



Research article

Herbal treatment of secretory diarrhea

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Abstract

The research study is conducted to understand interaction of illness, symptoms, context, patients response and the clinical skill vis a vis better management of secretory diarrhea. Specific aim of this study is to determine the impact of intensive medical intervention with herbal drug “Dirasif” (Test) and allopathic drug “Furoxone” (Control) to treat secretory diarrhea. This is randomized controlled clinical trial in primary care with an open intervention. All patients judged by the physician to need either herbal or allopathic medicine for secretory diarrhea are randomized in treatment therapy. Clinical trial was conducted on hundred patients from both groups i.e. 50 patient from control and 50 from experimental group having age between 12-40 year. Comparison of data recorded by participants relating to these variables showed significant differences between test and control groups ($p < 0.05$) despite the fact that no side effects were recorded in test group. Overall clinical success was observed in both treatment groups however the efficacy of the test treated medication (Dirasif) was superior as $p=0.03$. Dirasif is more effective than the Furoxone in the treatment of secretory diarrhea in Gadap community Karachi, Pakistan.

Keywords: Secretory diarrhea, efficacy, dirasif, furoxone

Introduction

Diarrhea diseases are one of the leading causes of morbidity and mortality in developing countries. According to UNICEF, diarrhea kills some 1.5 million children under the age of 5 year annually [1]. Infectious diseases contribute significant role in mortality and morbidity both to adult and child in Pakistan. Infection is the most common cause of secretory diarrhea in which there is increase in the active secretion, or inhibition of absorption. The most common cause of this type of diarrhea is a *cholera* toxin and *E.coli* those stimulate the secretion of anions, especially chloride ions. In

secretory diarrhea stool osmotic gap is less than 50 mOsm/kg. It is mediated by a cyclic adenosine monophosphate (cAMP) pathway best described in *Vibrio cholerae* enterotoxin [2, 3, 4, 5]. In chronic secretory diarrhea patients may present with large volumes of watery diarrhea.

The clinical presentation and course of illness depend on the etiology of the diarrhea and on the host.

Complementary and alternative medicine (CAM) is a group of diverse health care systems. There are many CAM therapies used to treat secretory diarrhea. It has been previously reported that *Myrtus communis* and *Aegle marmelos* have antidiarrheal effect and is commonly used for the

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treatment of secretory diarrhea [5, 6]. *Aegle marmelos* was assessed for its antibacterial, anti-giardial and antirotaviral activities. The effect of decoction of its fruit on adherence of enteropathogenic *Escherichia coli* and invasion of enteroinvasive *E. coli* and *Shigella flexneri* to HEp-2 cells were assessed as a measure of its effect on colonization. Major constituents are aegelin., marmorosin, imperatorin, altoimperatorin, xanthotoxin, scopoletin and tembamide. It significantly reduced bacterial adherence and invasion of HEp-2 cells. Some previous observations confirm the modes of action safety of *Aegle marmelos* in infectious forms of diarrhoea [7]. Recent research on *Myrtus communis* has revealed a substance in the plant that has an antibiotic action against *E. coli*, streptococcus and *Vibrio cholera* etc [8]. The plant is taken internally in the treatment of urinary infections, digestive problems, vaginal discharge, bronchial congestion, sinusitis and dry coughs and infectious diarrheal diseases [9]. Myrtenol, myrtucommulone-A, myrtucommulone-B, semimyrtucommulone, limonene (23%), linalool (20%), pinene (14%), cineol (11%) are the major constituents found in fruit extraction of *Myrtus communis*. *Punica granatum* and *Phyllanthus emblic* have also been reported as having antidiarrheal, antidysenteric, antibiotic, antiseptic, aromatic, astringent properties [10].

Materials and Methods

Study design

The study was based on an experimental, randomized, clinical trial. The study has been conducted according to the principal of good clinical practice i.e. an informed consent was obtained from the patients before the enrollment then proper history and clinical examination was done. The study was carried out from 1st April 2007 to 30th April 2009

Patients and dosage form design

Sample size estimated in clinical assessment on secretory diarrhea has been carried out based on general physical examination, general appearance of the patients, age, sex, and local examination of

the abdomen in a pilot study at Shifa ul Mulk Memorial Hospital Karachi. Clinical trial was conducted on 100 patients. One hundred patients of secretory diarrhea from both groups (50 patient from control and 50 from experimental group) between the age of 12-40 years irrespective of socioeconomic status.

The case group was presented herbal formulation Dirasif (500mg) which comprises of different herbal medicinal plants components such as *Myrtus communis*(150mg), *Aegle marmelos*(150mg), *Punica granatum*(75mg), *Phyllanthus emblica*(75mg) and *Berberis vulgaris*(50mg).. The control groups are subjected to allopathic dosage form design Furoxone (500mg).

Setting

The therapeutic evaluations of these medicines were conducted after the diagnoses of secretory diarrhea on clinical and biochemical evaluation at Shifa-ul-Mulk Memorial Hospital, for Eastern Medicine, Hamdard University. The patients were registered from the general O.P.D. and hospitalized to the clinical Research ward of the Hospital. All the patients selected for the study, were thoroughly examined and clinical history was recorded.

Sample selection

The sample was selected from the out patient department registered and enrolled in Shifa ul Mulk Memorial Hospital and on the basis of stool D/R and inclusion and exclusion criteria the patient fulfilling the secretory diarrhea criteria as candidates were selected. The study period include was from 2007 to 2009. Among this population all the patient suffering from secretory diarrhea were interviewed immediately and upon their consent to participate they were grouped as test and control groups.

Data collection

Data collected for this research work included filling of clinical trial proforma through personal interview, personal observation and use of case record, file and documents. The designed clinical

Table 1: Improvement response in symptoms after treatment

Complaints	Treatment Group		P value
	Test (n)	Control (n)	
Loose motion	90%	74%	0.037
Dehydration	87.5%	29.7%	0.00
Nausea & vomiting	92.59%	33.33%	0.00
Abdominal pain	100%	20%	0.00
Tenesmus	94.87%	27.03%	0.00
General weakness	100%	33.33%	0.05
Anorexia	100%	20%	0.016

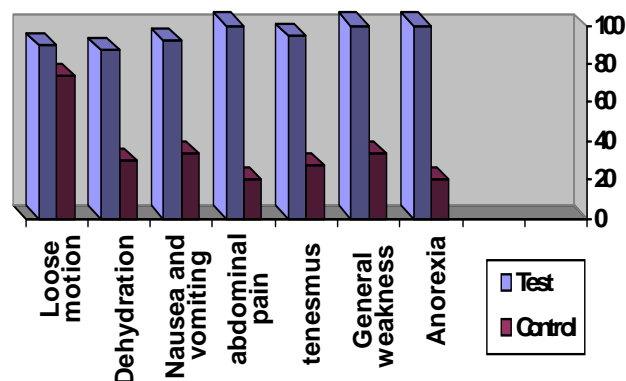
trial proforma specified the clinical feature and information to be filled by the physician for record and utilized in statistical assessment.

Assessment

Primary analysis was based on a stool D/R. Other important parameters include watery diarrhea, abdominal pain, tenesmus, dehydration, anorexia, nausea, vomiting, general weakness; irritability. The data was adjusted based on the number of cases in the light of demographic factor using statistical methods like multinomial logistic regression. The data was composed in separate groups. Statistical analysis were performed using SPSS and excel software, the Chi Square Test was determined. All differences were considered statistically significant by generating a 'p-value' from test statistics. The significant result with 'p-value' less than 0.05 was considered as statistically significant.

Patient characteristics

There are no significant differences in the mean ages between the treatment groups at the start of clinical trial. The mean age of patients prescribed Dirasif as calculated was 27.41 and 26.10 years of males and females respectively. The mean age of patients prescribed Furoxone as calculated was 26.60 and 28.45 years of males and females respectively

**Figure 1: Improvement Response in symptoms after treatment**

Results

Dirasif was prescribed to 50 patients for the reduction of loose motion, 45 patients showed reduction in their loose motion but five patients did not respond. Fifty patients were treated with Furoxone. Loose motion of 37 patients out of 50 reduced to normal. The reduction of loose motion and relief of abdominal pain, nausea and vomiting, dehydration, tenesmus general weakness and anorexia by both test and control drug is shown in Table 1 and Fig 1.

Chi-square test was applied and "p" value was calculated for the purpose of comparison so as to obtain a statistical significant data. According to the statistical analysis a significant difference was observed between two treated groups ($p < 0.05$) at the end of therapy. All differences that were equal to or more than the set cut-off values were considered clinically significant. The evaluation of treatment was significantly improved in the Dirasif (test group) compared with furoxone (control group) at the end of therapy. So it can be concluded that the efficacy of the Dirasif is highly significant and has long lasting effects

Discussion

Furoxone (Furazolidone) is commonly used in patient with secretory diarrhea but it exerts some side effects like headache, malaise, gastrointestinal intolerance and some allergic reactions etc. In order to overcome this problem, there is a great need to find new medicinal

agents, which have good efficacy and less adverse effects. The different medicinal herbs used in this study were selected on the basis of their traditional use in Unani system of medicine. The study was conducted for comparing the efficacy and safety of two different treatment modalities, coded herbal formulation Dirasif as test drug and allopathic treatment Furoxone as control drug for the treatment of secretory diarrhea. The collected data of 100 patients, the frequency of male patients were 60 while, 40 were of female patients were enrolled into the study. These 100 patients have been selected at baseline after the adjustment made out of 125 patients. The clinical assessment included loose motion, watery diarrhea, bloody diarrhea, nausea, vomiting, tenesmus, dehydration, abdominal pain, anorexia, general weakness, irritability, as well as physician and patient's opinions on improvement.

It has been previously reported that *Myrtus communis* and *Aegle marmelos* have antidiarrheal effect and is commonly used for the treatment of secretory diarrhea. So by taking advantage the coded herbal formulation Dirasif, contains a total five ingredients in which *Myrtus communis*, *Aegle marmelos*, *Punica granatum*, *Phyllanthus emblic* and *Berberis vulgaris* for the treatment of secretory diarrhea [7-10].

Basis improvement in the subjective signs and symptoms, clinical observations and pathological investigations at periodic intervals during the course of treatment were evaluated. Dirasif 5ml twice daily compared to Furoxone 5ml twice daily was prescribed on a total of 100 patients suffering from secretory diarrhea. Both preparations led to a decrease in the frequency of loose motion. Dirasif is more efficacious in reducing the frequency of loose motion than Furoxone. Reducing loose motion was due to antidiarrheal effect of Dirasif because Dirasif contain *Myrtus communis* and *Aegle marmelos* which acts as active ingredients and has antidiarrheal effect particularly against *E. coli* and *V. cholera* infection which are the major etiological factors. The effect of *Aegle marmelos* is on the adherence of enteropathogenic

Escherichia coli and invasion of enteroinvasive *E. coli* and *Shigella flexneri* to HEP-2 cells. *Myrtus communis* have also been evaluated as an antibacterial and antidiarrheal plant. Other ingredients of Dirasif also have antidiarrheal and antibacterial effect reducing the infection caused by *E. coli* and *V. cholera*. Tolerance of Dirasif was generally good and no serious side effects were observed. However further citations are required to observe the safety, toxicity and pharmacological actions of these medicinal plants

Conclusion

Dirasif is more effective than the Furoxone in the treatment of secretory diarrhea in Gadap community Karachi, Pakistan as determined by p value <0.03. Control drug showed lesser efficacy than the test drug in its compliance to treat secretory diarrhea. The control drug exhibited side effects like gastrointestinal intolerance, headache and malaise where the test drug did not show any untoward manifestation associated with the use of this medication and found acceptability by all treated patients.

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