statically differences between more or less dose of Senna in respect of treatment duration. These statistical analyses on vital factors showed that dose 18-22 mg of Senna could make significant changes in respiratory rate and blood factors such as PCV, RBC rate, WBC density, full and subtracted count of WBC, Neutrophil and Lymphocytes, in this group as compared with other group.

Groups A3	Respiratory 46± Rate per minute	Heart Rate 219 per minute	body 38± temperature	PCV % 38.	RBC* 10 <sup>6</sup> 6.2:	Hb gr/dl 12.	WBC/M lit 105	Nut % 59±	Lym % 35.	Mon % 2.5:	Eos % 1.3:	Baso % 0.5:	Band % 1.3:	
	13.4	)±16	±0.3	1±2.2	±0.4	5±0.7	5836±1828	±14.3	3±13.6	±1	±0.5	±0.5	±0.8	
B3	45±3.8	210±10	38±0.2	40±1	6.5±0.3	13±0.8	10916±1020	42.5±5.4	52.5±4.3	1.6±1.2	$1.1 \pm 0.7$	1±0.8	$1.1 \pm 0.4$	
C3	43±3.3	217±10	38.2±0.2	40.5±2.4	$1.5 \pm 0.4$	13.2±0.8	11083±970	47.3±6.8	46.1±7	2.3±0.8	2.1±1.9	$0.5 \pm 0.5$	1.5±9.5	
D3	51±4.8	221±9	37.8±0.2	42±2.7	6.8±0.6	13.8±1.1	11833±605	55.1±5.6	38.5±6	2.1±0.4	$1.3 \pm 0.5$	0.8±0.7	2.1±0.7	
E3	53±2.8	218±6	37.9±0.2	44±5.7	$7.5 \pm 1.1$	14.7±1.8	12333±683	61±9.5	32.1±9.2	2.8±0.7	1.3±0.5	0.3±0.5	$1.5 \pm 0.6$	

Table 3. The mean and the standard deviations of vital signs and hematology tests after treatment.

## ACKNOWLEDGMENTS

The authors would like to express their sincere thanks to Dr. Dariush Shirani of Department of Clinical Sciences, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran, Dr. Firoozeh Saghaei of Department of pharmacology, Faculty of Veterinary Medicine, Islamic Azad University, Shahrekord Branch, Shahrekord, Iran and Dr. Masoud Mirghaderi of Faculty of Veterinary Medicine, Islamic Azad University, Shahrekord Branch, Shahrekord, Iran for support me.

## REFERENCES

- 1. Kakino M., Tazawa S., Maruyama H., Tsuruma K., Araki Y., Shimazawa M., Hara H. (2010).Laxative effects of agarwood on low-fiber diet-induced constipation in rats. BMC Complement Altern Med.; 10: 68. doi: 10.1186/1472-6882-10-68.
- 2. Emmanuel A. (2011). Current management strategies and therapeutic targets in chronic constipation. Therapeutic Advances in Gastroenterology. 4(1) 37- 48. DOI: 10.1177/1756283X10384173.
- 3. Ettinger S.J., Feldman E.C. (2005) Textbook of Veterinary Internal Medicine, 6th edn. Elsevier Saunders, St Louis.
- 4. Morales M.A., Hern'andez D., Bustamante S., Bachiller I., Rojas A. (2009). Is Senna Laxative Use Associated to Cathartic Colon, Genotoxicity, or Carcinogenicity? Journal of Toxicology. Volume 2009, Article ID 287247, 8 pages. doi:10.1155/2009/287247.
- 5. Bum E.N., Nkantchoua G.N., Njikam N., Taiwe G.S., Ngoupaye G.T., Pelanken M.M., Nanga, Maidawa F., Rakotonirina A., Rakotonirina S.V. (2010). Anticonvulsant and sedative activity of leaves of Senna spectabilis in Mice.. Int. J. Pharmacol., 6: 123-128. DOI: 10.3923/ijp.2010.123.128.
- 6. Leung L., Kotecha J. (2011). Chronic Constipation: An Evidence-Based Review. J Am Board Fam Med. ; 24 (4):436–451.
- Voskuijl W., de Lorijn F., Verwijs W., Hogeman P., Heijmans J., Makel W., Taminiau J., Benninga M. (2004). PEG 3350 (Transipeg) versus lactulose in the treatment of childhood functional constipation: a double blind, randomised, controlled, multicentre trial. Gut.; 53:1590-1594.
- 8. Chen X., Zhai X., Kang Z., Sun X. (2012). Lactulose: an effective preventive and therapeutic option for ischemic stroke by production of hydrogen. Medical Gas Research.; 2: 3.

- 9. Passmore A.P., Davies K.W., Flanagan P.G., Stoker C., Scott M.G. (1993); A comparison of Agiolax and lactulose in elderly patients with chronic constipation. Pharmacology. Oct;47 Suppl 1:249-52.
- 10. Ewe K., Ueberschaer B., Press A.G. (1993); Influence of senna, fibre, and fibre + senna on colonic transit in loperamide-induced constipation. Pharmacology. Oct;47 Suppl 1:242-8.
- 11. Ramesh P.R., Kumar K.S., Rajagopal M.R., Balachandran P., Warrier P.K. (1998); Managing morphine-induced constipation: a controlled comparison of an Ayurvedic formulation and senna. J Pain Symptom Manage. Oct;16(4):240-4.
- 12. Kinnunen O., Winblad I., Koistinen P., Salokannel J. (1993); Safety and efficacy of a bulk laxative containing senna versus lactulose in the treatment of chronic constipation in geriatric patients. Pharmacology. Oct;47 Suppl 1:253-5.
- 13. Quah H.M., Ooi B.S., Seow-Choen F., Sng K.K., Ho K.S. (2006); Prospective randomized crossover trial comparing fibre with lactulose in the treatment of idiopathic chronic constipation. Tech Coloproctol. Jul;10(2):111-4. Epub 2006 Jun 19.

#### How to cite this article:

Saam T and Faham K. The Comparison of the Effects of Two Herbal Medicines, Namely Senna and Lactulose, on Induced Acute Constipation in Rabbits. Bull. Env. Pharmacol. Life Sci. 3 (4) 2014: 01-06