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Dealing With Irritable Bowel Syndrome

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Pages with reference to book, From 78 To 81

Treatment

i) Establish a successful physician patient relationship

It is of utmost importance to establish a successful physician patient relationship and help the patient to understand the benign nature of the illness. Physician should acknowledge the reality of patient's symptoms and have empathetic behaviour⁶⁶. Any concerns of the patient should be discussed. Some patients may be having fears of underlying cancer. Reassurance helps the patient cope with his symptoms. Emphasis should be on negative findings of the screening investigations.

The complex underlying pathophysiological and psychophysiological disturbances exist in patients with irritable bowel syndrome, treating them may be a difficult task. It has been shown that doctors underestimate patients expectations, anxiety and secondary complaints and overestimate patients' pain related attributions⁶⁷. Any exacerbating factors should be identified and appropriate changes made in the dietary habits and life style. Education of patient and reassurance is important⁶⁸.

ii) Look after Psychological Aspects

If the symptoms are clearly related to stresses and psychological strain, these patients may require anxiolytics and antidepressants e.g tricyclic antidepressants or Serotonin reuptake inhibitors. Sometimes need may arise to refer one of these patients to a psychiatrist. Before referring, the patient should be taken into confidence about the need of second opinion, with assurance of continuous medical care. Psychological treatment offered to the patient may include psychotherapy⁶⁹, hypnotherapy⁷⁰ and biofeedback⁷¹. Patients with overt psychiatric symptoms and those with diarrhea and intermittent pain exacerbated by stress, show a good response to psychotherapy⁷². In an analysis of controlled studies on psychological treatment, eight studies showed that psychological treatment was superior to the controlled therapy while five failed to detect a significant effect⁷³.

iii) Dietary Changes

Dietary changes are often effective in alleviating symptoms. Patients who have gaseous symptoms and bloating or diarrhea may be helped by avoiding smoking and caffeine, carbonated drinks, lactose containing foods, sweets and jams containing sorbitol or fructose. They should also avoid gas forming beans, cabbage, lentil and legumes which are fermented in the colon by the bacteria, ending up in gases.

iv) Fiber Supplements

Fiber supplements may help relieve constipation^{74,75}. Fiber should be introduced gradually to avoid excessive bloating. Bran, psyllium, ispaghula husk and methylcellulose have the ability to retain water thereby increasing stool weight, preventing hard stools and accelerating intestinal transit. Any benefit from Fiber supplementation may be a placebo effect⁷⁴⁻⁷⁶ but it seems reasonable to utilize this effect and give a trial of fibers to patients with IBS. The agents should be taken within an hour of the meal to allow blending with the fecal matter. A laxative may be given to the patients in constipation phase prior to bulking with Fiber supplements to avoid bloating and satiety and liquid should be consumed in excess alongwith dietary fiber.

v) Medical Treatment

A number of drugs are used in the treatment of IBS. Not a single drug is effective in all the patients⁷⁵. Individual patients may benefit from one of the drugs mentioned in the table 2.

Table 1. Diagnostic criteria for irritable bowel syndrome.

Manning's Criteria:

1. Abdominal distention.
2. Relief of abdominal pain with defecation.
3. More frequent stools with the onset of pain.
4. Looser stools with the onset of pain.
5. Passage of mucus.
6. Feeling of incomplete evacuation.

Rome Criteria:

Continuous or recurrent symptoms for at least three months.

1. **Abdominal pain or discomfort that is:**
 - A. Relieved with defecation or
 - B. Associated with change in frequency of stools or
 - C. Associated with change in consistency of stools.
 2. **Two and/or more of the followings at least 25% of the time:**
 - A. Altered stool frequency.
 - B. Altered stool form (hard or loose/watery).
 - C. Altered stool passage (straining urgency or feeling of incomplete evacuation).
 - D. Passage of mucus.
 - E. Bloating or feeling of abdominal distension.
-

Table 2. Pharmacotherapy for irritable bowel syndrome.

Smooth muscle relaxants:

Mebeverine, dicyclomine, peppermint oil, belladonna, cimetropium, pinaverium, trimebutine, octylonium, zamifenacin

Antidiarrhoal agents:

Loperamide, diphenoxylate, dioctahedral, smectite, cholestyramine, codeine phosphate.

Prokinetic agents:

Cisapride, naloxone, erythromycin.

Fiber supplements:

Bran, Psyllium, ispaghula, methylcellulose.

Antidepressants:

Amitriptyline, imipramine, doxepin, amoxapine, trazodone.

Benzodiazepines:

Deflatulants:

Simethicone, dimethylpolysiloxane.

Miscellaneous:

- Somatostatin analogue octreotide
 - Kappa opioid receptor antagonist fedotozine
 - Serotonin (5HT₃) receptor antagonists grainsetrone, ondansetron.
-

These drugs include tricyclic antidepressants, antidiarrheal agents, smooth muscle relaxants, prokinetic drugs, somatostatin agonists, 5HT₄ antagonists, Kappa opioid agonists, etc.

Low dose antidepressants are effective in improving global symptoms especially pain, a CNS mediated effect^{77,78}. Anticholinergic effect of these medications may also be a contributing factor in relieving abdominal pain. Antidepressants can also modulate intestinal motor function and may have therapeutic effect in IBS, unrelated to mood improvement⁷⁹. Patient should be reassured that these drugs are not being prescribed for any psychiatric illness but for the other useful effects.

Smooth muscle relaxants are effective in improving global symptoms and abdominal pain⁸⁰ but not constipation or abdominal distention. Mebeverine is a specific myorelaxant for colon and does not have the side effects of anticholinergic drugs⁸¹. Zamifenacin is a new potent gut M₃ selective muscarinic antagonist. It reduces colonic motility in IBS⁸². Loperamide has a relaxing effect on localized and segmental large bowel spasms. A double blind placebo controlled trial has shown its benefit with regards to stool frequency, stool consistency and the overall pain intensity⁸³. Morning dose of loperamide or mebeverine may particularly be helpful for patients who have increased frequency of bowel movements in the morning. Octreotide alters the conscious perception of rectal sensation and

may be useful in chronic pain syndromes⁸⁴. Fedotozine acts on the peripheral opioid receptors modulating sensory afferent pathways⁸⁵. A multicentre controlled trial has shown its effectiveness in reducing abdominal pain intensity^{86,87}. The effect of a Serotonin (5-HT₃) receptor antagonist, ondansetron has been assessed in a double blind placebo controlled trial in individuals with diarrhea predominant IBS. There was improvement in stool consistency but not in frequency^{75,88}. As there is high prevalence of adverse reactions to food in diarrheic IBS, treatment with oral cromolyn sodium may be of value in these patients^{76,89}. Cisapride, a prokinetic drug, has Serotonin receptor agonist (5HT₃) and antagonist (5-HT₄) actions. It influences interdigestive and postprandial small bowel motor activity⁹⁰, accelerates colonic transit and decreases the severity of constipation⁸⁹.

Conclusion

In short, treatment of IBS has to be individualized according to the predominant symptom of the patient. A combination of psychological support, dietary advice, change in the life style and appropriate selection from the armament of drugs help in effectively combating symptoms and misery of the patient. A positive physician patient interaction is associated with fewer return visits for IBS⁹². IBS patients with short duration and fewer psychological symptoms have a better prognosis than patients with a long history of IBS and associated psychological stresses⁹³.

References

1. Manning AP Thompson WG, Heaton KW, et al. Towards positive diagnosis of irritable bowel. *Br. Med. J.*, 1978;2:653-54.
2. Smith RC, Greenbaum DS, Vancouver JB. et al. Gender differences in Manning criteria in the irritable bowel syndrome. *Gastroenterology*, 1991;100:591-5.
3. Klauser AG, Voderhoizer WA, Schindlbeck NE, et al. Functional diagnostic work-up in patients with irritable bowel syndrome. *Z. Gastroenterol.*, 1996;34:273-8.
4. Taub E, Cuevas JL, Cook EW et al. Irritable bowel syndrome defined by factor analysis. Gender and race comparisons. *Dig Dis Sci* 1995;40:2647-55.
5. Thompson WG, Dotevall O, Drossman DA, et al. Irritable bowel syndrome: guidelines for the diagnosis. *Gastroenterol Int.* 1989;2:92-5.
6. Everhart JE, Renault PF. Irritable bowel syndrome in office-based practice in the United States. *Gastroenterology* 1991; 100:998-1005.
7. Harvey RF, Salih SY, Read AE. Organic and functional disorders in 2000 gastroenterology outpatients. *Lancet*, 1983; 1:632-4.
8. Hahn BA, Saunders WB, Maier WC. Difference between individuals with self-reported irritable bowel syndrome (IBS) and LBS-like symptoms. *Dig Dis Sci* 1997; 43: 2585-90.
9. Jones R, Lydeard S. Irritable bowel syndrome in the general population. *Br. Med. J.*, 1992; 304:87-90.
10. Gomborone J, Dewsnap P, Libby G, et al. Abnormal illness attitudes in patients with irritable bowel syndrome. *J Psychosom Res* 1995; 39:227-30.
11. Heaton KW, O'Donnell LJ, Braddon FEM, et al. Symptoms of irritable bowel syndrome in a British urban community; consulters and nonconsulters. *Gastroenterology* 1992;102: 1962-67.
12. Kruis W, Thierne CH, Weinzierl M, et al. A diagnostic score for irritable bowel syndrome. *Gastroenterology*, 1984;87: 1-7.
13. Drossman DA, Sandler RS, McKee DC, et al. Bowel patterns among subjects not seeking health care. *Gastroenterology*, 1982;83:529-34.

14. Hinds JP, Stoney B, Wald A. Does Gender or the menstrual cycle affect colonic transit? *Am. J. Gastroenterol.*, 1989;84:123-6.
15. Agreus L, Svardsudd K, Nyren O, et al. Irritable bowel syndrome and dyspepsia in the general population: Overlap and lack of stability over time. *Gastroenterology*, 1995; 109:671-80.
16. McKee DP, Quigley EMM: Intestinal motility in irritable bowel syndrome: Is IBS a motility disorder? Part I: definition of IBS and colonic motility. *Dig. Dis. Sci.* 1993;38:1761-72.
17. McKee DP, Quigley, EMM. Intestinal motility in irritable bowel syndrome: Is IBS a motility disorder? Part 2: motility of small bowel, esophagus, stomach and gall-bladder. *Dig. Dis. Sci.*, 1993;38:1773-82.
18. Galati iS, McKee DP, Quigley EMM. Response 'to intraluminal gas in irritable bowel syndrome. Motility versus perception. *Dig. Dis. Sci.*, 1995;40:1381-87.
19. Kellow JE, Phillips SF. Altered small bowel motility in irritable bowel syndrome is correlated with symptoms. *Gastroenterology*, 1987;92: 1885-93.
20. Kellow JE, Gill RC, Wingate DL. Prolonged ambulant recordings of small bowel motility demonstrate abnormalities in the irritable bowel syndrome. *Gastroenterology*, 1990;98: 1208-18.
21. Kellow JE, Eckersley GM, Jones M. Enteric and central contributions to intestinal motility in irritable bowel syndrome. *Dig. Dis. Sci.*, 1992;37:168-74.
22. Cairn PA, Read NW, Brown C, et al. Irritable bowel syndrome: Relationship of disorders in the transit of a single solid meal to symptom pattern. *Gut.*, 1983;24:405-11.
23. Vassallo M, Camilleri M, Phillips SF, et al. Transit through the proximal colon influences stool weight in irritable bowel syndrome. *Gastroenterology*, 1992; 102: 102-8.
24. Stivland T, Camikkeri M, Vassallo M, et al. Scintigraphic measurement of regional gut transit in idiopathic constipation. *Gastroenterology*, 1991; 101:107-15.
25. Hutchinson R, Notghi A, Smith NB, et al. Scintigraphic measurement of ileocaecal transit in irritable bowel syndrome and chronic idiopathic constipation. *Gut*, 1995;36:585-9.
26. Sullivan M, Cohen S, Snape WJ. Colonic myoelectrical activity in irritable bowel syndrome. Effect of eating and anticholinergics. *N. Engl. J. Med.*, 1978; 198: 878-83.
27. Latimer PR, Sarna SK, Campbell D, et al. Colonic motor and myoelectric activity: a comparative study of normal patients, psychoneurotic patients and patients with irritable bowel syndrome (IBS). *Gastroenterology*, 1981; 80: 893-901,
28. Beareroft CP, Perrett D, Farthing Mi. Postprandial plasma 5-hydroxytryptamine in diarrhea predominant irritable bowel syndrome: a pilot study. *Gut.*, 1998; 42:42-6.
29. Prior A, Maxton DO, Whorwell PJ. Anorectal manometry in irritable bowel syndrome: Differences between diarrhea and constipation predominant subjects. *Gut.*, 1990;31:458-62.
30. Ritchie J. Pain from distention of the pelvic colon by inflating a balloon in the irritable bowel syndrome. *Gut.*, 1973;14:125-32.
31. Phillips SF, Talley NJ, Camilleri M. The irritable bowel syndrome. In: Anuras S ed. *Motility disorders of the gastrointestinal Tract*. New York, Raven, 1992:299-326.
32. Mertz H, Naliboff B, Munakata J, et al. Altered rectal perception is a biological marker of patients with irritable bowel syndrome. *Gastroenterology*, 1995; 109:40-52.
33. Slater BJ, Plusa SM, Smith AN, et al. Rectal hypersensitivity in the irritable bowel syndrome. *Int. J. Colorectal. Dis.*, 1997; 12: 29-32.
34. Accarino AM, Azpiroz F, Malagelada JR. Selective dysfunction of mechanosensitive intestinal afferents in irritable bowel syndrome. *Gastroenterology*, 1995;108:636-43.
35. Silverman DHS, Munakata JA, Ennes H, et al. Regional cerebral activity in normal and pathologic perception of visceral pain. *Gastroenterology*, 1997; 112: 55-63.
36. Trimble KC, Farouk R, Pyrd A, et al. Heightened visceral sensation in functional gastrointestinal disease is not site specific. Evidence for a generalized disorder of gut sensitivity *Dig. Dis. Sci.*, 1995;40:1607-13.

37. Whitefield WE, Bosinajian L, Zonderman Act a!. Role of psychologic distress associated with Irritable bowel syndrome. Comparison of community and medical clinic samples. *Gastroenterology*, 1988;95 :709-14.
38. Sandler RS, Drossman DA, Nathan HP,et al. Symptom complaints and health care seeking behavior in subjects with bowel dysfunction. *Gastroenterology*, 1984;87:314-8.
39. Francis CY, Duffy iN, Whorwell PJ,et al. High prevalence of irritable bowel syndrome in patients attending urological out patient department. *Dig. Dis. Sci.*, 1997; 42: 404-7.
40. Pass R, Fullerton S, Naliboff B, et al. Sexual dysfunction in patients with irritable bowel syndrome and non-ulcer dyspepsia. *Digestion*, 1998;59:79-85.
41. Whitehead WE, Crowell MD, Robinson JC,et al Effect of stressful life events on bowel symptoms: Subjects with irritable bowel syndrome compared with subjects without bowel dysfunction. *Gut.*, 1992;33:825-30.
42. Drossman DA, Sandler RS, McKee DC, et al. Bowel patterns among subjects not seeking health care: Use of a questionnaire to identify a population with bowel dysfunction. *Gastroenterology*, 1982;83 :529-34.
43. Masand PS, Kaplan DS, Gupta S,et a!. Major depression and irritable bowel syndrome: is there a relationship? *J. Clin. Psychiatry.*, 1995;56:363-7.
44. Newcomer AD, McGill DB. Irritable bowel syndrome. Role of lactose deficiency. *Mayo Clin. Proc.* 1983;59:339-41.
45. Vernia P, Ricciardi MR. Frandina C. et al. Lactose malabsorption and irritable bowel syndrome. Effect of a long tenu lactose free diet. *Ital J Gastroenterol.*, 1995;27:117-21.
46. Vesa TH, Seppo UM, Marteau PR, et a!. Role of irritable bowel syndrome in subjective lactose intolerance. *Am. J. Clin. Nutr.*, 1998; 67: 7 10-5.
47. Rumessen JJ, Gudmand-Hoyer E. Functional bowel disease: Malabsorption and abdominal distress after ingestion of fructose, sorbitol and fructose -sorbitol mixtures. *Gastroenterology*, 1988;95:694-700.
48. Hyams JS, Sorbitol intolerance: An unappreciated cause of functional gastrointestinal complaints. *Gastroenterology*, 1983;84:30-3.
49. Alun Jones V, McLaughlan P, Shorthouse M, et at. Food intolerance: A major factor in the pathogenesis of irritable bowel syndrome: *Lancet*, 1982;ii: 1115-7.
50. Nanda R, James R, Smith H,et al. Food intolerance and the irritable bowel syndrome. *Gut.*, 1989;30:1099-1104.
51. Merrick MW, Eastwood MA, Ford Mi. Is bile acid malabsorption underdiagnosed? An evaluation of accuracy of diagnosis by measurement of SeHCAAT retention. *Br. Med. J.*, 1985;290:665-8.
52. Oddsson E, Rask-Madsen J, Krag E. A secretory epithelium of the small intestine with increased sensitivity to bile acids in irritable bowel syndrome associated with diarrhea. *Scand. J. Gastroenterol.*, 1978;13:409-16.
53. Spiller RC, Brown ML, Phillips SF. Decreased fluid tolerance, accelerated transit, and abnormal motility of the human colon induced by oleic acid. *Gastroenterology*, 1986; 91:100-7.
54. Snape WJ, Materazzo SA, Cohen S. Effect of eating and gastrointestinal hormones on human colonic myoelectrical and motor activity. *Gastroenterology*, 1978; 75: 373-8.
55. Thompson WG, Creed F, Drossman DA, et al. Functional bowel disorders and chronic functional abdominal pain. *Gastroenterology, Int.*, 1992; 5: 75-91..
56. Gricknik KP, Ferrante FM. The difference between acute and chronic pain. *Mt. Sinai. J. Med.*, 1991;58:217-20.
57. Holtmann G, Goebell H, Talley NJ. Functional dyspepsia and irritable bowel syndrome: is there a pathophysiological basis. *Am. J. Gastroenterol.*, 1997;92:954-9.
58. Nyhlin H, Merrick MV, Eastwood MA, et a!. Evaluation of ileal function using 23-selena-25-homotaurocholate, a gamma labelled conjugated bile acid. *Gastroenterology*, 1983;84:63-8.

59. Bond JH, Levitt MD, Prentiss R. Investigation of small bowel transit time in man utilizing pulmonary hydrogen (H₂) measurements. *J. Lab. Clin. Med.* 1975;85:546-55.
60. Cann PA, Read NW, Brown C, et al. Irritable bowel syndrome: Relationship of disorders in the transit of a single solid meal to symptoms patterns. *Gut.*, 1983;24:405-11.
61. Proano M, Camilleri M, Phillip SF, et al. Transit of solids through the human colon. Regional quantification in the unprepared bowel. *AM. J. Physiol.*, 1990;258: G 856-62.
62. Stivland T, Camilleri M, Vassallo M, et al. Scintigraphic measurement of regional gut transit in idiopathic constipation. *Gastroenterology*, 1991; 101:107-15.
63. Pemberton JH, Phillips SF. Constipation and diarrhea. In: Moody FG, ed. *Surgical Treatment of Digestive Disease*. 2nd ed. Chicago: Year Book Medical Publishers; 1990,pp. 39-52.
64. Awad RA, Martin J, Guevara M, et al. Defecography in patients with irritable bowel syndrome and healthy volunteers. *Int. J. Colorectal. Dis.*, 1997; 12: 91-94.
65. Ritchie J. Pain from distention of the pelvic colon by inflating a balloon in the irritable bowel syndrome. *Gut.*, 1973;14:125-32.
66. Sharpe M, Peveler R, Mayon R, The psychological treatment of patients with functional somatic symptoms: A practical guide. *J. Psychosom. Res.*, 1992;36;5 15-29.
67. Van Dulmen AM, Fennis JF, Mookink HG, et al. Doctors perception of patients' conditions and complaints in irritable bowel syndrome at an outpatient clinic. *J. Psychosom. Res.*, 1994;38:581-90.
68. Drossman DA. Diagnosing and treating patients with refractory functional gastrointestinal disorders. *Ann. Intern. Med.*, 1995; 123: 688-97.
69. Guthrie EA, Creed F, Dawson D, et al. A randomised controlled trial of psychotherapy in patients with refractory irritable bowel syndrome. *Br. J. Psychiatry*, 1993;163:315-21.
70. Harvey RF, Hinton RA, Gunary RM, et al. Individual, and group hypnotherapy in treatment of refractory irritable bowel syndrome. *Lancet.*, 1989;i:424-5.
71. Whitehead WE, Biofeedback treatment of gastrointestinal disorders. *Biofeedback self Regul.*, 1992;17:59-76.
72. Guthrie E, Creed F, Dawson D, et al. A controlled trial of psychological treatment for the irritable bowel syndrome. *Gastroenterology*, 1991; 100:450-7.
73. Talley NJ, Owen BK, Boyce P, et al. Psychological treatments for irritable bowel syndrome: a critique of controlled treatment trials. *Am. J. Gastroenterol.*, 1996; 91: 277-83.
74. Snook J, Shephard HA. Bran supplementation in the treatment of irritable bowel syndrome. *Aliment Pharmacol. Ther.*, 1994;8:511-4
75. Klein KB. Controlled treatment trials in the irritable bowel syndrome: A critique. *Gastroenterology*, 1988;95:232-41.
76. Cook IJ, Irvine EJ, Campbell D, et al. Effect of dietary Fibers on symptoms and rectosigmoid motility in patients with irritable bowel syndrome: A controlled crossover study. *Gastroenterology*, 1990;98:66-72.
77. Clouse RE, Lustman PJ, Geisman RA, et al. Antidepressant therapy in 138 patients with irritable bowel syndrome: A five year clinical experience. *Aliment Pharmacol. Ther.*, 1994;8:409-16.
78. Mertz FIR, Fass R, Hirsh T, et al. Amitriptyline for functional dyspepsia: Effect on symptoms, gastric sensitivity and sleep (abstract). *Gastroenterology.*, 1994;108:649.
79. Gorard DA, Libby GW, Farthing MJ. Effect of tricyclic antidepressant on small intestinal motility in health and diarrhea - predominant irritable bowel syndrome. *Dig. Dis. Sci.*, 1995;40:86-95.
80. Poynard T, Naveau S, Mory B, et al. Meta-analysis of smooth muscle relaxants in the treatment of irritable bowel syndrome. *Aliment Pharmacol. Ther.*, 1994;8:499-510.
81. Van-Outryve M, Mayeur S, Meertis M, A, et al. A double blind crossover comparison study of the safety and efficacy of mebeverine with mebeverine sustained release in the treatment of irritable bowel syndrome. *J. Clin. Pharm. Ther.*, 1995;20:277-82.
82. Houghton LA, Rogers J, Whorwell PJ, Zamifenacin (UK-76, 654) a potent gut M₃ selective

- inuscarnic antagonist, reduces colonic motor activity in patients with irritable bowel syndrome. *Aliment Pharmacol. Ther.* 1997; 11: 561-8.
83. Efskind PS, Bernkler I, Vatn MH. A double blind placebo controlled trial with loperamide in irritable bowel syndrome. *Scand J Gastroenterol.*, 1996;31:463-8.
84. Hasler WL, Soudah HC, Owyang C. Somatostatin analog inhibits afferent pathways mediating perception of rectal distention. *Gastroenterology*, 1993;104:1390-7.
85. Gue M, Junien JL, Bueno L. The kappa agonist fedotozine modulates colonic distention - induced inhibition of gastric motility and emptying in dogs. *Gastroenterology*, 1994;107: 1327-34.
86. Dapoigny M, Abitbol JL, Merle G, et al. Fedotozine in irritable bowel syndrome: Results of a 6 week placebo - controlled multicenter therapeutic trial. *Gastroenterology*, 1995;108:A588.
87. Dapoigny M, Abitbol JL, Fraitag B. Efficacy of peripheral Kappa agonist fedotozine versus placebo in treatment of irritable bowel syndrome. A multicentre dose-response study. *Dig. Dis. Sci.*, 1995;40:2244-49.
88. Steadman CJ, Talley NJ, Phillips SF, et al. Selective 5 - hydroxytryptamine type 3 receptor antagonism with ondansetron as treatment for diarrhea - predominant irritable bowel syndrome: A pilot study. *Mayo Clin. Proc.*, 1992;67:732-8.
89. Stefanini OF, Saggiaro A, Alvisi V, et al. Oral cromolyn sodium in comparison with elimination diet in the irritable bowel syndrome, diarrheic type. Multicenter study of 428 patients. *Scand. J. Gastroenterol.*, 1995;30:535-41.
90. Evans PR, Bak YT, Kellow JE. Effect of oral cisapride on small bowel motility in irritable bowel syndrome. *Aliment Pharmacol., Ther.*, 1997; 11: 837-44.
91. Wiseman L, Faulds D. Cisapride: An update review of its pharmacology and therapeutic efficacy as a prokinetic agent in gastrointestinal motility disorders. *Drugs.*, 1994; 47: 116-152.
92. Owens DM, Nelson DK, Talley NJ. The irritable bowel syndrome: Long term prognosis and the physician - patient interaction. *Ann. Int. Med.*, 1995;122:107-12.
93. Lembo T, Fullerton S, Dietl D, et al. Symptom duration in patients with irritable bowel syndrome. *Am J Gastroenterol.*, 1996;91 :898-905.