

## IBS a motility and sensitive disorder: Beneficial effect of a gastrointestinal; selective calcium antagonist

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Functional gastrointestinal disorders, such as Irritable Bowel Syndrome (IBS) characterized by abdominal pain, transit disturbances and intestinal discomfort, are very common in the world population. IBS is widely regarded as a disorder of intestinal motor activity and it is known to also affect other regions of the gastrointestinal (GI) tract. Nowadays, hypothesis concerning the mechanisms implicated in these disorders brings to the role of visceral afferents mediating hypersensitivity of the gut in addition to GI hypermotility generally evoked. Patients with IBS respond to stimulation with exaggerated intestinal motor responses accompanied by abdominal symptoms. Stimuli implicated in this regard are GI mediators such as cholecystikinin (CCK), gastrin, substance P *etc.* Calcium antagonists, which are known to act when the cell membrane is depolarized following electrical stimulation, have recently been demonstrated to be effective when digestive hormones or mediators are involved<sup>[1]</sup>. Pinaverium bromide (PB) Dicitel, a GI selective calcium antagonist, that acts by interfering with the (-1 subunit of the intestinal L-Type calcium channel, has been intensively investigated<sup>[2]</sup>. Its effect on the stimulation of colonic motility induced by a meal, involving CCK and by a CCK injection, was evidenced in rats chronically fitted with intraparietal electrodes on the proximal colon and previously treated or not by capsaicin. The inhibition of postprandial colonic motility by PB given orally, occurring from the very low dose of 2 mg/kg, involves a CCK-dependent pathway which needs the integrity of sensitive afferents<sup>[3]</sup>. These data confirm prove us results showing

that PB has a marked inhibitory effect on GI contractile activity both in the postprandial and in the interdigestive phase<sup>[4]</sup>. This also supports the *in vitro* findings obtained in isolated single intestinal smooth muscle cells contracted by GI hormones or mediators<sup>[1]</sup>. In human, a pharmacology study performed by means of an intraluminal electromyographic probe recording long spike burst activity (LSB), in IBS patients, after a meal stimulation, showed that PB significantly inhibited LSB induced-increase *vs* placebo, illustrating its effect on colonic motor response to eating. Several other studies, measuring intraluminal pressure following a test meal, in dicatate that PB reduces overall motility in the sigmoid region and colon in human without adversely affecting normal propulsive activity. In conclusion, since the two main characteristics of the Irritable Bowel Syndrome are abnormal colonic motility and hypersensitivity of the gut, an inhibitory action of pinaverium bromide, a GI selective calcium antagonist, on postprandial motility through a mechanism involving sensory afferent neurons could explain the efficacy of this compound in the Irritable Bowel Syndrome, *via* its action both on motility and hypersensitivity of the gut.

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