Plantago ovata: Clinical study of overuse

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Abstract: The objective of the study was to undertake evidence-base study to evaluate clinical manifestation of the over-estimated use of herbal drug *Plantago ovata* and to compare it with placebo for the efficacy and adverse effects. The patients of both genders were included. Blood urea, creatinine, ALT, Serum B12, CP, ESR and liver function tests were performed. The data was statistically analyzed in both groups for differential symptomatology. In anorexia test verses control results showed that *Plantago ovata* husk and placebo showed the affected ratio as 81 percent and 50 percent, correspondingly. Whereas in clinical performance of heart burning, pain in epigastrium, low libido, body pain, dyspepsia, fever, burning sensation in palm and sole in test drug showed affected response as adverse effect 90%, 88% and as control drug, 36%, 29%, 22%, 25%, 38%, 30%, 33%, 57%, respectively. The results were highly marked in test drug i.e. in comparison with placebo. This is clearly evident from data analysis that effect observed in test arm is far more superior hence null hypothesis was rejected clearly. Similarly serological and biochemical reports study i.e. (ALT, Vit. B1 and Vit A) revealed that there is no hepatotoxic and neurotoxic effect found in both the drugs.

Keywords: *Plantago ovata*, constipation, husk, herbal drug, hepatotoxic, neurotoxic.

INTRODUCTION

Dietary fibers are largely consumed for a variety of ailments like chronic constipation (Voderholzer *et al.*, 1997, HM Alvi 1282 Hijra), diarrhoea (Bliss *et al.*, 2001, HM Naseer, 1881), hemorrhoids (Perez-Miranda *et al.*, 1996), dysentery (AZ Gyahan, 1390), ulcerative colitis (Fernandez-banares *et al.*, 1999), irritable bowel syndrome (Jones *et al.*, 1982), reduced appetite (Turnbull *et al.*, 1995), hyperlipidemia (Chan *et al.*, 1998), hyperglycemia (Anderson *et al.*, 1999), atherosclerosis (JW Anderson, 1987), obesity (Rigaurd *et al.*, 1998), cancer of the stomach, colon and liver (Nardgaard *et al.*, 1996; Rodriguez-Cabezas *et al.*, 2003) and for removing toxic effects (as detoxificant, Cheallier *et al.*, 1996). The fibers are in abundance in variety of herbs. Amongst them the majority uses *Plantago ovata* as a good natural fiber source. Its seeds are rich in mucilage and fiber, hence used in variety of preparations as laxative. Approximately 10-30 present mucilage is found in the seeds. Husk and seeds have been used for the above-mentioned problems and modern day medicine has not only recommended its daily use but has regularly attempted to prove its worth. Certain ancient and modern authors have mentioned its side effects and contraindications. In Unani medicine the temperament of husk has been mentioned as cold and moist grade II *(Sard wa Tar Darja Doem)*. The husk has been mentioned to be cold and moist in order III (HM Nasir, 1847, Ibn Sina, 1906).

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MATERIALS AND METHODS

The study was conducted to observe its effect in human sufferers particularly those using *Plantago ovata* for more than six months to one year in different ailments. Furthermore to compare the effect of placebo and the test drug to evaluate side effect of both drugs.

An experimental randomized clinical trial was conducted to execute this research study in the period of June 2009 to 2012. The trials were carried out in, Matab Hamdard Defense and Al Qudrat Matab Gulshan Iqbal, Shifaul Mulk Memorial Hospital for Eastern Medicine, Hamdard University, Karachi. Only those cases were enrolled for this study, which fulfilled the inclusion criteria and referred from the physician to investigator after documenting their details in clinical trial protocol. The most difficult task in this study was to observe the ethical quandary to decide about using best-known effect of the treatment. The single blinded randomized control trials were conducted, no control arm alike the experimental group (treated with husk) and with regard to follow up that conditions are reserved similar for these groups.

Sample size

160 patients ranging the age 20-55 years were preliminary screened. The study duration was 4 years. Patients of all socioeconomic classes were taken from out patient departments of different health centers mentioned above.

STATISTICAL ANALYSIS

All the data collected at the three clinical centres including Al-Qudrat Matab Gulshan, Defense and Shifa ul

Mulk Memorial Hospital for Eastern Medicine, Hamdard University, Karachi. The data were entered into different softwares like Microsoft Office Vista, EPI info (SPSS for Windows version 12.0). The statistical analysis was performed by chi square test via SPSS.

Ethical issues and clinical trial approval

Study was conducted following the approval of Ethical Committee (EC) of Shifa-Ul-Mulk Memorial Hospital, Faculty of Eastern Medicine, Hamdard University Karachi, Pakistan. Study design and protocols were cleared by the Ethical Committee (EC) and permission was sought before the start of the clinical trial.

Clinical diagnosis of constipation (Inclusion criteria)

To diagnose constipation a complete proforma was followed having all details of patients' history and lab reports.

Treatment

The patient's recruited through set inclusion/exclusion criteria after careful diagnosis. It was observed that anaemia was mild to moderate with moderate leukocytosis in enrolled cases. Study populations were randomized into test and control groups. Control group treated with placebo while the test group received *Plantago ovata*.

Efficacy evaluation criteria

Completely affected

Those patients who got relief in constipation after 6 months treatment

Not affected

Those patients who didn't get relief in constipation after 02 weeks treatment. Otherwise utilized for the criteria of assessment in the four categories as indicated in different tables further specified as follows.

Inclusion criteria

- The patients having Chronic Constipation were taken.
- Patient's between age group of 20 to 55 years.
- Patients found normal in OPD check-up were included.
- Residents of Karachi, Pakistan.
- All socio-economic groups who signed the consent form.

Exclusion criteria

- The patients of Chronic Medical illness were not taken.
- Patients having history of known diseases or complications i.e. uncontrolled hypertension and diabetes or esophageal varices, ascites and other bleeding ailments.
- Patients with known pyrexia usually of high grade.
- Cases suffering from abscess of liver.
- Patients with severe systemic disease i.e. liver, kidney or heart disorders.
- Patients with hepatic or renal impairment, cardiac disorder.

RESULTS

Patient characteristics

The study was conducted in June 2009 to June 2012. The trial was performed according to good clinical practices (GCP). Total 160 patients were screened for this study. The frequency of male verses female was 33 (42%) verses 47 (58%). The patients were randomly distributed and 80 patients were treated with herbal coded drug (Test group) *Plantago ovata* while remaining 80 patients treated with a drug Placebo (Control Group). The improvement in efficacy was checked by the set of signs and symptoms including anorexia, heart burn, epigastric pain, low libido, body ache, joint pain, burning micturition and fever. The efficacy response of medication was done on the basis of "affected" in the improvement of signs and symptoms, clinical outcome and investigations at regular intervals during the course of treatment. Overall 9- symptoms were noted and cross checked for their status of either 'affected' or 'not affected'. These included heart burn, epigastric pain, low libido, body-ache, joint pain, burning micturition, fever, and neuropathy. All these are included in the list of traditionally identified side or after effects and have been subjected to confirmation in this study. Results reveal that 71% were found not affected in anorexia, 61% in heart burn, 56% in epigastric pain, 79% in body-ache, 66% in joint pain, 30% in burning maturition, 10% in fever and 61% in neuropathy.

By summarizing data of the herbal coded drug and placebo their effects observed on the patients in subjective signs and symptoms was subjected to SPSS for window 12 and has been mentioned in table 1. After statistical analysis it was observed that the rate of recovery is markedly effective withdrawing treatment with *Plantago ovata* or in comparison with placebo.

The biochemical and serological analyses were also performed as illustrated in tables 2 and 3. After compilation of the data statistically, coded drug revealed that biochemical and serological parameters were not altered by the coded drug of *Plantago ovata* ($p=0.5$). The patients were categorized on the basis of relief of signs/symptoms in a period of 6 months for Constipation, the dealt cases were divided into not affected and affected according to the drug and placebo used. No untoward manifestations of drugs were observed in trial patients within a period of 2 weeks with Constipation. The comparative, biochemical oriented observation reveals as follows in table 2.

DISCUSSION

Psyllium had been used in western countries as laxative. The plant fiber has also been prescribed at large in colon cancer for the treatment of hypercholesterolemia. It was noted in a case control study that a women of 40 years

Table 1: Comparative data between *Plantago ovata* and Placebo.

Presenting complaint		Treatment Group		P value
		Test	Control	
Anorexia	Completely Affected	79	9	0.01
	Not Affected	21	91	
Heart Burn	Completely Affected	61	5	0.00
	Not Affected	39	95	
Epi-gastric Pain	Completely Affected	84	29	0.00
	Not Affected	16	71	
Low Libido	Completely Affected	79	21	0.00
	Not Affected	21	78	
Body-Ache	Completely Affected	89	25	0.00
	Not Affected	11	75	
Joint Pain	Completely Affected	81	38	0.00
	Not Affected	19	62	
Burning Micturation	Completely Affected	79	30	0.00
	Not Affected	21	70	
Fever	Completely Affected	16	3	0.00
	Not Affected	84	97	

Table 2: Comparative biochemical data between *Plantago ovata* and Placebo.

Biochemical Analysis		Treatment Group		P value
		Test	Control	
ALT	Completely Affected	5	4	0.5
	Not Affected	95	96	
BUN	Completely Affected	5	4	0.5
	Not Affected	95	96	
Serum Creatinine	Completely Affected	5	4	0.5
	Not Affected	95	96	

Table 3: Comparative serological data between *Plantago ovata* and Placebo.

Serological Analysis		Treatment Group		P value
		Test	Control	
Serum B12	Completely Affected	32	2	0.024
	Not Affected	68	98	

age, who taken *Psyllium* as laxative, developed pruritic macular, papular and urticarial covering on her whole body except the face. However there was also a related complaint of swelling around lips and tightening in chest and throat. These complaints vanished after *Psyllium* stoppage and recurred without delay on start up of challenge test. It was further observed through biochemical tests that IgE was raised, RAST for *Psyllium*-specific IgE was present (antigen).

In another study on the arabinoxylans, which was studied for fecal bulking effect on 07 healthy candidates who had taken either small amount of fiber diet or placebo or 18 gram per day of Ispaghula (husk) for the period of 15 days. It was observed at the end of study that there was no difference in gut transit time, gas excretion or flatus. However, fecal weight risen significantly after Ispaghula intake. Similarly increased fatty acid was found and there was also increase in molar proportions of propionic and acetic acids. The author explained that the polymerized Ispaghula had taken 4 hours to reach at caecum and its fecal bulk is due to arabinose and xylose, the digestibility of sugars were 24 (11) and 53% (6), respectively (mean (SEM)).

Conclusively, *Psyllium* is well reported in humans and more resistant to fermentation. Its bulk laxative effect is due to the intact material. A study was conducted in adolescence and children living in developed countries. The output of the study also revealed that the dietary advice containing low glycemic index foods and fiber might be the solution of impaired glucose homeostasis in children. The postprandial glucose values dramatically change in *Psyllium* treated type 2 diabetes cases as -12.2 to -20.2%. The values of change in LDL-cholesterol in *Psyllium* treated children were 2.78 to 22.8%; the HDL

cholesterol was 4.16 to 3.05% and the triglycerides were dropped from 8.49 to 19.54%. In order to verify the inhalant allergen activities of Psyllium powder the dietary plant fibers i.e. xylan, husks, wheat bran, pectin and alfalfa studied. In an *in vitro* study with GIT enzymes like pepsin, trypsin, chymotrypsin, lipase, α amylase, maltase and lactase in buffer solutions at concentrations of 1-5% for 10-30 min at 37 degrees. The said activity of the plant has been proved especially in the workplace. In another case control study conducted on atopic woman of aged 31 years who had used a home prepared laxative of *Psyllium* on the advice of her mother (twice daily), the skin prick test detected positive. Furthermore IgE antibodies were also detected positive via ELISA. While only moderate mild bronchial hyper responsiveness (PC20=1.5mg/ml) seen on methacholine inhalation test. Similarly early asthmatic responses were also confirmed of certain role of *Psyllium* powder. SDS-PAGE and immune blotting method also revealed several allergenic components having molecular weight of 66, 60, 36-20 and 14kDa.

In further studies cross-reaction was not detected between *P. ovata* seed and *P. lanceolata* pollen confirmed by ELISA-inhibition. Hence, *Psyllium* might cause a strong inhalant allergenic action and may elicit asthma, either in an occupational situation, or in a domestic environment where workers are constantly facing its exposure.

CONCLUSION

The finding from this study demonstrated the following salient clinical assessment; there was statistically significant difference when comparing the effectiveness of herbal medicine *P. ovata* with placebo for the treatment of constipation. This is clearly evident that *P. ovata* possesses a therapeutic value for the treatment of constipation and it's also having fewer hazards as evident by biochemical and serological study.

The *Psyllium* inner seed endospore contains some allergens which are protein in nature but the plant husk is entirely free from these allergins. The literature search revealed that though *Psyllium* recovers glucose homeostasis, lipid and lipoprotein profile but, more research is required to be done to elucidate its effects and the mechanisms involved. It is also observed that it enhances water secretion, urea, sodium chloride, and uric acid. The purpose of this study was to identify the toxicity of *Plantago ovata* (Husk) overestimated use. The contemporary medicine describes the use of Isapghol as a non-absorptive fiber, which even if over dosed would not cause any harm to the body. In contrast the Unani medicine has forbidden its overestimated use in all those conditions where permanent temperamental variations occur and where body's physiology leads to disease conditions which are due to excess moisture in the body thus leading to a number of disorders, which has been justified on the basis of clinical studies.

REFERENCES

Ali Zargari, *Gyahan darui* (1390), 3rd Volume Pub: Danishgah Tehran, Iran. pp.803-805.

Anderson JW, Allgood LD and Turner J *et al* (1999). Effects of *Psyllium* on glucose and serum lipid responses in men with type 2 diabetics and hypercholesterolemia. *Am. J. Clin. Nutr.,* **70**: 466-473.

Bliss DZ, Jung HJ and Savik K (2001). Supplementation with dietary fiber improves fecal incontinence. *Nurse. Res.,* **50**: 203-213.

Chan Ek and Schroeder DJ (1998). School of pharmacy University of California, San Francisco 94143, US. *Psyllium* in hypercholesterolemia. *Lipids,* **33**(6): 573-582.

Cheallier A and Remove Toxin (1996). The Encyclopedia of Medicinal Plants. Dorl Kindarsley London. ISBN 9-780751-303148

Fernandez-banares F Hinojosa J and sanchez-Lombrana JL *et al* (1999). Randomized clinical trial of seeds (dietary fiber) as compared with mesalamine in maintaining remission in ulcerative colitis. *Am. J. Gastroenterol.,* **94**: 427-423.

Hakeem Muhammad and Alvi Khan (1282 Hijra), *Khulastul Tijarat*: Publisher Matba Muhammadi, Luknow India. p.237.

Hakeem Muhammad Naseer (1881). *Farhang e Nasria*, Munshi Naval Kishore, Owadh India. P.17.

Hakeem Muhammad Nasir (1847). *Mufridat-e-Nasiri* Pub Gulzar Muhammadi, Lucknow, India p.9.

Ibn e Sina (1906). Al Qanoon. Volume III: Pub: Mutaba Al Nami, Lucknow, India, p.39.

Jones VA Mclaughlan P and Shorthouse M *et al*. (1982), Food intolerance: A major factor in the pathogensis of irritable bowel syndromes. *Lancet,* **2**: 1115-1117.

Anderson JW (1987). Dietary fiber, lipids and atherosclerosis. *Am. J. Cardiol.,* **60**: 17G-22G.

Nordgaard I, Hove H, Clausen M R, Mortensen P B, (1996) Colonic production of butyrate in patients with previous colonic cancer during long-term treatment with dietary fibre *(Plantago ovata* seeds). *Scandinavian Journal of Gastroenterology* 31:10, 1011-1020.

Perez-Miranda M and Gomez A (1996). Leon-Colombo Gastroenterology Dept Spain. Effect of fiber supplement on internal bleeding Hemorrhoids, pp.1504-1507.

Rigaurd D, Paycha F, Meulemans A and Merrouche M (1998). Effect of *Psyllium* on gastric emptying, hunger feeling and food intake in normal volunteer, Service de Gastroenterologist et Nutrition. *Hospital Bichat. Paris. France,* **52**(4): 239-245.

Rodriguez-Cabezas ME, Galvez J, Camuesco D, Lorente MD and Concha A (2003). Intestinal anti-inflammatory activity of dietary fiber (seeds) in HLA B27 transgenic rats. University of Granada Spain. *Clinical Nutrition,* **22**(5): 463-471.

Turnbull WH, Thomas HG. The effect of a Plantago ovate seed containing preparation on appetite variables, nutrient and energy intake. *Int. J. Obes Relat Metab Disord* ., **19**:338-342.

Voderholzer WA, Schatke W and Muhldorfer BE *et al* (1997). Clinical response to dietary fiber treatment of choronic constipation. *Am. J. Gastroenterol.*, **92**: 95-98.