Clinical Efficacy of Dexlansoprazole vs Esomeprazole in Gastro-Oesophageal Reflux Disease: A Randomized Clinical Trial.

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ABSTRACT

Background: Gastro-Esophageal reflux disease (GERD) is a very common problem in a gastrointestinal clinical setting. Still, the best treatment for it remains debatable as there are many new drugs that have evolved for its treatment in addition to dietary modification.

Objective: To compare the clinical efficacy of Dexlansoprazole (modified-release 60 mg) and esomeprazole (40 mg) for the resolution of symptoms of GERD after 2 weeks of therapy.

Material and Methods: This randomized controlled trial or intervention was conducted for comparing the clinical efficacy of Dexlansoprazolevs Esomeprazole for the symptomatic treatment of GERD.A total of 100 endoscopically diagnosed patients were selected and were randomly allocated to two groups each containing 50 patients. Group 'A' contained 50 patients who were given 60 mg Dexlansoprazole for 2 weeks and group 'B' also contained the same number of patients receiving the treatment with Esomeprazole 40 mg for the same duration.After informed consent, a validated tool FSSG (Frequency Scale for the Symptoms of GERD) was used to collect the responses of patients.The data was analyzed using SPSS version 23. The Chi-square test was used to compare the responses of two groups considering a P-value of <0.05 as significant.

Results: Among domains of frequency scale for the symptoms of GERD, only dysphagia was significantly better in Dexlansoprazole group, P-valueof< 0.05 while rest of the symptoms were statistically same with a p-value of > 0.05.

Conclusion: This study concluded that the symptomatic relief of GERD after 2 weeks of therapy with Esomeprazole and Dexlansoprazole was the same except for dysphagia.

Keywords: Dexlansoprazole, Esomeprazole,Gastroesophageal reflux disease.

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INTRODUCTION

Gastroesophageal reflux disease is nothing new gastroenterology setting and it has prevalence of 10-20% in the West and an yearly incidence of 0.38-0.45%. [1]Its prevalence in North America is 18.1-27.8% and 8.8-25.9% in entire Europe. [2]Most studies have reported that such patients have a decrease in workplace productivity with a direct impact on quality of life.[3] This in turn is a financial burden on patients as treatment may last for months and maybe even more complicated in refractory cases. [4]

It can cause a variety of symptoms such as burning in the chest, regurgitation of food and sometimes symptoms of asthma.[5] Acid suppression therapy forms the cornerstone of the treatment with eminent superiority.[6] Overall, proton pump inhibitors (PPIs) have shown significant relief of complainsand better healing of esophagitis as well as considerable relief in theagony of patients with GERD. The PPIs are the cornerstone for GERD treatment,, and in that, they can provide 56-76% considerable relief of symtoms and 80-85% rates of healing for oesophageal lesions, which can decrease the incidence of dangerous sequalae.[7] However, it is reported that around 30% of affected patients continue to have symptoms on conventional doses of PPIs once daily.

Therefore twice-daily doses of PPI are essential for symptomatic relief. The recurrence of symptoms is a problem frequently reported by patients questioning the compliance of therapy even with double dose and partly the non-adherence to the right diet contributing as well. [8]The latest guidelines have advised weight loss and raising the head end of the patient's bed to decrease the symptoms of reflux. [9]The evolution of newer PPIs have provided gastroenterologists more options in terms of the treatment of such patients. Due to the dual delayed release formation of dexlansaprazole it can be used as a step down therapy for patients having reflux symptoms.[10] Therefore I want to do this study as dexlansaprazole is a new drug and there are

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fewer studies when it comes to comparing it with other PPIs.This study compares the clinical efficacy of Dexlansoprazolevs Esomeprazole for the symptomatic treatment of GERD.

MATERIAL AND METHODS

Operational Definition:

GERD:

Gastroesophageal reflux disease (GERD) occurs when stomach acid frequently flows back into the tube connecting your mouth and stomach (esophagus).[6]

After ethical approval on 28th Dec 2018, this randomized control intervention study was conducted in tertiary care hospital affiliated with Kabir Medical College (Town Teaching Hospital Peshawar) from 1st January 2019 to 30th December 2019. Inclusion cases were all patients with symptoms of GERD like heart burn and regurgitation of food diagnosed clinically and on upper gastrointestinal endoscopy based on LA classification. Endoscopic findings were noted which can be as follows: 1. esophageal erosions which will be graded as per the Los Angeles (LA) classification system as follows: Grade A: more than one mucosal break no longer than 5 mm, none of which extends between the tops of the mucosal folds; Grade B: more than one mucosal break more than 5 mm long, none of which extends between the tops of two mucosal folds; Grade C: mucosal breaks that extend between the tops of two or more mucosal folds, but involve less than 75% of esophageal circumference; and Grade D: mucosal breaks involving at least 75% of the esophageal circumference. Pregnant ladies, diabetic patients already on proton pump inhibitors and those having associated peptic ulcer disease and gastrointestinal tumour were excluded from the study.Sample size of 104 patients was calculated with 80% confidence interval, 80% power of test and by taking expected GERD score with Dexlansoprazole and Esomeprazole as 13.1±3.8 and 16.5±10.9 respectively.[14] Following formula was used to calculate sample size

$$n = \frac{(Z\alpha_{/2} + Z_{\beta})^2 \times 2\sigma^2}{(\mu_1 - \mu_2)^2}$$

In both treatment groups 4 patients were lost to follow up so the final analysis was carried out on 100 patients (50 patients in each group).

Group 'A' contained 50 patients who were given 60 mg Dexlansoprazole for 2 weeks and group 'B' also contained the same number of patients receiving the treatment with esomeprazole for the same duration. After informed consent, a validated tool FSSG (Frequency Scale for the Symptoms of GERD)[3] was used to collect the responses of patientson follow up or using electronic contact using a mobile phone, Whatts app and e-mail.The data analysis was through SPSS latest version.The age of the participants was taken as quantitative variable while gender was qualitative variable. The drug effectiveness was based on the response of patients and their improvement of symptoms being assessed clinically on followup visits. The Chi-square test got applied to compare the responses of two groups considering a P-value of leass than 0.05 as significant.

RESULTS

The mean age of patients in the Esomeprazole group was 32.86 ± 9.21 years and in the Dexlansoprazole group was 33.50 ± 8.58 years, with no significant difference, p-value > 0.05. In the Esomeprazole group, there were 27(54%) male and 23 (46%) female cases while in the Dexlansoprazole group there were 20 (40%) male and 30(60%) females. The mean total score (symptoms severity score) of the frequency scale for the symptoms of GERD in the Esomeprazole group was 25.57 ± 10.46 years and in the Dexlansoprazole group was 21.38 ± 13.53, although the total score was higher in the Esomeprazole group but was not statistically, significant difference, p-value > 0.05.This p-value was calculated to compare age of patients in both treatment groups. The purpose was to see if the age of patients in both treatment groups was statistically different or same.Presenting symptoms were compared in both treatment groups to see which group had higher or less frequency for a said symptoms. To compare each symptoms severity in both treatment groups we groups we have calculated p value to show that which group is better in terms of resolution of certain symptoms.Among domains of frequency scale for the symptoms of GERD, only dysphagia was significantly better in Dexlansoprazole group, p-value < 0.05 while rest of the symptoms were statistically same, p-value > 0.05.The improvement in dysphagia was assessed clinically by taking history from the patient.

Table 1. Comparison of Age and Total Score of Frequency Scale for the Symptoms of GERD in Both Groups

	Study Groups	Mean	S.D	P-value
Age (years)	Esomeprazole (n=50)	32.86	9.21	0.072
	Dexlansoprazole(n=50)	33.5	8.58	
Total Score	Esomeprazole(n=50)	25.57	10.46	0.088
	Dexlansoprazole(n=50)	21.38	13.53	

Table 2. Comparison of Scale for the Symptoms of GERD in Both Groups

		Study groups		P-value
		Esomeprazole (%)	Dexlansoprazole (%)	
Heartburn	Never	1(2)	10(20)	0.076
	Occasionally	14(28)	11(22)	
	Sometimes	12(24)	10(20)	
	Often	13(26)	12(24)	
	Always	10(20)	7(14)	
Bloating	Never	5(10)	12(24)	0.241
	Occasionally	9(18)	12(24)	
	Sometimes	17(34)	11(22)	
	Often	11(22)	7(14)	
	Always	8(16)	8(16)	
Heaviness	Never	3(6)	8(16)	0.353
	Occasionally	10(20)	13(26)	
	Sometimes	15(30)	9(18)	
	Often	13(26)	13(26)	
	Always	9(18)	7(14)	
Rubbing Chest	Never	1(2)	13(26)	0.005
	Occasionally	15(30)	11(22)	
	Sometimes	9(18)	8(16)	
	Often	22(44)	12(24)	
	Always	3(6)	6(12)	
Feeling Sick Post Meals	Never	2(4)	6(12)	0.672
	Occasionally	12(24)	12(24)	
	Sometimes	11(22)	11(22)	
	Often	18(36)	15(30)	
	Always	7(14)	6(12)	

Unusual burning sensation	Never	0(0)	5(10)	0.149
	Occasionally	13(26)	14(28)	
	Sometimes	12(24)	14(28)	
	Often	17(34)	11(22)	
	Always	8(16)	6(12)	
Burning Throat Sensation	Never	5(10)	9(18)	0.716
	Occasionally	9(18)	7(14)	
	Sometimes	13(26)	15(30)	
	Often	13(26)	12(24)	
	Always	10(20)	7(14)	
Fullness Post-meal	Never	35(70)	43(86)	0.174
	Occasionally	8(16)	5(10)	
	Sometimes	6(12)	2(2)	
	Often	0(0)	0(0)	
	Always	0(0)	0(0)	
Dysphagia	Never	0(0)	7(14)	0.006
	Occasionally	10(20)	11(22)	
	Sometimes	18(36)	11(22)	
	Often	15(30)	15(30)	
	Always	7(14)	6(12)	
Bitter Taste	Never	2(4)	9(18)	0.198
	Occasionally	9(18)	11(22)	
	Sometimes	15(30)	10(20)	
	Often	18(36)	15(30)	
	Always	6(12)	5(10)	
Burping	Never	2(4)	9(18)	0.273
	Occasionally	13(26)	11(22)	
	Sometimes	13(26)	10(20)	
	Often	17(34)	15(30)	
	Always	5(10)	5(10)	
Heartburn after overeating	Never	2(4)	9(18)	0.273
	Occasionally	13(26)	11(22)	
	Sometimes	13(26)	10(20)	
	Often	17(34)	15(30)	
	Always	5(10)	5(10)	

DISCUSSIONS

Almost all the PPIs are effective agents for suppression of acid secretion which is responsible for symptoms of GERD with brilliant symptomatic relief to the patients. [11]The cardinal feature of Dexlansoprazole is by its dual release formation enhances the concentration and subsequently extending the suppression of acid secretion, therefore, providing double dose effect. The same was found by Metz in patients having a first dose of Dexlansoprazole had effective control of heartburn accounting for more than 90% relief of reflux symptoms.[12] Moreover, Sharma et al, also reported almost similar figures of 92%-95% of patients had complete relief of symptoms by using Dexlansoprazole MR for 2 months.[13] On the other hand, esomeprazole (40 mg) possessing a delayed-release formation with single-release features producing high titres 1.6 hours after the administration of the dose.About75% of patients didn't complain of any heartburn during the treatment and 85%-91% had symptoms free nights after they had 40 mg of esomeprazole for a month. [14]In addition to this patients who were given 40 mg esomeprazole did achieve great rates of healing (87%-94.1%) for erosive esophagitis after 2 months of therapy.

Both Dexlansoprazole and esomeprazole are very useful medications with tremendous relief for symptoms of GERD.[15] The main benefit of Dexlansoprazole-MR is that it uses new method via which its dual delayed-release (DDR) formulation enhances the blood conctentration and as well as the time of supression of acid thereby relieving the symptoms. However, there is little data about the symptomatic relief of reflux symptoms Dexlansoprazole with a dose 60 mg and that of esomeprazole at a dose 40 mg. A study tiltled"First-week clinical responses to dexlansoprazole 60 mg and esomeprazole 40 mg for the treatment of grades A and B gastroesophageal reflux disease" was conducted by Seng-KeeChuah in 2017.[16] This study aimed to To compare the one-week clinical effects of single doses of dexlansoprazole and esomeprazole on grades A and B erosive esophagitis. The study enrolled 175 adult patients diagnosed with gastroesophageal reflux disease. The patients were randomized in a 1:1 ratio into 2 groups to define the sequence or order in which they were given single doses of dexlansoprazole (n = 88) and esomeprazole (n = 87) for an intention-to-treat analysis. The primary endpoints were the complete symptom resolution (CSR) rates at days 1, 3, and 7 after drug administration. The overall CSR for GERD patients was similar at days 1-7 for both the dexlansoprazole and esomeprazole groups, although a higher incidence of CSR was observed on day 3 in female patients who received a single dose of dexlansoprazole.

Wu et al did a comparative research that showed that the Dexlansoprazoleat 30 mg had a greater effect than esomeprazole at a dose of 20 or 40 mg (RR = 2.01, 95%CI: 1.15-3.51; RR = 2.17, 95%CI: 1.39-3.38, respectively) indivuals with patients with non erosive esophagitis after one month of treatment.[17] However, there wasn't significant difference in patients with erosive esophgitis in terms of their healing rates. A single day comparative pH study revealed that dexlansoprazolehad a greater percentage of time with a pH > 4 when compared to esomeprazole (58% and 48%, P = 0.003) at 1 day post-dose.[17]

CONCLUSION

This study concluded that the symptomatic relief of GERD after 2 weeks of therapy with Esomeprazole and Dexlansoprazole was the same except for dysphagia.

These results do have important implications for clinicians while dealing patients with GERD. There are newer guidelines for treatment of this diseases in breast feeding women as well.[18] This issue is due to studies having a little sample size. There is a huge potential for further studies based on latest available guidance.[19] Therefore, studies with large sample size are required to establish an effective correlation between dexlansaprazole and other proton pump inhibitors.

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AUTHOR'S CONTRIBUTION
The following authors full fill authorship criteria as per ICMJE guidelines;

Ayub JU, Qaisar A:	Idea conception, drafting the work, final approval, agreed to be accountable for all the work.
Amin S, Zaman M:	Design of the work, data acquisition, critical rivision, final approval, agreed to be accountable for all the work.
Shah AZ:	Data analysis, drafting of the work, final approval, agreed to be accountable for all the work.
Ahmed F:	Data interpretation, critical revision, final approval, agreed to be accountable for all the work.