



EFFECT OF DOMPERIDONE ON SERUM PROLACTIN LEVELS IN FUNCTIONAL DYSPEPSIA PATIENTS

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ABSTRACT **Background:** Dyspepsia is diagnosed when symptoms originating from gastro-duodenal region are present which include epigastric pain and burning, post prandial fullness and early satiation. Functional dyspepsia poses a burden on our healthcare system and drugs used it also lead to various described side effects such as hyperprolactinemia.

Materials And Methods: The Study was conducted, over a period of 12 months. 97 study subjects were recruited from the outdoor patient department, with a primary diagnosis of functional dyspepsia after obtaining informed consent from the patients and after ethical clearance from institutional ethics committee. Patients more than 18 years of age and with functional dyspepsia sine alarm symptoms were included in the study. Patient with alarming GIT symptoms, pregnant and lactating women were excluded. Prolactin levels were measured before starting empirical treatment with PPI and prokinetic and 2nd sample was taken at the end of 4 weeks and suitable inference was made comparing the 2 values.

Results: Mean age in the study was 45.85 +/- 16.50 years ranging from 18 years to 80 years. Males constitute 61.9% and females constitute 38.1%. Hyperprolactinemia on day 28 was present in 80.4% of the patients.

Conclusion: Empirical therapy of 4 weeks duration in functional dyspepsia leads to significant elevation of serum prolactin levels.

KEYWORDS : Functional dyspepsia ,domperidone, hyperprolactinemia.

INTRODUCTION

Dyspepsia is a common complaint in the population visiting the healthcare facilities. Dyspepsia is diagnosed when symptoms originating from gastro-duodenal region are present which include epigastric pain and burning, post prandial fullness and early satiation. Before the diagnosis of dyspepsia is made by upper gastro-intestinal endoscopy the patients are said to have un-investigated dyspepsia¹.

Throughout the world magnitude of dyspepsia is worrisome as the number of patients visiting outdoor facilities with complaints of dyspepsia is huge. The prevalence of this disorder is said to be ranging from 20 to 30 percent worldwide². Various studies in India report a prevalence of 30.4%³. Indian studies conducted primarily for studying the clinical profile of irritable bowel syndrome found frequency of dyspeptic symptoms at 49 percent in the population⁴. Inhibitors of proton pump and prokinetic agents are the mainstays of the treatment of functional dyspepsia⁵.

The functional dyspepsia guidelines in the Asia-Pacific region and the United States of America advice 4 weeks of empirical treatment with prokinetic agent and proton pump inhibitor before considering any other treatment. Duration of 4 weeks for empirical treatment been used in many trials⁶.

The prokinetic effect of domperidone is mediated through the blockade of enteric inhibitory dopamine-2 receptors. Domperidone has various adverse effects, hyperprolactinemia and extra pyramidal symptoms have been reported along with mastalgia, galactorrhoea, stomach cramps, diarrhoea⁷. Galactorrhoea due to domperidone was reported from Britain in 1983 and from India in 1991^{8,9}. Gynaecomastia has been reported, more in case of non-specific D2 antagonists such as metoclopramide¹⁰. Study by Fujino T et al concluded that domperidone is an effective stimulator of prolactin levels in human beings¹¹. A Brazilian study concluded that therapy with domperidone leads to very high serum prolactin levels¹².

Functional dyspepsia poses a burden on our healthcare system and drugs used to treat the above said problem also lead to various described side effects such as hyper-prolactinemia.

MATERIAL AND METHODS

The Study was conducted in the Department of General Medicine, over a period of 12 months. Ninety seven study subjects were recruited from the Medicine OPD, with a primary diagnosis of functional dyspepsia after obtaining informed consent from the patients and after

ethical clearance from institutional ethics committee. Age more than 18 years and patients with Primary diagnosis of functional dyspepsia without alarm symptoms were included in this study. Patient with alarming GIT symptoms, pregnant and lactating women were excluded.

ROME IV criteria was used to make a probable diagnosis of functional dyspepsia. Detailed history regarding the symptoms, their duration was taken. Personal history including addiction and history of any drug intake for the above symptoms and for any other concomitant illness are recorded. Females were asked about their menstrual history and history of breast feeding and recent breast examinations, other relevant history was asked for. A thorough general physical examination was conducted. The patient was then informed regarding the probable diagnosis of functional dyspepsia and the empirical therapy with PPI and domperidone 30 mg per day was instituted after taking blood samples for Serum Prolactin.

The therapy with domperidone was continued for 4 weeks. On follow-up a serum prolactin sample was withdrawn. The prolactin levels of the sample at day zero and day twenty-eight are compared and suitable inference was made.

Data entry was done using M.S. Excel and it statistically analysed using Statistical package for social sciences (Version 16) for M.S Windows. Descriptive statistical analysis was carried out to explore the distribution of several categorical and quantitative variables. Categorical variables were summarized with n (%), while quantitative variables were summarized by mean ± S.D. All results are presented in tabular form and are also shown graphically using bar diagram or pie diagram as appropriate. The difference in the two groups was tested for Statistical Significance by t test and categorical variables tested by chi square test. P-value less than 0.05 was considered to be statistically significant.

RESULTS

Majority of the patients belonged to the age group of <40 years (41.2%), followed by 41-60 years (36.1%) and 61-80 years (22.7%). Mean age in the study was 45.85 + 16.50 years ranging from 18 years to 80 years.

Males constitute 61.9% and females constitute 38.1%. 88.7% were married and 11.3% were unmarried. 11.3% subjects belonged to high socioeconomic status, 77.3% belong to middle socioeconomic status and 11.3% belong to lower socioeconomic status.

Table 1 : Showing Demographic Details Of The Study Population

		Frequency	Percent
Age Category (Years)	<40	40	41.2%
	41-60	35	36.1%
	61-80	22	22.7%
	Total	97	100.0%
Marital status	Married	86	88.7%
	Unmarried	11	11.3%
	Total	97	100.0%
Gender	Male	60	61.9%
	Female	37	38.1%
Socioeconomic status	High Class	11	11.3%
	Middle Class	75	77.3%
	Lower Class	11	11.3%
	Total	97	100.0%

Table 2 : Showing Symptom Prevalence Of Functional Dyspepsia (epigastric Pain Syndrome Type Was More Prevalent In Our Study)

	Frequency	Percent
Bothersome post prandial Fullness	45	46.4%
Bothersome Early Satiety	43	44.3%
Bothersome Epigastric Pain	61	62.9%
Bothersome Epigastric Burning	57	58.8%

Table 3 : Descriptive Statistics Of Weight, Height And BMI : Statistical Significance Was Found Between Weight And Serum Prolactin Levels On Day 28

Parameters	Prolactin Day28 (ng/mL)	Mean	SD	T Test	P Value
Weight (kg)	<20	74.895	7.651	2.39	0.01
	>=20	68.513	10.949		
Height (cm)	<20	172.158	5.241	1.69	0.09
	>=20	168.744	8.361		
BMI (kg/m2)	<20	25.281	2.479	1.74	0.08
	>=20	23.992	2.971		

Table 4 : Prolactin Levels On Day 0 And 28 Respectively : Hyperprolactinemia Was Present In 78 Subjects At Day 28.

		Frequency	Percent
Prolactin-Day 0 (ng/mL)	<20	59	60.8%
	>=20	38	39.2%
Prolactin- Day 28 (ng/mL)	<20	19	19.6%
	>=20	78	80.4%

DISCUSSION

Functional dyspepsia turns out to be the most common and widespread digestive diseases in the clinics, occurring without age boundaries, closely related to the factors such as gastrointestinal motility disorder, gastric electric rhythm disorders and gastric paresthesias^{13,14,15,16}. Treatment of functional dyspepsia is time-consuming which may increase worries of the patients and increase anxiety and depression which under the regulation of the central nervous system inhibit gastrointestinal peristalsis, reduces secretion and eventually leads to gastrointestinal dysfunction with precipitation of dyspepsia symptoms^{17,18}. In the clinical treatment, this disease is more often treated with medicine to control symptoms and meanwhile, the patients should pay attention to lifestyle modifications¹⁹.

The main drugs used for treatment of functional dyspepsia include proton pump inhibitors and prokinetic agents both of which are readily available over the counter and have various effects some known and studied, some less known and ignored for example hyperprolactinemia²⁰.

In our study, Mean age was 45.85 +/- 16.50 years ranging from 18 years to 80 years. Majority of the patients with hyperprolactinemia on day 28 belong to the age group of <40 years (41%) followed by 41-60 years (33.3%) and 61-80 years (25.6%) patients. Same was seen in a study by Jain C et al., comparing the efficacy of 2 prokinetic agents in treatment of functional dyspepsia, most patients of dyspepsia belonged to age group of 20-40 years (69%), only 15% patients were more than 60 years of age and mean age was 30 ± 10 years²¹. In a study by Narayanan V et al., on efficacy and tolerability of acotiamide a prokinetic agent in functional dyspepsia patients it was observed that 60% of the patients belonged to age group of ≥ 40 years and which also indicates higher incidence of functional dyspepsia and more visits to outdoor department with complaints of dyspepsia in age group of 40-

60 years²². In a study on use of combination of prokinetic agent and proton pump inhibitor for treatment of dyspeptic symptoms due to gastrointestinal disorder by Ndraha S, it was observed that 43% of patients of dyspepsia were in age group of 40-60 years similar to age distribution seen our study^{23,24}.

In our study, Males were more than females. Majority of the patients with hyperprolactinemia on day 28 were males (57.7%) followed by females (42.3%). Similar results were seen in a study by Jain C et al., 122 patients were male and 49 were female and male preponderance (71.35%) was found²¹. But certain studies suggest that the incidence of functional dyspepsia is more in females than males contrary to the results of our study. Jones RH et al., observed in a study on dyspepsia in England and Scotland that there is a slight excess of female predominance²⁵. In another study by Jones R, it was observed that prevalence of functional dyspepsia in men and women is almost equal²⁶.

In our study, Bothersome post prandial fullness was present in 46.4% patients. Bothersome Early Satiety was present in 44.3% patients. Bothersome Epigastric Pain was present in 62.9% patients. Bothersome Epigastric Burning was present in 58.8% patients. Our study suggested the predominance of epigastric pain syndrome type of functional dyspepsia in the study population contrary to the previous studies described hence forth. In a study by Jain C et al., most common symptom seen was abdominal fullness (88.8%), post prandial bloating (86.5%), early satiety (74.8%), nausea (74.8%), heartburn (42.3%) & other symptoms like regurgitation (12.9%), belching (7%) were among less common symptoms suggesting post prandial distress to be more common type of functional dyspepsia subtype²¹. Zagari RM et al., observed in a study of 114 patients with FD 77(67%) had postprandial fullness and early satiation and 55(48.2%) had epigastric pain suggesting post prandial distress to be more common type²⁸. Matsueda K et al., observed that among 405 patients, 232(57.3%) had postprandial fullness, 94(23.2%) of patients had bloating and 79(19.5%) of patient had early satiation which indicates a predominance in postprandial syndrome in most of the patients unlike what was found in our study²⁹.

In our study, on day 0, prolactin levels were less than 20 in 60.8% patients and more than 20 in 39.2% patients. On day 28, prolactin levels were less than 20 in 19.6% patients and more than 20 in 80.4% patients. There was significant increase in prolactin levels on day 28 irrespective of baseline prolactin levels. Similarly in a study by Fujino et al., it was found that domperidone is an effective stimulator of prolactin levels in human beings¹¹. Findings by Vilar L et al., were also similar to our study, it was observed that domperidone lead to very high serum prolactin levels¹². Cho E et al., also demonstrated that domperidone resulted in higher prolactin levels than at the time of admission, thus supporting findings of our study³⁰. Results similar to our study were reported by Ochoa-Amayaa BE et al., they observed that domperidone caused hyperprolactinemia, which resolved on its cessation³¹. Domperidone as a culprit causing hyperprolactinemia was also reported in a study by Talley NJ et al., where in the 2 pro-kinetic drugs i.e., metoclopramide and domperidone caused hyperprolactinemia in almost 50% of patients³⁰. In a study by Cann P et al., It was found that during treatment with domperidone there were high levels of prolactin in 15 out of 18 thus supporting the findings of our study⁸. Agarwal P et al., also reported a case of domperidone induced galactorrhea in a 28- year female, which improved on cessation of therapy thus demonstrating the endocrinal adverse effects of the mentioned drug⁹. In a study by Poovathingal M et al., a 19 year old female during work up for irregular menstrual cycle she was found to have raised prolactin levels, which were attributed to domperidone use for her recently diagnosed gastrointestinal problem other causes of hyperprolactinemia were ruled out and it was thus ascertained that therapy with domperidone leads to raised prolactin levels as suggested in our study¹⁰.

CONCLUSION

Functional dyspepsia is a common and worrisome problem, the treatment is simple and safe with proton pump inhibitors and prokinetic agents. Usually no adverse effects are seen with treatment of functional dyspepsia but, hyperprolactinemia is common. When missed hyperprolactinemia due to domperidone can lead to costly investigations which are unnecessary. It can be concluded that empirical therapy of 4 weeks duration in functional dyspepsia leads to significant elevation of serum prolactin which is not related to baseline prolactin level.

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