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The Effect of Probiotic Supplement as Adjuvant Therapy on Dyspeptic Symptoms and Quality of Life during *Helicobacter pylori* Eradication Therapy in a Sample of Iraqi Patients with Peptic Ulcer Disease

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Abstract:

Infection with Helicobacter pylori (H. pylori) had been associated with development of certain symptoms in addition to the use of standard eradication triple therapy has resulted in the increased incidence of undesirable side effects, which can lead to reduced compliance. Probiotics have been proposed to contribute to their efficacy in increasing H. pylori eradication and decreasing side effects when used together with eradication therapy. This study was intended to minimize the side effects of antibiotics therapy and the symptoms associated with peptic ulcer disease (PUD) and improving patient's quality of life (QOL). This interventional prospective randomized- controlled, open-label study was carried out on 77 patients diagnosed with positive H. pylori infection during the period from September 2017 to April 2018. The incidence and intensity of symptom score that caused by adverse effects of both infection and therapy were highly significantly decrease in terms of epigastric pain, bloating, flatulence, taste disturbance, loss of appetite, nausea, vomiting, and heartburn after 2 months of treatment within each study group correspondingly all domains of the quality of life were significantly improved in all patients after H. pylori eradication within each study group. From the present study concluded that the administra¬tion of probiotics as adjuvant to standard triple therapy may suggest a role in improving the symptoms and reduce the adverse effects accompanying with the eradication therapy for H. pylori thus improving patient's quality of life.

Key words: Peptic Ulcer Disease, H. pylori, Probiotics.

تأثير مكمل البروبايوتك كعلاج مساعد على أعراض عسر الهضم ونوعية حياة المرضى أثناء العلاج القاضي للبكتيريا الملوية البوابية فى عينة من المرضى العراقيين المصابين بمرض القرحة الهضمية

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الخلاصة:

الأصابة بعدوى البكتيريا الملوية البوابية قد ارتبطت بظهور بعض الأعراض بالإضافة إلى استخدام العلاج الثلاثي القياسي القاضي على البكتريا أدى إلى زيادة في حدوث آثار جانبية غير مرغوب فيها ، مثل الإسهال المرتبط بالمضادات الحيوية والغثيان أو القيء ، وبالتالي عدم التزام المرضى للعلاج. وقد تم اقتراح استخدام البروبايوتك للمساهمة في فعاليتها في القضاء على البكتريا الملوية البوابية والقضاء على الآثار الجانبية عند استخدامها جنبا إلى جنب مع العلاج الثلاثي. تهدف هذه الدراسة إلى تقليل الآثار الجانبية للمضادات الحيوية والأعراض المرتبطة بمرض القرحة الهضمية بالإضافة الى زيادة نوعية حياة المرضى. اجريت هذه الدراسة التداخلية العشوائية المحتملة المسيطر عليها والمفتوحة التسمية على 77 مريضاً تم تشخيص إصابتهم بالعدوى الملوية البوابية خلال الفترة من سبتمبر 2017 إلى أبريل 2018. انخفضَ حدوث

وشدة الاعراض الناجمة عن الآثار االجانبية لكل من العدوى والعلاج انخفاضاً كبيراً للغاية من حيث الم المعدة ، انتفاخ البطن ، اضطراب الذوق ، فقدان الشهية ، الغثيان ، التقيؤ ، والحرقة بعد شهرين من العلاج داخل كل مجموعة من مجاميع الدراسة في المقابل تحسنت جميع مجالات نوعية الحياة في جميع المرضى بشكل ملحوظ بعد القضاء على البكتريا الملوية البوابية في كل مجموعة. من الدراسة الحالية نستنتج إلى أن اضافة البروبايوتك كمساعد للعلاج الثلاثي القياسي قد يظهردوراً فعالاً في تحسين الأعراض والحد من الآثار الجانبية المصاحبة للعلاج االثلاثي القياسي القاضي على البكتريا الملوية البوابية وبالتالي تحسين نوعية حياة المرضى.

الكلمات المفتاحية : مرض القرحة الهضمية ، البكتريا الملوية البوابية ،البروبايوتك

Introduction:

Gastric colonization with *H. pylori* induces histologic gastritis in all infected indiv-iduals, but the disease remains asympt-omatic, as only a minority of patients (10-15%) develops any apparent clinical signs of this colonization [1]. When symptoms occur, they may include a burning pain in the middle or upper stomach between meals or at night, bloating**,** heartburn**,** nausea or vomiting [2]. In addition to The administration of antibiotics for 10-14 days and high-dose PPI (twice a day) has been recommended for *H. pylori* eradication therapy by the Maastricht IV consensus conference [3], this has resulted in the incr-eased incidence of undesirable side effects, such as antibiotic-associated diarr-hea, nausea or vomiting, during anti-*H. Pylori* therapy, which can lead to reduced compliance and thereby eradication failure [4]. Consequently, new therapies or adjun-ctive treatments to standard erad-ication regimens are needed [5]. Probiotics as defined by the Food and Agricultural Organization (FAO) and World Health Organization (WHO) are live microor-ganisms which when administered in adeq-uate amounts confer a health benefit on host. *Lactobacillus* and *Bifidobacterium* species were the most extensively studied probiotics for treating and/or preventing gastrointestinal diseases [6]. *H. pylori* infection might subclinically impair various mental and physical aspects of a patient's QOL. Several authors have reported that the QOL of patients with epigastric symptoms was improved after the eradication of *H. pylori* [7]. The QOL domains include : Physical Functioning (PF) to assess both the presence and extent of physical limitation, Role-Physical (RP) to assess role limitations due to physical health problems, Bodily Pain (BP) to measure the severity of bodily pain exper-ienced by the respondent during the indicated interval of time, General Health (GH) to capture an overall rating of health, Vitality (VT) to captures differences in subjective well-being by measuring the respondent's energy level, Social Funct-ioning (SF) to Assess health-related effects on the quantity of social activities, in terms of the impact of physical health and emoti-onal problems on such activities, Role-Emotional (RE) to assess role limitations owing to personal or emotional problems. Like the RP scale, it captures the impact of role limitations on performing work or other usual activities and Mental Health (MH) [8]. Probiotics have been proposed to contribute to their efficacy in increasing *H. pylori* eradication and decreasing side effects when used together with eradic-ation therapy [9].

Patients and methods

An interventional prospective randomized-controlled, open-label study designed to minimize the side effects of antibiotics therapy and the symptoms associated with PUD in addition to improving patients QOL. A total of 77 patients diagnosed with *H. pylori* infection (44 males and 33 females) who attended the private clinic of the consultant gastroenterologist and Al-Dawly private hospital were enrolled in the study after signing a written consent with ethical approval released by the institution scientific committee. The eligible patients were allocated into 4 groups:

Group 1: include (23) patients treated with standard *H. pylori* eradication triple therapy (clarithromycin 500 mg tablets,

amoxicillin 1g capsules, esomeprazole 20mg tablets) to be given twice daily for 14 days duration plus probiotic supplement to be given one capsule twice daily for 14 days", which represents 'same', i.e. probiotic administration simultaneously with the standard eradication regimen for a total period of 14 days.

Group 2: include (19) patients treated with probiotic supplement monotherapy to be given one capsule twice daily for 14 days, and then continue concurrently with the standard *H. pylori* eradication triple therapy, which represents 'before', i.e. probiotic used prior to the eradication regimen then continuing until the end of the eradication treatment for a total period of 28 days.

Group 3: include (18) patients treated with standard *H. pylori* eradication triple therapy plus probiotic supplement to be given one capsule twice daily for 14 days, followed by probiotics monotherapy for other 14 days, which represents: 'after', i.e. probiotic administered concomitantly with the eradication treatment and then continuing as a monotherapy when the eradication regimen has ended.

Group 4: include (17) patients treated with only standard *H. pylori* eradication triple therapy for 14 days period, which represent the control group.

The probiotic supplement includes acidophilus probiotic blend 1 billion culture with the prebiotic fructooli-gosaccharide (FOS), designed to aid in the maintenance of probiotic activity in the intestine. The amoxicillin and clarithromycin were administered after breakfast and dinner, esomeprazole was taken before breakfast and dinner, and meanwhile probiotic was given before the breakfast and dinner. All patients continue on esomeprazole only and were followed for 8 weeks.

All patients enrolled in this study were asked to answer a validated questionnaire about dyspeptic symptoms, and also the potential symptoms caused by the adverse effects of treatment. The questionnaire was carried out before treatment, on the day 7, day 30, and day 60 after completion of treatment course. Each symptom was quantified as absent =zero, mild =1, moderate =2 and severe =3. The incidence and intensity of symptoms in all patient were evaluated thereafter.

The patients' QOL was evaluated using the short form 8(SF-8) questionnaire. The SF-8 consists of 8 questions for the following domain: (PF, RP, BP, GH, VT, SF, RE, MH). The patient must provide one answer for each of the 8 questions. The scores for 2 summaries (the physical component summary [PCS] and the mental component summary [MCS]) are calculated. The SF-8 questionnaire carried out at baseline and 8 weeks later [7].

Scoring the SF-8 health domain scales consists of assigning the mean SF-36v2 scale score, from the 1998 U.S. general population, to each response category of the SF-8 item measuring the same concept [8]. The mean SF-36v2 standard form scores assigned to each SF-8 item's response categories yield T-score means of 50 for each SF-8 scale, based on the 1998 U.S. general population normative data. Each item is then considered a scale, with higher scores indicating better health. Scoring of the SF-8 is available through Quality Metric Incorporated or its authorized resellers [8]. The SPSS 21.0 was used to make the statistical analysis. ($P > 0.05$) are not significant while ($P < 0.05$) significant and ($P < 0.01$) are highly significant

Results

Demographic data and disease characteristics

The gender distribution of the study groups (female: male) ratio was as follows: Group 1 (30.43% vs 69.57%), group 2 (68.42% vs 31.58%), group 3 (38.89% vs 61.11%), and group 4 (35.29% vs 64.71%) respecttively. The duration of symptoms of **< 1** years was reported from (35.29%) to (63.16%), duration of symptoms between (1-5) years reported from (10.53%) to (47.06%), and duration of symptoms **> 5** years reported from (4.35%) to (22.22%)

among patients in the present study. There was no statistically significant difference in the mean values of gender, age, BMI and duration of symptoms between the study group's patients ($P > 0.05$), (Table1).

Table (1): Demographic data and disease characteristics of patients with *H. pylori* induced peptic ulcer

Variable	Study groups				*P* value
	Group 1 (n=23)	Group 2 (n=19)	Group 3 (n=18)	Group 4 (n=17)	
	n %	n %	n %	n %	
Gender [a]:					
Female	7 (30.43)	13 (68.42)	7 (38.89)	6 (35.29)	
Male	16 (69.57)	6 (31.58)	11 (61.11)	11 (64.71)	0.07^{NS}
Total	23 (100)	19 (100)	18 (100)	17 (100)	
Age [b]:					
21-30	4 (17.39)	5 (26.32)	8 (44.44)	8 (47.06)	
31-40	8 (34.78)	5 (26.32)	6 (33.33)	3 (17.65)	
41-50	4 (17.39)	3 (15.79)	0 (0.00)	4 (23.53)	0.29^{NS}
51-60	5 (21.74)	2 (10.53)	1 (5.56)	1 (5.88)	
61-70	2 (8.70)	4 (21.05)	3 (16.67)	1 (5.88)	
BMI [c] kg/m^2	27.72± 4.74	28.49± 5.51	24.46±4.32	26.40±4.35	0.06^{NS}
Symptoms duration [b]:					
< 1	12 (52.17)	12 (63.16)	7 (38.89)	6 (35.29)	
1-5	10 (43.48)	5 (26.32)	7 (38.89)	8 (47.06)	0.44^{NS}
> 5	1 (4.35)	2 (10.53)	4 (22.22)	3 (17.65)	

Data presented as Mean ±SD, (n) is the number of patients and (%) is a percentage. (a): Pearson chi-square test, (b): Fisher exact probability test, (c): One-way ANOVA test. NS: Nonsignificant ($P>0.05$).

Incidence and Intensity of Dyspeptic Symptoms in Patients with *H. pylori*-Induced PUD throughout the study Intervals

The mean incidence and intensity of epigastric pain, bloating and flatulence throughout the study intervals from the baseline, 7 days, 1 month, and 2 months within each study group showed considerable significant improvement and decrease in intensity ($P<0.01$), however, there were no differences in the incidence of epigastric pain between the study groups over study intervals except in groups 1 patient were notably decreased after 1 month though not significant ($P>0.05$) and except in groups 2 and 4 patient bloating was notably decreased after 1 month and significantly after 2 months ($P<0.01$). In addition, there were no differences in the incidence of flatulence over study intervals but only in groups 2 patient flatulence was significantly decreased after 2 months ($P<0.01$), (Table 2).

Table (2): Incidence and Intensity of Epigastric pain, Bloating and Flatulence in Patients with *H. pylori*- Induced PUD throughout the study Intervals

Epigastric pain									
Study Groups / Study Interval	Group 1 (n=23)		Group 2 (n=19)		Group 3 (n=18)		Group 4 (n=17)		*P* value
	Incidence n (%)	Intensity	Incidence n (%)	Intensity	Incidence n (%)	Intensity	Incidence n (%)	Intensity	
Baseline	16(69.56)	3.46	16(84.2)	3.68	17(94.44)	3.75	14(82.35)	3.65	0.19^{NS}
7 day	9(39.13)	2.57	8(42.1)	2.32	12(66.66)	2.36	12(70.58)	2.53	0.17^{NS}
1 month	4(17.39)	2.0	6(31.57)	1.97	9(50.00)	2.11	7(41.17)	2.11	0.09^{NS}
2 month	3(13.04)	1.98	5(26.31)	2.03	7(38.88)	1.78	4(23.52)	1.71	0.20^{NS}
Percent of change	-42.77%		-44.83%		-52.53%		-53.15%		
P value	0.00^{**}		0.00^{**}		0.00^{**}		0.00^{**}		
Bloating									
Baseline	21(91.3)	3.70	19(100)	3.92	18(100)	3.86	15(88.23)	3.76	0.08^{NS}
7 day	13(56.52)	2.22	12(63.1)	2.39	12(66.66)	2.03	11(64.7)	2.50	0.34^{NS}
1 month	12(52.17)	1.93	8(42.1)	1.82	13(72.22)	2.11	4(23.52)	1.88	0.09^{NS}
2 month	15(65.21)	2.15	9(47.36)	1.87	14(77.77)	2.00	5(29.41)	1.85	0.02^{**}
Percent of change	-41.89%		-52.29%		-48.18%		-50.79%		
P value	0.00^{**}		0.00^{**}		0.00^{**}		0.00^{**}		
Flatulence									
Baseline	22(95.65)	3.76	19(100)	3.92	18 (100)	3.86	15(88.23)	3.76	0.16^{NS}
7 day	16(69.56)	2.35	12(63.1)	2.45	11(61.11)	1.97	11 (64.7)	2.47	0.41^{NS}
1 month	13(56.52)	1.83	7(36.84)	1.79	13(72.22)	2.17	4 (23.52)	1.85	0.05^{*}
2 month	16(69.56)	2.07	8 (42.1)	1.84	13(72.22)	2.00	6 (35.29)	1.91	0.02^{**}
Percent of change	-44.95%		-53.06%		-48.18%		-49.20%		
P value	0.00^{**}		0.00^{**}		0.00^{**}		0.00^{**}		

Data presented as mean rank (intensity), (n) is the number of patients and (%) is a percentage. Fisher exact probability test to compare variables between study groups, Friedman test to compare variables in the same group at different periods, NS: Not significant ($P>0.05$), (**) ($P<0.01$) is considered highly significant.

The mean incidence and intensity of taste disturbance and loss of appetite throughout the study period from the baseline, 7 days, 1 month, and 2 months within each study group showed considerable significant improvement and decrease in intensity ($P<0.01$), however, there were no differences in the incidence of taste disturbance between the study groups over study intervals ($P>0.05$), (Table 3).

Table (3): Incidence and Intensity of Taste disturbance and Loss of appetite in Patients with *H. pylori*- Induced PUD throughout the study Intervals

Taste disturbance									
Study groups / Study intervals	Group 1 (n=23)		Group 2 (n=19)		Group 3 (n=18)		Group 4 (n=17)		
	Incidence n%	Intensity	Incidence n%	Intensity	Incidence n%	Intensity	Incidence n%	Intensity	*P* value
Baseline	10(43.47)	2.93	14(73.6)	3.39	14(77.77)	3.39	14(82.35)	3.41	0.19^{NS}
7 day	10(43.47)	2.89	9(47.36)	2.47	13(72.22)	2.97	13(76.47)	2.82	0.29^{NS}
1 month	1(4.34)	1.98	5(26.31)	2.03	3(16.66)	1.83	5(29.41)	1.88	0.10^{NS}
2 months	4(17.39)	2.20	5(26.31)	2.11	3(16.66)	1.81	4(23.52)	1.88	0.93^{NS}
Percent of change	-24.91%		-32.57%		-46.61%		-44.87%		
P value	0.00^{**}		0.00^{**}		0.00^{**}		0.00^{**}		
Loss of appetite									
Baseline	12(52.17)	3.17	11(57.8)	3.11	14(77.77)	3.53	9(52.94)	3.06	0.16^{NS}
7 day	7(30.43)	2.57	4(21.05)	2.13	10(55.55)	2.53	5(29.41)	2.29	0.06^{NS}
1 month	2(8.69)	2.09	5(26.31)	2.32	5(27.77)	2.03	3(17.64)	2.29	0.33^{NS}
2 months	3(13.04)	2.17	6(31.57)	2.45	5(27.77)	1.92	4(23.52)	2.35	0.85^{NS}
Percent of change	-31.55%		-21.22%		-45.61%		-23.20%		
P value	0.00^{**}		0.01^{**}		0.00^{**}		0.04^{**}		

Nausea except and vomiting were significantly decreased in the mean incidence and intensity of throughout the study intervals from the baseline, 7 days, 1 month, and 2 months within each study group (P<0.01) in group 1 patients, however, no differences in vomiting between the study groups over study intervals was noticed (P>0.05), (Table 4).

Table (4): Incidence and Intensity of Nausea and Vomiting in Patients with *H. pylori*- Induced PUD throughout the study Intervals

Nausea									
Study group / Study intervals	Group 1 (n=23)		Group 2 (n=19)		Group 3 (n=18)		Group 4 (n=17)		
	Incidence n%	Intensity	Incidence n%	Intensity	Incidence n%	Intensity	Incidence n%	Intensity	*P* value
Baseline	5(21.73)	2.70	11(57.8)	3.21	15(83.33)	3.58	9(52.94)	3.18	0.01^{**}
7 day	3(13.04)	2.34	8(42.1)	2.34	7(38.88)	2.39	7(41.17)	2.53	0.21^{NS}
1 month	3(13.04)	2.39	7(36.84)	2.21	4(22.22)	2.11	3(17.64)	2.24	0.43^{NS}
2 month	4(17.39)	2.48	6(31.57)	2.24	3(16.66)	1.92	2(11.76)	2.06	0.43^{NS}
Percent of change	-8.15%		-30.21%		-46.36%		-35.22%		
P value	0.44^{NS}		0.00^{**}		0.00^{**}		0.00^{**}		
Vomiting									
Baseline	1(4.34)	2.57	4(21.05)	2.82	8(44.44)	3.11	5(29.41)	2.94	0.05^{*}
7 day	0(0.0)	2.48	1(5.26)	2.45	2(11.11)	2.39	2(11.76)	2.47	0.62^{NS}
1 month	0(0.0)	2.48	0(0.0)	2.37	1(5.55)	2.31	0(0.0)	2.29	0.46^{NS}
2 month	0(0.0)	2.48	0(0.0)	2.37	1(5.55)	2.39	0 (0.0)	2.29	0.46^{NS}
Percent of change	-3.50%		-15.96%		-23.15%		-22.10%		
P value	0.39^{NS}		0.01^{**}		0.00^{**}		0.00^{**}		

There was highly significant decrease in the mean incidence of heartburn in the early study intervals in group 1 and 2 patients particularly on 7 day visit (P<0.01) compared to group 3 and 4 patients, and the heartburn significantly decreased in the mean incidence and intensity of throughout the study intervals from the baseline, 7 days, 1 month, and 2 months within each study group (P<0.01), however, the symptom recurred again after 2 months in all study groups with the least incidence in group 1 and 2 patients, (Table 5).

Table (5): Incidence and Intensity of Heartburn in Patients with *H. pylori*- Induced PUD throughout the study Intervals

Heartburn									
Study groups / Study intervals	Group 1 (n=23)		Group 2 (n=19)		Group 3 (n=18)		Group 4 (n=17)		
	Incidence n%	Intensity	Incidence n%	Intensity	Incidence n%	Intensity	Incidence n%	Intensity	*P* value
Baseline	14(60.86)	3.26	11(57.8)	3.26	16(88.88)	3.78	14(82.35)	3.47	0.09^{NS}
7 day	1(4.34)	2.09	4(21.05)	2.37	7(38.88)	2.06	9(52.94)	2.38	0.00**
1 month	4(17.39)	2.22	1(5.26)	2.03	6(33.33)	2.03	6(35.29)	2.09	0.11^{NS}
2 month	6(26.08)	2.43	4(21.05)	2.34	8(44.44)	2.14	7(41.17)	2.06	0.52^{NS}
Percent of change	-25.46%		-28.22%		-43.38%		-40.63%		
P value	0.00**		0.00**		0.00**		0.00**		

The mean incidence and intensity of diarrhea and constipation were signify-cantly decreased throughout the study intervals from the baseline, 7 days, 1 month, and 2 months within study group 3 only (P<0.01) compared to other groups, however, there was no differences in diarrhea between the study groups over study intervals (P>0.05), (Table 6).

Table (6): Incidence and Intensity of Diarrhea and Constipation in Patients with *H. pylori*- Induced PUD throughout the study Intervals

Diarrhea									
Study group / Study intervals	Group 1 (n=23)		Group 2 (n=19)		Group 3 (n=18)		Group 4 (n=17)		
	Incidence n%	Intensity	Incidence n%	Intensity	Incidence n%	Intensity	Incidence n%	Intensity	*P* value
Baseline	5(21.73)	2.74	4(21.05)	2.66	7 (38.88)	2.86	2 (11.76)	2.59	0.66^{NS}
7 day	4(17.39)	2.57	4(21.05)	2.61	6 (33.33)	2.64	2(11.76)	2.53	0.86^{NS}
1 month	1(4.34)	2.30	2(10.52)	2.32	3 (16.66)	2.33	1 (5.88)	2.44	0.75^{NS}
2 month	2(8.69)	2.39	3(15.78)	2.42	2 (11.11)	2.17	1 (5.88)	2.44	0.85^{NS}
Percent of change	-12.77%		-9.02%		-24.13%		-5.79%		
P value	0.10^{NS}		0.36^{NS}		0.02**		0.73^{NS}		
Constipation									
Baseline	3 (13.04)	2.63	2 (10.52)	2.61	5(27.77)	2.92	1 (5.88)	2.53	0.14^{NS}
7 day	1 (4.34)	2.43	2 (10.52)	2.50	0(0.0)	2.36	0 (0.0)	2.41	0.15^{NS}
1 month	1 (4.34)	2.43	2 (10.52)	2.50	0(0.0)	2.36	1 (5.88)	2.56	0.36^{NS}
2 month	2 (8.69)	2.50	1 (5.26)	2.39	0 (0.0)	2.36	1 (5.88)	2.50	0.84^{NS}
Percent of change	-4.94%		-8.43%		-19.18%		-1.18%		
P value	0.51^{NS}		0.49^{NS}		0.00**		0.71^{NS}		

Assessment of Quality of Life (QOL) of Patients with *H. pylori*- Induced PUD treated with Eradication Triple Therapy Alone or in Combination with Probiotic

After 8 weeks of treatment, there was highly significant increase in the eight domains of the SF-8 score (PF, RP, BP, GH, VT, SF, RE, MH, PCS and MCS) in all 4 groups compared to pretreatment (P<0.01), but no significant difference between the study groups after treatment was noticed (P>0.05) (Figure 1)

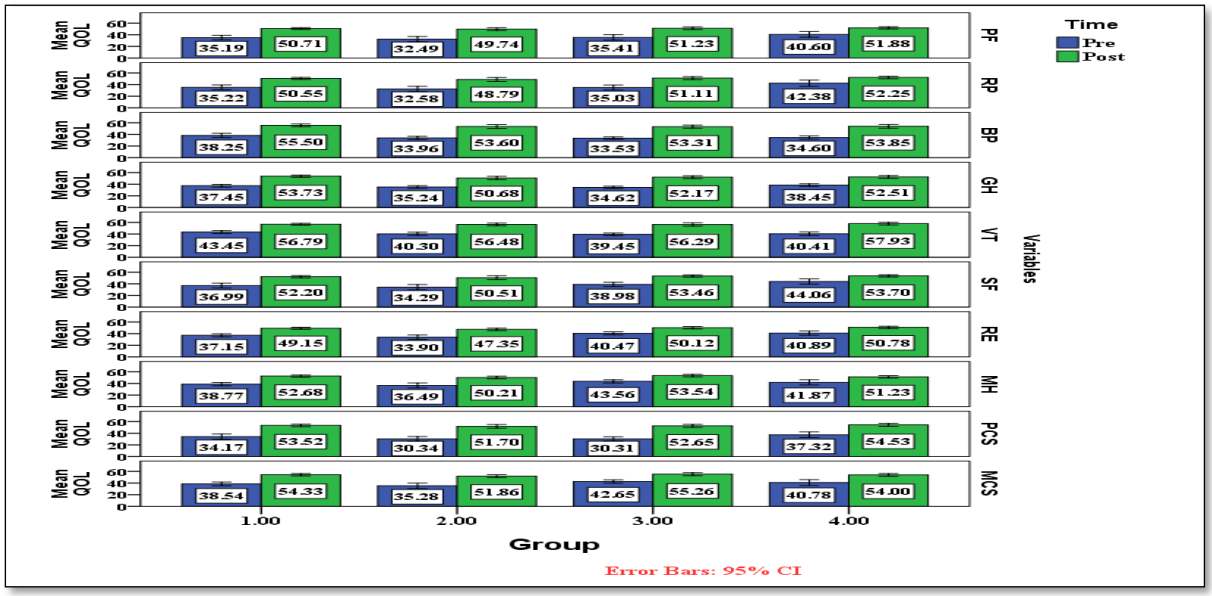

Figure (1): Comparison of QOL mean scores of the SF-8 questionnaire in study groups patient's pre and post-treatment

Discussion

Demographic Data and Disease Characteristics of Patients with *H. pylori* Induced Peptic Ulcer Disease

In the present study and in other studies, both genders have a higher rate of infection with *H. pylori* micro-rganism with slight predominance towards male patients in this study and others [10, 11], or towards female gender in other studies [12-14]. Moreover, *H. pylori* infection mostly presents within (21-40) years age groups in this study, and a lower prevalence rate of *H. pylori* infection was noticed in the elderly among all study groups. Two hypotheses have been proposed to explain these findings; the first, in old age *H. pylori* could be present in a small number or low activation which might not be detected, and second, the history of *H. pylori* infection may be overlapped by the development of an unfavorable gastric environment with aging [15]. Most patients in the present study were slightly overweight among the study groups. Comparable results were found in other studies where individuals with a higher BMI were more likely to be positive for *H. pylori* infection than those with a lower BMI or with an increased risk [16], and a positive relation between obesity and *H. pylori* infection were revealed [17]. Majority patients in the current study presented with duration of symptoms of less than one year where the patients presented with high intensity of dyspeptic symptoms.

Assessment of Dyspeptic Symptoms of PUD Patients on *H. pylori* Eradication Triple Therapy Alone and in Combination with Probiotics

Presence and intensity of a number of symptoms caused by *H. pylori* infection should be monitored [18]. Increasing intensity in the symptoms during and after treatment was considered as adverse effects, and low compliance, mainly because of adverse events due to antibiotics is a substantial problem that requires a different line of treatment [19, 20]. Probiotics could represent a valid support to the standard triple therapy, and such a combination means that the patient still receives a certain ''gold standard'' in terms of therapy, and potentially get a benefit from probiotics adjuvant addressing both issues that affect standard triple therapy efficacy via reducing the frequency of side-effects of antibiotic hence increasing patient compliance in one arm [21, 22], and eliminating the need for additional antibiotics, thus greatly reduce possibility for antibiotic resistance in another arm [20].

The results of the current study revealed that there was highly significent decrease ($P < 0.01$) in the incidence and intensity of symptom score caused by adverse effects of both infection and therapy in terms of epigastric pain, bloating, flatulence, taste disturbance, loss of appetite, nausea, vomiting, and heartburn after 2 months of treatment within each study group. The improvement in the bloa-ting and flatulence was noticed in patients receiving 14 days probiotics prior combining to standard *H. pylori* triple therapy (before) compared to other protocols of therapy (-52.29% and -53.06%) ($P < 0.01$) after 2 months respectively, meanwhile the improvement in the intensity of epigastric pain score was noticed in this group of patients early after one month only and no significant difference between groups thereafter. Also, no significant difference between groups in respect to taste disturbance, loss of appetite, nausea, and vomiting ($P > 0.05$), except for the intensity of heartburn was significantly reduced within 7 days inpatient on probiotic supplement of all protocols compared to the standard *H. pylori* eradication triple therapy ($P < 0.01$). The incidence and intensity of diarrhea and constipation were significantly decreased in patients continue for 14 days probiotics therapy after combining to standard *H. pylori* triple therapy (after) compared to other protocols of therapy ($P < 0.01$), and the least percent of change was found in patients on standard *H. pylori* eradication triple therapy. These findings were inconsistent with that of Hauser *et al.* (2015), where adding probiotic supplement containing *Lactobacillus rhamnosus* GG (LGG1) and *Bifidobacterium* (BB-121) in the concentration of 10^8 to 10^{10} CFU to the standard *H. pylori* eradication triple therapy produced more pronounced reduction in disease symptoms in the probiotic arm (7 out of 10 symptoms $P < 0.05$) as early as at 2 weeks of treatment, that is to say, after the discontinuation of antibiotic and before continuing on PPI monotherapy for 3 weeks [18].

On the contrary, Navarro-Rodriguez *et al*. (2013) in his study found that probiotics (*Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Bifidobacterium bifidum* and *Streptococcus Faecium*), which are similar to those used in the present study, when administered for 30 days after combining to antibiotic regimen (Lansoprazole 30 mg, Tetracycline 500 mg and Furazolidone 200 mg administered twice a day for 7 days) did not show any increase in bacterial eradication effectiveness or decrease in

adverse effects of *H. pylori* eradication treatment among Brazilian patients [19]. Several meta-analysis concluded that the administration of probiotics can ameliorate the symptoms and reduce the adverse effects associated with eradication therapy for *H. pylori*, such as diarrhea, vomiting, nausea and epigastric pain [23-25].

Assessment of QOL of PUD Patients on *H. pylori* Eradication Triple Therapy Alone and in Combination with Probiotics

The role of QOL assessment has gained increased attention among gastrointestinal researchers in recent years. The SF-8 generates a health profile of eight discrete scores descryibing health-related quality of life (HRQL), which are summarized into PCS and MCS continuous summary scores [26].

In the present study, the SF-8 questionnaire showed that both the PCS and MCS scores including all components were significantly improved in all patients after *H. pylori* eradication within each study group ($P<0.01$), though, there was no significant difference in the QOL score between study groups in all domains ($P>0.05$) post-treatment.

Many other previous studies reported the improvement of QOL in patients with peptic ulcers treated with standard *H. pylori* eradication triple therapy, but no available report deals with the impact of probiotic as monotherapy or as an adjuvant on patients QOL. Nevertheless, with reference to the improvement in the dyspeptic symptoms particularly in bloating and flatulence which was noticed in patients receiving 14 days probiotics prior combining to standard *H. pylori* triple therapy (before) after 2 months in this study compared to other protocols of therapy and the improvement in the intensity of epigastric pain score early after one month, consequently may potentially improve the QOL of PUD patients.

A recent report by Taguchi *et al.* (2017), the SF-8 questionnaire of both the PCS and MCS scores were significantly improved after standard *H. pylori* eradication triple therapy (Rabeprazole, 10mg; Amoxicillin, 750 mg; Clarithromycin, 200mg; b.i.d. for 7 days) by using the SF-8 Japanese version, where (PCS; P = 0.04, MCS; P = 0.004) in all patients. This improvement in *H. pylori*-positive patients was regardless of the presence or absence of epigastric symptoms [7].

Wen *et al*. (2014) also reported that patients with chronic gastritis had poor QOL compared to patients with peptic ulcers (except for PF domain), and both groups had lower QOL score compared to population norms (except for MH domain). After treatment, both groups experienced improved QOL after treatments (except for RP domain for both diseases) [27].

In a recent study by Kabakambira *et al.* (2018) evaluated the impact of HR QOL using the Short Form Nepean Dyspepsia Index (SF-NDI) questionnaire of PUD patients on standard antibiotic based triple therapy for 10 days, the improvement was much less in the metronidazole-based triple therapy than in the standard of care [28].

Conclusion

From the present study concluded that the administration of probiotics as adjuvant therapy to the standard *H. pylori* eradication triple therapy may suggest a significant role in improving the symptoms and reduce the adverse effects accompanying with the eradication therapy for *H. pylori* thus improving patient's quality of life.

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