Efficacy of rifaximin in patients with abdominal bloating or distension: a systematic review and meta-analysis

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Introduction

- Abdominal bloating is a functional gastrointestinal complaint with high prevalence and significant impact on quality of life.
- Bloating is often underestimated because it co-exists with other functional GI disorders(FGIDs)
- This is especially in the case of IBS where it affects 66-90% of patients.
- Treatment protocols for abdominal bloating and distension usually involve dietary modification with low FODMAP diet
- Rifaximin is a semi-synthetic oral antibacterial drug belonging to the rifamycin class.
- It possesses activity against the bacterial RNA polymerase.

Aims and Objectives

- We aimed to perform a systematic review and meta-analyses on the effects of rifaximin in abdominal bloating.
- Primary outcomes: Improvement in symptoms of abdominal bloating or distension at the end of follow-up
- Secondary outcomes: Comparison of reduction in objectively measured patient reported outcomes (PROs) using bloating/distension scores.
- Subgroup analysis: Dose response relationships using different Rifaximin regimens

Methods and Materials

Databases	MEDLINE, EMBASE, Web of Sciences, and SCOPUS (inception up to 01/08/2020).
Inclusion Criteria	• Human studies, adults/adolescents aged >/=14 years, in any language. • RCTs examining the role of rifaximin in patients with FGIDs.
Exclusion Criteria	FGID in the background of IBD and diverticular disease of the colon.
Intervention	Active arm- oral rifaximin therapy; Control arm- Administered placebo.
Meta-analysis	• Data was pooled using the random-effects inverse-variance model with DerSimonian-Laird estimate of tau^2. • Pooled risk ratios from binomial variables and standardized mean difference (SMD) from PRO measures were used to generate forest plots.

Results

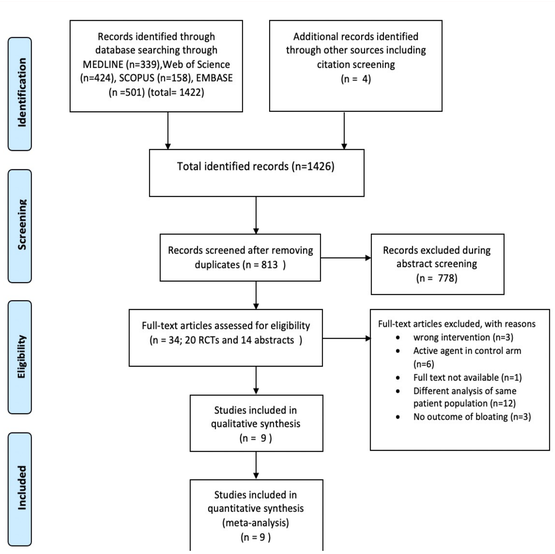

Figure 1: PRISMA flow chart for selection of studies included

Characteristics of studies	• 9 studies: 3326 patients (Rifaximin: 1672, Control: 1654); Mean age- 37.7-52.2 years (Figure 1) • Rifaximin dose- 800mg/1 week (2 studies), 400mg/10 days(1 study), 800mg/2 weeks(1 study), 1200mg/2weeks(1 study), 1100mg/2weeks(2 studies), 1650mg/2weeks(2 studies)
Improvement in Bloating/Distension	• 6 studies: RR 1.22, 95% CI 1.11, 1.35 at doses 1100-1650mg/2 weeks (homogenous for outcome) • Control arm (n/N=437/1199, 36.4%) and rifaximin arm (n/N=536/1202, 44.6%) whose bloating or distension improved: number needed to treat (NNT) of 12.2. (Figure 2)
Effect of Dose and Duration on improvement in bloating	• ≤1200 mg/day: binomial outcome- pooled RR 1.16, 95% CI 0.98, 1.38, p=0.09; scores- pooled SMD -0.31, 95%CI -0.75, 0.13, p=0.17 (Figure 3,4) • 1650 mg/day: binomial outcome- pooled RR 1.25, 95%CI 1.11, 1.4, p<0.001; scores- pooled SMD -0.27, 95% CI -0.51, -0.1, p=0.002 • Meta regression showed no effect of male sex (p=0.54), duration of follow-up (p=0.28), or the dose of rifaximin per tablet (p=0.56)
Improvement in Bloating scores	• 8 studies: different scales; pooled SMD -0.30, 95% CI -0.51, -0.10, p=0.04; significant heterogeneity

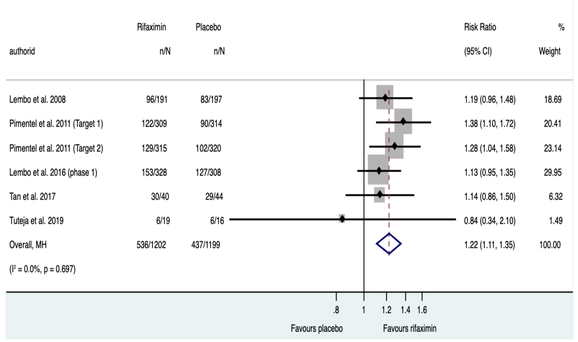

Figure 2: Forest plot depicting the proportion of patients demonstrating improvement in abdominal bloating or distension in each study.

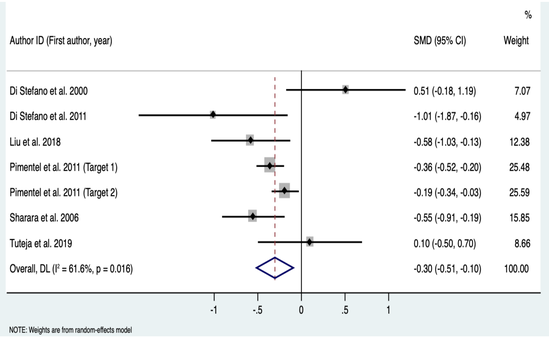

Figure 3: Forest plot depicting standardized mean difference of post-treatment bloating scores between rifaximin vs. placebo.

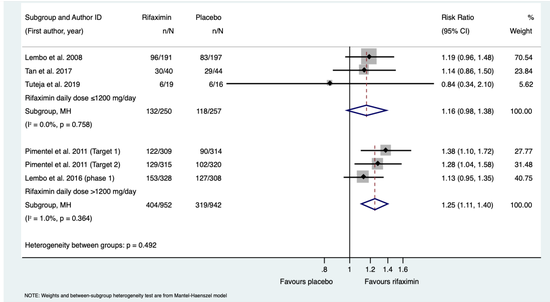

Figure 4: Forest plot of the same outcome as in Figure 2, depicting the subgroup analysis of different daily doses of rifaximin (≤1200 mg/day and >1200 mg/day).

Discussion

Strengths of this study

Focused on the symptom complex of bloating or distension	Incorporated more recent well-conducted trials
Included FGID other than IBS	Assessed the effect on bloating or distension in FGID irrespective of diagnosis.

Rifaximin showed improvement in bloating symptoms (3201 patients, pooled RR 1.22)

Rifaximin reduces the bloating or distension severity or duration (1553 patients, pooled SMD= -0.30)

Rifaximin doses >1200 mg/day + duration of 2 weeks showed improvement in bloating subjectively and a reduction in quantitative scores

Rifaximin is relatively safe (negligible GI absorption) and cost of generic form is low but may need reduction in the US

Conclusions

- Rifaximin effectively improves the symptoms of bloating or distension in patients with functional GI disorders, including IBS.
- It increases the likelihood of symptomatic relief compared to placebo and reduces the severity of these symptoms.
- It may be offered to patients with FGIDs symptomatic with bloating or distension who fail to improve on diet modification alone.

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References

1. Wu M, Zhao Y, Wang R, Zheng W, Guo X, Wu S, et al. Epidemiology of Functional Abdominal Bloating and Its Impact on Health Related Quality of Life: Male-Female Stratified Propensity Score Analysis in a Population Based Survey in Mainland China. PLoS ONE [Internet]. 2014 Jul 18 [cited 2020 Jun 26];9(7). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4103840/
2. Lacy BE, Cangemi D, Vazquez-ARoque M. Management of Chronic Abdominal Distension and Bloating. Clin Gastroenterol Hepatol [Internet]. 2020 Apr 1 [cited 2020 Jul 20]; Available from: http://www.sciencedirect.com/science/article/pii/S154235652030433X