Irritable Bowel Syndrome

The Gastro-intestinal System
The gastro-intestinal (G.I) system extends from the mouth to the anus. It is responsible for the passage and digestion of food and liquid from their entry at the mouth to the exit of solid waste at the anus. The full length of the G.I. tract is 5-6 times a person's height. The content within the G.I. tract is propelled by peristalsis, which is a series of coordinated, rhythmic smooth muscle contractions that occur throughout the G.I tract.

The colon is the last area of absorption in the G.I tract. It absorbs water, nutrients and salts from the partially digested food that enters from the small intestines. What is left over at the rectum is feces.

Irritable Bowel Syndrome
Irritable bowel syndrome or IBS is a disturbance in the regulation of the colon that results in the hypersensitivity and hyperactivity of the smooth muscle. About 1 out of 10 people suffers from IBS. IBS is twice more likely seen in women than men.

IBS is characterized by symptoms of abdominal distension or pain, or altered bowel habit. The abdominal distension or pain is usually relieved by defecation. Diarrhea may present itself with accompanying bowel spasms. Diarrhea may alternate with constipation. Some patients may even complain of a feeling of incomplete evacuation after a bowel motion. IBS is now diagnosed as either constipation-dominant or diarrhea-dominant.

The actual cause of IBS is unknown. IBS patients have a colon that is hypersensitive and reactive. The normal functioning of the colon is regulated by a host of hormones and neurotransmitters. Serotonin (5-HT) is thought to be the key chemical that acts on the lining of colon. People with abnormal levels of serotonin are more susceptible to IBS. Studies have also shown that IBS usually follows after a bout of gastroenteritis. This is usually due to the use of antibiotics. IBS is not caused by stress. But, stress can aggravate the symptoms of IBS.

Initially, the Manning Criteria were used to diagnose IBS. In 1999, the Rome II Criteria for IBS were developed. They now form the standard for IBS diagnosis.

The Rome II Criteria for IBS:
At least 12 weeks or more, which need not to be consecutive, in the past 12 months, of abdominal discomfort or pain, that has 2 out of 3 features:
1. relieved with defecation
2. onset associated with a change in frequency of stool
3. onset associated with a change in appearance/ form of stool

IBS is a benign disorder. However, it can seriously compromise a person's quality of life. The symptoms can disrupt personal or professional activities, upset emotional well-being and limit individual potential.

Treatment Options
At the moment, there is no cure for IBS. Symptomatic treatments are usually prescribed to relieve symptoms associated with IBS.

Medications such as loperamide or diphenoxylate are given to relieve diarrhea. Bisacodyl and senna are often used in constipation. Other forms of laxative such as lactulose and polyethylene glycol (PEG) are good choices to avoid cathartic colon. Bulking agents such as psyllium husk and oat bran may also be of help.

Antispasmodics are prescribed to relieve spasms and abdominal pain. Traditionally, peppermint oil is used to treat bowel spasms. Administered in the capsule form, it can cause heartburn or oesophageal irritation. Antimuscarinic drugs such as hyoscine and dicyclomine are often associated with unpleasant side-effects. Patients often complain of dry mouth, urinary retention, diluted pupils and giddiness. Patients with
prostate hypertrophy and glaucoma should never be prescribed with this group of drugs. Instead, non-cholinergic acting drugs such as mebeverine are more suitable. Mebeverine belongs to the group of drugs called musculotropic antispasmodics. They act directly on the smooth muscle cells of the G.I. tract. They relieve bowel spasms, minus the unpleasant anti-cholinergic effects. Antispasmodics in combination with barbiturates or sedatives are used to relax stressed patients in addition to relieving spasms. These drugs are prone to habit-forming, so their use should be monitored by a physician.

Novel approach to IBS treatment is targeted at the serotonin receptor in the G.I. tract. Currently, the only available drug is tegaserod. Tegaserod is a selective 5-HT4 agonist. It is indicated for the short term treatment of constipation-dominant IBS. It acts to stimulate and restore the gut motility. Tegaserod is available as a 6mg-tablet which is taken twice daily for 4-6 weeks. Aloxetron and cilasetron, both 5-HT3 antagonists, are still undergoing clinical studies and are indicated for diarrhea-dominant IBS.

Changes in Diet
A high-fiber diet may help to relieve some symptoms of IBS, especially constipation. Whole-grain breads and cereals, fruits and vegetables are good sources of fiber. The fiber helps to bulk the stool so that it is easily passed out. It also keeps the colon mildly distended to reduce the spasms. Drinking 6-8 glasses of water also prevent the formation of hard stool. High-fiber diets may cause flatulence and bloating but these symptoms usually go away within 1-2 weeks.

Eating small, frequent meals may also be beneficial to some IBS sufferers. Large meals tend to cause bloating. Eating and drinking too quickly can lead to swallowing air which leads to gas. There are some foods and beverages that need to be avoided or minimized in IBS. Oily and spicy food, dairy products, alcohol, caffeinated beverages and artificial sweeteners can aggravate symptoms of IBS. It is suggested that IBS patients keep a food diary to monitor the food and beverages that trigger IBS symptoms. By doing so, they can avoid or minimise the intake of the triggering factors.

Alternative treatments that include probiotics and acupuncture are still very much under scrutiny as there are still inconclusive data on these treatments. Nevertheless, a healthy lifestyle with the occasional pharmacological help can keep IBS at bay.

References:
1. http://www.aboutibs.org
4. The Merck Manual of Diagnosis and Therapy, 17th Edition

LEZPAIN
Mebeverine HCl
135 mg   F.C. TABLETS

Relieve spasm of various origin
& improve symptoms of IBS

HELP RELIEVE:
- Abdominal pain/cramps due to gastrointestinal spasm
- Bowel disturbances
- Intestinal discomfort related to irritable bowel syndrome
Benzodiazepines

Introduction

The benzodiazepines are a class of drugs with hypnotic, anxiolytic, anticonvulsant, amnestic and muscle relaxant properties. Benzodiazepines are used primarily in the short-term treatment of generalized anxiety and panic disorders. They are believed to act on the (GABA)-type A-chloride receptors in the central nervous system, the activation of which produces a state of relaxation and induces anterograde amnesia.

History

In 1960, chloridiazepoxide was the first benzodiazepine released, followed by diazepam in 1963. Chloridiazepoxide became the major agents for treatment of anxiety. Oxazepam, one of the active metabolites of chloridiazepoxide and diazepam, was later released as a separate entity in 1965. In the 1970s, many benzodiazepines were released including flurazepam (1970), clorazepate (1972), clonazepam (1975), prazepam (1976), and lorazepam (1977).

Besides treatment of anxiety, benzodiazepines quickly became preferred over short-acting barbiturates and other agents for use as hypnotics. While flurazepam was widely used as a hypnotic, pharmaceutical manufacturers began searching for benzodiazepines with shorter elimination half-life to avoid the hangover effect commonly reported with flurazepam. Several such agents were released in the early 1980s: alprazolam and temazepam in 1981 and triazolam in 1982. Other benzodiazepines that have been marketed include halazepam (1981), quazepam (1985), and midazolam (1985).

Use of Benzodiazepines

Benzodiazepines are commonly used to manage the symptoms associated with acute anxiety disorders, anxiety associated with depression, acute insomnia not due to a secondary medical condition such as apnoea, agitation and anxiety occurring secondary to dementia, and to manage symptoms associated with acute ethanol withdrawal. Benzodiazepines are also

ALPRANAX alprazolam 0.5mg tablets

Introducing one of the most popular benzodiazepines for anxiety

- Efficacy of benzodiazepines in the treatment of anxiety is well established.\(^2\)
- Fast onset of symptom relief (within first week)\(^1\)
- Low potential for dependency or abuse\(^1,2\)

References:
Meloxicam – A COX-2 Preferential Inhibitor

An Oxicam Derivative
Meloxicam is an oxicam derivative that is a member of the onolic acid group of NSAIDs. In models, meloxicam exhibits anti-inflammatory, analgesic, and antipyretic activities. Meloxicam has been shown, especially at its low therapeutic dose, to preferentially inhibit COX-2 over COX-1 (refer to table 1 for a comparison between meloxicam and other NSAIDs on the degree of inhibition of COX-2 relative to COX-1). Therefore, meloxicam offers a better advantage in terms of gastrointestinal safety profile. In clinical trials, GI adverse events overall were reported less frequently with both 7.5mg and 15mg.

An Effective NSAID
Clinical trials have shown that meloxicam at 7.5 – 15 mg/day is as effective as diclofenac, piroxicam and naproxen as an anti-inflammatory and analgesic, and was associated with fewer GI adverse effects (perforations, ulcers or bleeding).

Safety Profile
Clinical studies have shown that, with respect to all GI adverse events, meloxicam 7.5 and 15 mg were significantly better than all comparators (piroxicam 20 mg, diclofenac 100 mg slow release and naproxen 750-1000 mg) in a pooled analysis of double-blind studies in rheumatoid arthritis and osteoarthritis.

Safety Profile
Clinical studies have shown that, with respect to all GI adverse events, meloxicam 7.5 and 15 mg were significantly better than all comparators (piroxicam 20 mg, diclofenac 100 mg slow release and naproxen 750-1000 mg) in a pooled analysis of double-blind studies in rheumatoid arthritis and osteoarthritis.

Table 1: The degree of inhibition of COX-2 relative to COX-1 for NSAIDs

<table>
<thead>
<tr>
<th>NSAID type</th>
<th>COX-2 selectivity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>COX-2 selective inhibitors</td>
<td></td>
</tr>
<tr>
<td>Rofecoxib</td>
<td>80</td>
</tr>
<tr>
<td>Etodolac</td>
<td>23</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>11</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>9</td>
</tr>
<tr>
<td>Nonselective NSAIDs</td>
<td></td>
</tr>
<tr>
<td>Diclofenac</td>
<td>4</td>
</tr>
<tr>
<td>Sulindac</td>
<td>3</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>2</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>0.4</td>
</tr>
<tr>
<td>Naproxen</td>
<td>0.3</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>0.3</td>
</tr>
<tr>
<td>Ketonolac</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Note: COX = cyclooxygenase, NSAID = nonsteroidal anti-inflammatory drug. *The 90% inhibitory concentration ratios of COX-2 relative to COX-1 in human whole blood assays.


Clinical Uses
Meloxicam is used for anti-inflammatory and analgesic effects in the symptomatic treatment of osteoarthritis or rheumatoid arthritis in adults and for the management of the signs and symptoms of pauciarticular or polyarticular course juvenile rheumatoid arthritis in children 2 years of age or older. Meloxicam is also used in the management of ankylosing spondylitis.
Antioxidants and Free Radicals

Introduction
Antioxidants are involved in the prevention of cellular damage—the common pathway for cancer, aging and a variety of diseases. They help to protect the body from free radical damage.

Free Radical Damage
Free radicals are atoms or group of atoms with an odd (unpaired) number of electrons and can be formed when oxygen interacts with certain molecules. They are very unstable and always trying to capture the needed electron to gain stability. Generally free radicals attack the nearest stable molecule by "stealing" its electron. When the "attacked" molecule loses its electron, it becomes a free radical itself, beginning a chain reaction.

In very high volumes free radicals can alter the genetic code material of cells themselves. Mutations that are formed by free radicals can lead to leukaemia and other types of cancer as well as a host of other diseases. Free radicals can also damage the cell membrane. This leads to retention of fluids in the cells, which is involved in the aging process.

Sources of Free Radicals
Free radicals come from two major sources: (a) endogenous and (b) exogenous. Endogenous free radicals are produced in the body from the normal metabolism of oxygen-requiring nutrients. Mitochondria, the intracellular powerhouses which produce the universal energy molecule, adenosine triphosphate (ATP), normally consume oxygen in this process and convert it to water. However, unwanted by-products, such as the superoxide anion, hydrogen peroxide and the hydroxyl radical, are inevitably produced, due to incomplete reduction of the oxygen molecule.

Exogenous sources of free radicals include air pollution, of which industrial waste and cigarette smoke are major contributors. Radiation and trace metals, notably lead, mercury, iron and copper, are also major sources of free radical generation. Normal diets containing plant foods with large quantities of certain compounds such as phenols and even caffeine may contribute to the exogenous supply of free radicals to the body.

Antioxidants Prevent Against Free Radical Damage
Antioxidants are our own army to defense against free radicals. They neutralize free radicals by donating one of their own electrons, ending the electron "stealing" reaction. The antioxidant nutrients themselves do not become free radicals by donating an electron because they are stable in either form.

Antioxidants can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. Although there are several enzyme systems within the body that scavenge free radicals, the principle micronutrient (vitamin) antioxidants are vitamin E, beta-carotene, and vitamin C. Additionally, selenium, a trace metal that is required for proper function of one of the body's antioxidant enzyme systems, is sometimes included in this category.

Vitamin E: The most abundant fat-soluble antioxidant in the body. It is one of the most efficient chain-breaking antioxidants available. Vitamin E is primary defender against oxidation and lipid peroxidation (creation of unstable molecules containing more oxygen than is usual).

Vitamin C: The most abundant water-soluble antioxidant in the body. It acts primarily in cellular fluid. Vitamin C helps in combating free-radical formation caused by pollution and cigarette smoke. It also helps return vitamin E to its active form.

Beta-carotene is a precursor to vitamin A (retinol). It protects dark green, yellow and orange vegetables and fruits from solar radiation damage, and is thought to play a similar role in the human body.

Continue on page 6
Combination of Antioxidants

Although many antioxidants can be obtained from food sources such as sprouted grains and fresh fruits and vegetables, it is difficult to get enough of them from these sources to hold back the free radicals constantly being generated in our polluted environment. We can minimize free radical damage by taking supplements of key nutrients. A high intake of antioxidant nutrients appears to be especially protective against cancer. Antioxidants work synergistically in giving protection against free radical damage, so it is better to take smaller doses of several different antioxidants than a large amount of only one. For example, while beta-carotene by itself is an excellent antioxidant, a mix of natural carotenoids provides more health benefits than beta-carotene alone. There are many good combination formulas available that make it easy to take multiple antioxidants everyday.

References:

shine®
Your Antioxidant’s Army

- Combination of natural mixed carotenoids, vitamin C, natural vitamin E and selenium.
- Helps to prevent diseases and aging.

Bio A.C.E
with Selenium
Film Coated Tablet
used as an adjunct for the relief of acute musculoskeletal problems (spasm, spasticity, or tetanus) and convulsion disorders (including status epilepticus and febrile seizures); for the relief of preoperative anxiety; and to induce sedation, light anesthesia, antegrade amnesia and conscious sedation in intensive care settings (eg., midazolam).

The Different Types of Benzodiazepines
Benzodiazepines differ from each other in duration of action and pharmacokinetics. However, the duration of action is usually considerably shorter than the half-life. Whereas long-acting benzodiazepines may produce day-time hangover, short-acting agents are more often associated with dependence, rebound insomnia, early morning insomnia, daytime anxiety, and serious withdrawal effects, such as seizures.

The following general characterizations can be made:
- Intermediate- and short-acting benzodiazepines are characterized by half-lives of 4 to 24 hours.
- Short-acting benzodiazepines are characterized by the following:
  - Few active metabolites.
  - Rarely, accumulation with multiple doses.
  - Minimal effect on drug clearance by age and liver disease.
- Long-acting benzodiazepines are characterized by the following:
  - Half-lives of longer than 24 hours.
  - Pharmacologically active metabolites
  - Accumulation with multiple dosages.
  - Impaired clearance in older patients and those with liver disease.

With most benzodiazepines, noticeable effects usually wear off within a few hours.

Alprazolam
Alprazolam is a benzodiazepine derivative that is currently used in the treatment of generalized anxiety, panic attacks with or without agoraphobia, and anxiety associated with depression. Alprazolam has a fast onset of symptom relief (within the first week); it is unlikely to produce dependency or abuse. No tolerance to its therapeutic effect has been reported. At discontinuation of treatment, withdrawal and rebound symptoms are common. Hence, alprazolam discontinuation must be tapered.

Conclusion
Few drugs can compete with benzodiazepines in efficacy, rapid onset of action and low acute toxicity. In short-term use, benzodiazepines can be valuable, sometimes even life-saving, across a wide range of clinical conditions.

References:

The following general characterizations can be made:
- Intermediate- and short-acting benzodiazepines are characterized by half-lives of 4 to 24 hours.
- Short-acting benzodiazepines are characterized by the following:
  - Few active metabolites.
  - Rarely, accumulation with multiple doses.
  - Minimal effect on drug clearance by age and liver disease.
- Long-acting benzodiazepines are characterized by the following:
  - Half-lives of longer than 24 hours.
  - Pharmacologically active metabolites
  - Accumulation with multiple dosages.
  - Impaired clearance in older patients and those with liver disease.

With most benzodiazepines, noticeable effects usually wear off within a few hours.

Alprazolam
Alprazolam is a benzodiazepine derivative that is currently used in the treatment of generalized anxiety, panic attacks with or without agoraphobia, and anxiety associated with depression. Alprazolam has a fast onset of symptom relief (within the first week); it is unlikely to produce dependency or abuse. No tolerance to its therapeutic effect has been reported. At discontinuation of treatment, withdrawal and rebound symptoms are common. Hence, alprazolam discontinuation must be tapered.

Conclusion
Few drugs can compete with benzodiazepines in efficacy, rapid onset of action and low acute toxicity. In short-term use, benzodiazepines can be valuable, sometimes even life-saving, across a wide range of clinical conditions.

References:
4. www.medscape.com

Continued from page 3

Continued from page 4

When examining non-serious GI events, severe GI events, discontinuous due to GI events, dyspepsia, abdominal pain and upper GI events, both meloxicam doses were significantly better than comparator NSAIDs in most cases. With respect to upper GI perforations, ulcerations and bleedings, the most serious of NSAID-associated side-effects, meloxicam was better tolerated than the comparators, reaching statistical significance for piroxicam and naproxen. Meloxicam's improved GI safety profile is likely to be due to its preferential inhibition of inducible COX-2 relative to constitutive COX-1.

Initiating Meloxicam Therapy
As with other NSAIDs, the potential benefits and risks should be considered prior to initiating meloxicam therapy. The lowest possible effective dosage and shortest duration of therapy consistent with treatment goals of the patient should be employed. Dosage of meloxicam must be carefully adjusted according to individual requirements and response, using the lowest possible effective dosage.

References:
4. www.medscape.com

7
**Fish Oil**
Natural Vitamin E

- Molecularly Distilled

- Best Source of Omega-3
  - Reduces risk of heart disease
  - Reduces hardening of arteries
  - Lowers triglycerides and VLDL levels
  - Lowers blood pressure
  - Reduces joint stiffness and swelling in rheumatoid arthritic patients

**Evening Primrose Oil**
Natural Vitamin E

- The Treasure For All Women
  - Eases all discomforts from
    - Mastalgia
    - Menopause
    - Flashes
    - Fluid retention
    - Menstrual cramps
  - The natural tonic & nourishment
    - Antioxidant
    - Relieves inflammation
    - Essential fatty acids
    - Prostaglandin
    - Skin conditioning & moisturizing
    - Prevents arthritis and all joint problems

**Natural Vitamin E**
Cod Liver Oil

- Youth & Beauty Essence
  - Slows the aging process of our skin and body organs
  - Freshens up the brain
  - Boosts up body metabolism
  - Smoothens your breath
  - Better skin condition
  - Improves eyesight
  - Clean & non-polluted

**Dailivite**
Multivitamins Minerals

- Keeps Your Body Healthy & Vital
  - Essential for growth and development
  - Protects the cells from damage and cellular aging
  - Aids in energy production and metabolism
  - Plays a major role in overall health

---

**ENDORSEMENT:**

- C&MF
- QA
- QC
- USP Compliance

---

Y.S.P. INDUSTRIES (M) SDN. BHD.
Toll Free: 1 800 88 3679
A Subsidiary of Y.S.P.SAH

we value life 我們尊重生命