Probiotics as the Treatment for the Visceral Pain in Gastrointestinal Disorders

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Introduction

Visceral pain

Visceral pain is the most common form of pain that human beings suffer throughout a lifetime. This kind of pain has important clinical characteristics:

- Is a pain originating in the internal organs but not evoked from all viscera.
- Diffuse and poorly localized.
- Not always linked to injury of the tissue.
- Referred to somatic structures.
- Intense motor and autonomic responses.

Irritable Bowel Disease (IBS) is mainly characterized by presence of visceral hypersensitivity and affects 3-25%[1] of the population. Among the wide variety of treatment options of the visceral pain, **probiotics** appear to be one of the best options.

Probiotics

"Live microorganisms which when administered in adequate amounts confer a health benefit on the host". For being effective, they need the following conditions:

- Non pathogenic and non toxic.
- Able to maintain good viability.
- Able to survive the passage through the digestive system.
- Able to attach to the intestinal epithelia and colonize temporarily.
- Capable of exerting a proven beneficial effect on the host.
- Remain stable and viable during processing, storage and use.

The species most widely used → ***Lactobacillus*** and ***Bifidobacterium.***

Aims

- To evaluate whether the treatment with the probiotic species *Lactobacillus* and *Bifidobacterium* is effective reducing the intestinal hyperalgesia in IBS patients.
- Compare the efficacy of using probiotics composed with a single strain or with multispecies.
- To elucidate the probiotics' main mechanisms that promote the intestinal antinociception.

Materials and methods

This project has been made by the search and extended reading of recent papers obtained from **PubMed**, **Sciencedirect** and **Scopus** databases, also consulting some doctoral thesis and books. The information was selected according to their relevance and date. The **main key words** used were: "*visceral hypersensitivity*", "*probiotic*", "*probiotic AND visceral pain*"," *probiotic AND IBS*".

Results

Efficacy of probiotics reducing the intestinal hyperalgesia in IBS patients

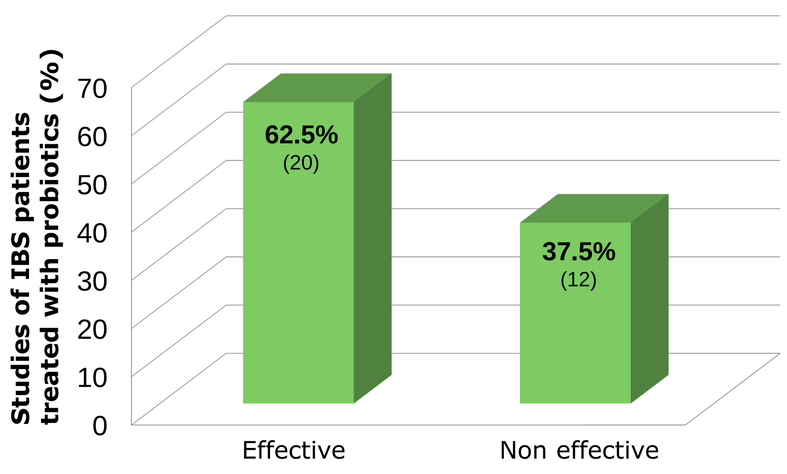

Figure 1. Percentage of studies that showed efficacy or non efficacy to the probiotical treatment. There are more studies that showed good response and a reduction of the visceral pain (62.5%) than studies that didn't show effectiveness (37,5%) to the treatment with probiotics.

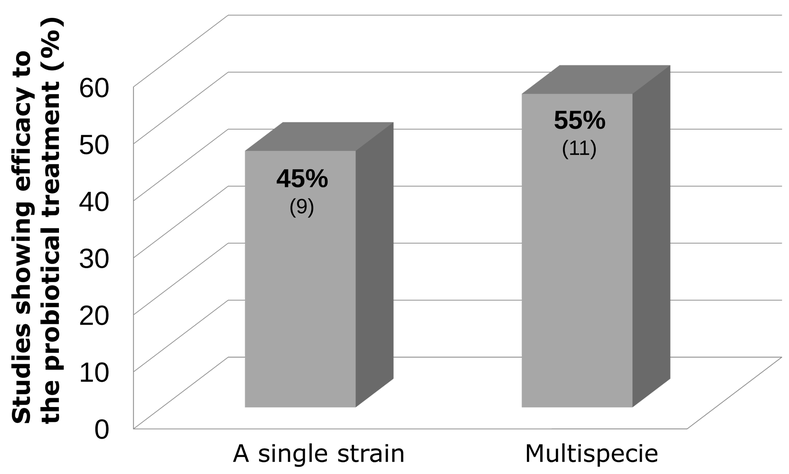

Figure 2. Efficacy comparison between the use of a single probiotic strain vs multispecies. From all studies where patients showed an improvement in the visceral pain, 45% used a single probiotic strain and 55% multispecies. There aren't efficacy differences between them.

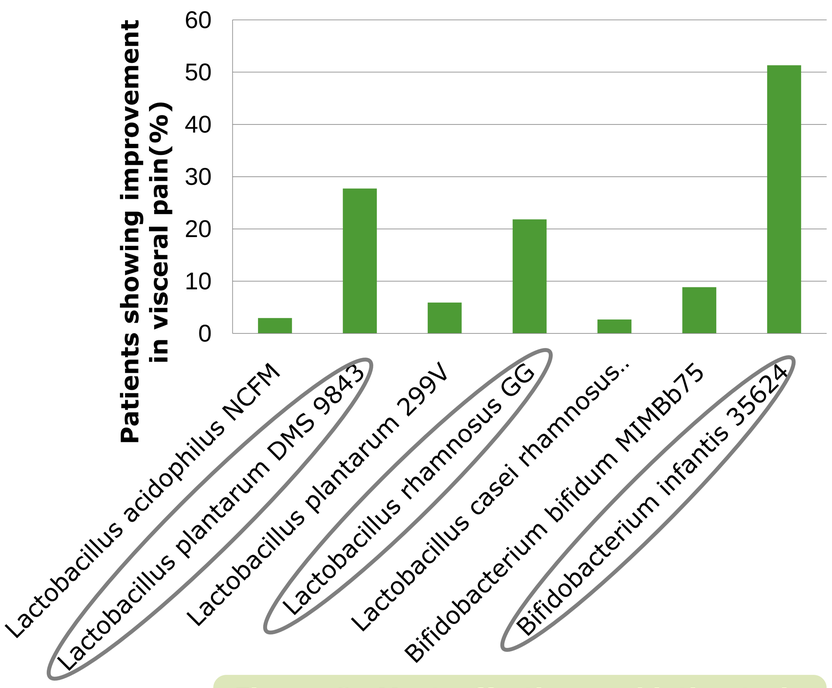

Figure 3. Most effective probiotic strain reducing the visceral pain.

Mechanism of action of probiotics

Current evidence indicates that different probiotic strains mediate their effects by a variety of **different mechanisms** that are dependent on the dosage employed , the **specific strain**, as well as the frequency of delivery.

Although the exact mechanisms of action of probiotics for the reduction of visceral pain are not known, several have been proposed.

PROBIOTICS ⇨ **IBS- related visceral pain**

- **↑ Expression of:**
  - **CB2 Receptor**
  - **μ-opioid Receptor**
- **Enhancement of the barrier function** [2]
  - **Release of Nitric oxide**
  - **↓ Apoptosis**
  - **↑ Expression of tight junction proteins :**
    - **Occludin**
    - **Zonula occludens – 1 (ZO1)**
- **Immunomodulation** → **Modify the cytokine profiles** → **↑ ratio IL-10/IL-12** → **Anti-inflammatory effect**[3]
- **Modulation of the microbiome- gut-brain axis** → **Changes in neurotransmitters levels in the SNC** [4] → **↑ Serotonin, Noradrenaline, Dopamine**

Further studies needed…

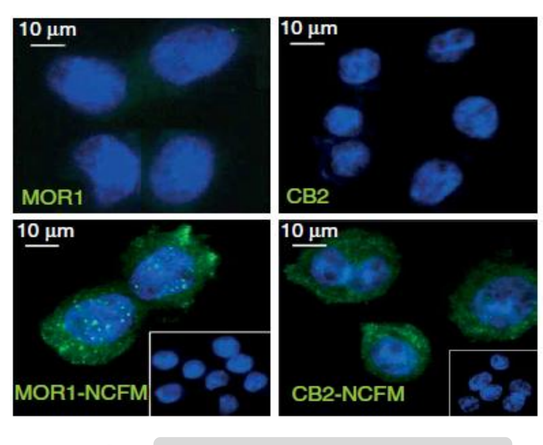

Figure 4. *Lactobacillus acidophilus* NCFM induces the expression of MOR1 and CB2 in epithelial cells.
Rousseaux C *et al. Nat. Med.* **13,** 35–7 (2007).

Conclusions

- Evidence suggests that probiotics offer a promise for the treatment of IBS patients. They have shown **efficacy** reducing the visceral pain and there are several mechanisms involved in this effect that are specie-specific.
- Future studies are needed about best strains, use of single or mixtures probiotics, dosis and to understand better the mechanisms involved in antinociception.

References

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2. Menningen R *et al. Am J Physiol Gastrointest Liver Physiol*.**296**, G1140-G1149(2009).
3. O'Mahony L *et al*. *Gastroenterology*.**128**, 541–51 (2005).
4. Kannampalli P *et al*. *Neurogastroenterol Motil*. **26**, 1694-704 (2014).