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Comparative Effectiveness of Lactobacillus Reuteri Supplementation in Eradicating Helicobacter Pylori Infection: a Meta-Analysis of Randomized Controlled Trials

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INTRODUCTION

Helicobacter pylori (H. pylori) infection is a worldwide disease causing many disease. The rate of H. pylori eradication therapy declined in recent decades owing to the escalating antibiotic resistance. Thus, it is needed to apply new agents to improve the efficacy of H. pylori eradication. Lactobacillus reuteri (L. reuteri) have been demonstrated to reduce H. pylori bacterial load and suppress the binding of H. pylori to gastric epithelialium.

AIM

The aim of our research is to explore the effectiveness of L. reuteri supplementation for helping H. pylori eradication.

METHOD

A systematic search of studies on L. reuteri for combination in H. pylori eradication was conducted up to December, 2020. Our investigations were limited to randomized controlled trials (RCTs). The odds ratio of H. pylori eradication rate of L. reuteri supplementation versus placebo was treated as the primary outcome, whereas the standardized mean difference (SMD) of gastrointestinal symptom rating scale (GSRS) of L. reuteri supplementation versus placebo after the end of H. pylori eradication comprised the secondary outcome.

RESULTS

The meta-analysis included eight randomized controlled trials comprising 511 participants in total (Table 1). The pooled odds ratio of H. pylori eradication rate in the L. reuteri supplementation arm compared with the placebo arm was 1.55 (95% confidence level [CI]: 1.03 to 1.55, *p*=0.037), indicating a improvement in L. reuteri for combination in H. pylori eradication. The quantitative analysis showed a significantly lower GSRS of L. reuteri supplementation versus placebo after the end of H. pylori eradication (SMD: -0.83; 95% CI: -1.15 to -0.51, p=0).

Study	Age	Total cases (exp/cont)	H. pylori infection diagnosis (initial/rechecking)	Eradication regimen (duration)	Lactobacillus Reuteri (duration)	Follow-up time	%Eradication (exp/cont)	Gastrointestinal Symptom Rating Scale (exp/cont)
Lionetti E (2006)	Children (3.3–18 years)	40 (20/20)	Histology, RUT, ¹³ C-UBT/ ¹³ C-UBT	Sequential therapy (10 days)	L. reuteri ATCC 55730 2x10 ⁸ CFU/day (20 days)	8 weeks	85%/80%	3.2±2/5.8±3.4
Francavilla R (2008)	Adults (35–68 years)	40 (20/20)	Histology, RUT, ¹³ C-UBT, HpSA/ ¹³ C-UBT, HpSA	Sequential therapy (10 days)	L. reuteri ATCC 55730 10 ⁸ CFU/day (28 days)	4 weeks	88%/82%	7.9±4.1/9.7±8.7
Scaccianoce G (2008)	Adults (19-71 years)	33 (17/16)	Histology/ ¹³ C-UBT	Standard triple therapy (7 days)	L. reuteri ATCC 55730 2x10 ⁸ CFU/day (7 days)	4-6 weeks	53%/62%	NA
Ojetti V (2012)	Adults (18-65 years)	90 (45/45)	¹³ C-UBT/ ¹³ C-UBT	Standard triple therapy (7 days)	L. reuteri ATCC 55730 3x10 ⁸ CFU/day (2 weeks)	6 weeks	80%/62%	NA
Emara MH (2014)	Adults (18–60 years)	70 (35/35)	Histology, RUT, HpSA/ ¹³ C-UBT	Standard triple therapy (14 days)	L. reuteri DSM 17938 and ATCC PTA 6475 2x10 ⁸ CFU/day (4 weeks)	4 weeks	74.3%/65.7%	4.8±2.4/9.0±5.3
Francavilla R (2014)	Adults (18-65 years)	88 (44/44)	Histology, RUT, ¹³ C-UBT/ ¹³ C-UBT	Standard triple therapy (7 days)	L. reuteri DSM 17938 and ATCC PTA 6475 2x10 ⁸ CFU/day (96 days)	8 weeks	75%/65.9%	4±3.1/6.8±2.9
Shahraki T (2016)	Children (5–14 years)	50 (25/25)	Histology, HpSA/ 13C-UBT	Standard triple therapy (14 days)	L. reuteri DSM 17938 and ATCC PTA 6475 10 ⁸ CFU/day (4 weeks)	4 weeks	88%/76%	NA
Poonyam P (2019)	Adults (18-65 years)	100 (50/50)	Histology, RUT, Culture/ 13C-UBT	Bismuth containing quadruple therapy (7-14 days)	L. reuteri DSM 17938 and ATCC PTA 6475 2x10 ⁸ CFU/day (7-14days)	4 weeks	82%/80%	NA

CONCLUSIONS

Lactobacillus reuteri supplementation significantly give a rise to the improvement of H. pylori eradication therapy and reduce the incidence of gastrointestinal symptoms.

Study name	Stat	istics for	r each :	study	Odds ratio and 95% CI	
	Upper lim it	Lower lim it	Odds	p-Value		
Lionetti E (2006)	7.342	0.273	1.417	0.678	-	
Francavilla R (2008)	9.417	0.275	1.610	0.597	ł	
Scaccianoce G (2008)	2.709	0.168	0.675	0.579	Ŧ	
Ojetti V (2012)	6.847	1.039	2.667	0.041	+	
Emara MH (2014)	4.224	0.538	1.507	0.435	+	
Francavilla R (2014)	3.910	0.616	1.552	0.351	+	
Shahraki T (2017)	10.543	0.509	2.316	0.278	ł	
Poonyam P (2019)	3.097	0.419	1.139	0.799	+	
	2.341	1.026	1.550	0.037	•	

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Study name Statistics for each study Odds ratio and 95% Funder Lower Odds Upper Lower Odds Upper Lower Odds Lonentic (2006) 7.342 0.273 1417 0.573 Faraxvalla R (2006) 9.417 0.573 150 0.547 Faraxvalla R (2006) 9.417 0.573 150 0.547 Faraxvalla R (2012) 6.847 1.039 2667 0.541 Faraxvalla R (2014) 3.907 0.419 1.309 0.545 Ponyman (2014) 1.036 0.565 0.531 0.57 Ponyman (2014) 1.036 0.560 0.533 0.501 1.039 Ponyman (2014) 1.036 0.530 0.531 0.531 0.531 Ponyman (2014) 1.036 1.330 0.739 0.531 0.531 Ponyman (2014) 1.036 0.550 0.530 0.531 0.531 0.531 Ponyman (2014) 1.036 0.530 0.531 0.531 0.531 0.531 Ponyman (2014)	Statistics for each study Statistics for each study Study name Statistics for each study Stat diff Lower Upper Ionetti E (2006) -0.932 -1.585 0.280 0.005 -0.935 -1.041 Francanila R (2014) -0.923 -1.041 -1.041 -1.540 -0.933 -1.040 Francavila R (2014) -0.933 -1.041 -1.041 -1.540 -0.000 Francavila R (2014) -0.933 -1.041 -1.041 -1.540 -0.000 Paracenila R (2014) -0.933 -1.146 -0.510 0.000 -2.00 -0.000 Paracenila R (2014) -0.828 -1.146 -0.510 0.000 -2.00 -2.00 -1.00 -2.00 -	
with or without L. reuteri.	symptom rating scale with or without L. reuteri.	ACKNOWLEDGEMENTS

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