Effect of Domperidon on Gastric Emptying in Diabetic Patients with Gastroparesis

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✔ The effect of Domperidon on gastric emptying time in 20 diabetic patients with gastroparesis was evaluated and compared to a control group consisting of 10 patients. In the control group; none of the patients had any gastrointestinal symptoms and their barium roentgenograms were normal. Preliminary to our study all patients have been evaluated using radiology, endoscopy and dynamic scintigraphic examination. After this evaluation domperidon (molitium) (eczacıbaşı) has been started 4x10 mg daily. Two weeks after the radioisotopic baseline study and under domperidon medication, the patients were questioned about their symptoms and the gastric emptying times were restudied employing the same protocol. In conclusion, it is found that domperidon treatment in diabetic patients with gastroparesis is effective symptomatically and shortens significantly the gastric emptying time without any side effects.

Key words: Gastric emptying, Domperidon, Radioisotope

✔ Diyabetik gastroparetik hastalarda domperidon'un mide boşalma zamanına etkisi araştırıldı. Çalışma 20 diyabetik hasta üzerinden yapıldı. Endoskopik, radyolojik ve sintigrafik çalışma ile diyabetik gastroparezis tanımlanmış hastalarda domperidon (Motilium–Eczacıbaşı) 40 mg/gün dozda başlandı. 15 gün süre ile hastalar yan etki, semptomatik iyileşme yönünden gözlendi. 15. gün sintigrafik olarak mide boşalma zamanı yinelendi. Sonuç olarak; diyabetik gastroparezis'li hastalarda uzamış mide boşalma zamanının domperidon ile normale döndüğü ve ilaca bağlı yan etki gözlenmediği, hastalarda semptomatik iyileşme sağlandığı tespit edildi.

Anahtar Kelimeler: Mide boşalma, Domperidon, Radyoizotop

Gastroparesis is a motor disorder characterized by delayed emptying of the gastric content without any mechanical obstruction. The pathophysiology of gastroparesis is a complex incident consisting of electrophysiological, hormonal, peripheral and central neural mechanisms[1]. It is known that dopamin has an important role as a neurotransmitter in gastric emptying[2-3]. A delayed gastric emptying time can be corrected by dopamin receptor blockers like metoclopramid, but it is known that these drugs have central side effects[4].

Domperidon is a dopamin receptor blocker which does not penetrate the blood–brain barrier and for this reason has no central side effects. It increases lower esophageal sphincter pressure and decreases gastric emptying period[5-9]. It has been found useful in the therapy of symptomatic diabetic gastroparethic patients[1-11].

The aim of our study was to evaluate the effects of domperidon on gastric emptying time on diabetic gastroparethic cases.

MATERIALS AND METHODS

20 diabetic patients between the ages of 25–65 (median 50) were included in our study. Three of these patients were type 1 diabetics taking insulin, 17 were type 2 diabetics using oral hypoglycemic drugs. All patients had symptoms of nausea, vomiting, abdominal bloting, lack of appetite, untimely hunger satisfaction. Symptom fre-

quency 1–2 per week is accepted as light (score 1), 3–4 medium (score 2) and over as heavy (score 3) cases. In the control group; none of the patients had gastrointestinal symptoms and their barium roentgenograms were normal.

Preliminary to our study, the probability of anatomical obstruction, active ulcers, cancer and other structures were excluded in all patients using radiology and endoscopy. Ten days prior to and during our study period, use of drugs which might effect the gastric motility were prohibited. After a 12 hour period of hunger all patients were examined following the ingestion of a semisolid food.

The semisolid food was prepared including, an egg, a piece of cheese, bread and 60 ml of milk. 1 mCi of Tc-99m Sulfur Colloid was added in to the milk and the patient was asked to begin chewing the solid parts of the food, taking some milk into the mouth chewing again and then swallowing but never drinking the milk directly. A kinetic study was performed with the patient lying in supine position; taking 120 frames in 60 minutes each frame being 30 seconds. Using the data obtained, a region of interest (ROI) was drawn along the borders of the stomach and a time activity curve was obtained for each patient. On the time activity curves which show exponential decrease, first the decrease constanst (X) were calculated for each patient using the formula $At=A_0.e^{-xt}$ where A_0 is the activity at T_0 and At is the activity at T_{60} min. Then $T_{1/2}$ was calculated using the formula $T_{1/2}=0.693/X$ [12].

After the study was over, domperidon (motilium) (eczacıbaşı) was started to be given 4x10 mg daily. After two weeks the patients were questioned about their symptoms and their gastric emptying times were restudied with the same protocol. Statistical evaluation of these quantitative results and the scoring before and after domperidon therapy were done by paired t tests.

RESULTS

In 20 patients the mean gastric emptying time was calculated as 102.05±65.51 (±SD) minutes before domperidon and 70.85±26.52 minutes after domperidon. In the control group; the mean gastric emptying time was found to be 66±18. The difference was statistically significant ($p<0,001$) (Figure 1). Mean symptom score was 3±0 before treatment and 1.65±0.67 after treatment and the result was again statistically significant ($p<0.001$) (Figure 2). No side effects were detected.

DISCUSSION

In diabetic patients gastroparesis impairs the plasma glucose regulations. In the treatment of gastroparesis prokinetic agents such as metoclopromide, sisaprid, domperidon, eritromisin, bethanecol are used to increase the intestinal transit time [13]. Domperidon is a derivative of benzimidasol and antagonizes the inhibitor effect of dopamin on the upper gastrointestinal system[14]. As the blood-brain barrier penetration is weak, it does not cause extrapyramidal symptoms and dystony. It might the level of prolactin being usually subclinically[15]. Gynecomasty occurrence in male patients is rare.

In various clinical studies it has been observed that domperidon treatment of the diabetic patients with gastroparesis was beneficial by oral treatment of 10 mg domperidon every 4 hours. Heer and colleagues showed that there was improvement in gastric symptoms severely[11]. Mc Calleum and colleagues has proven that by oral and intravenous treatment of domperidon gastric emptying time decreases and symptoms disappear[13]. Our results also show that, domperidon treatment decreases the delayed gastric emptying time of the diabetic patients with gastroparesis.

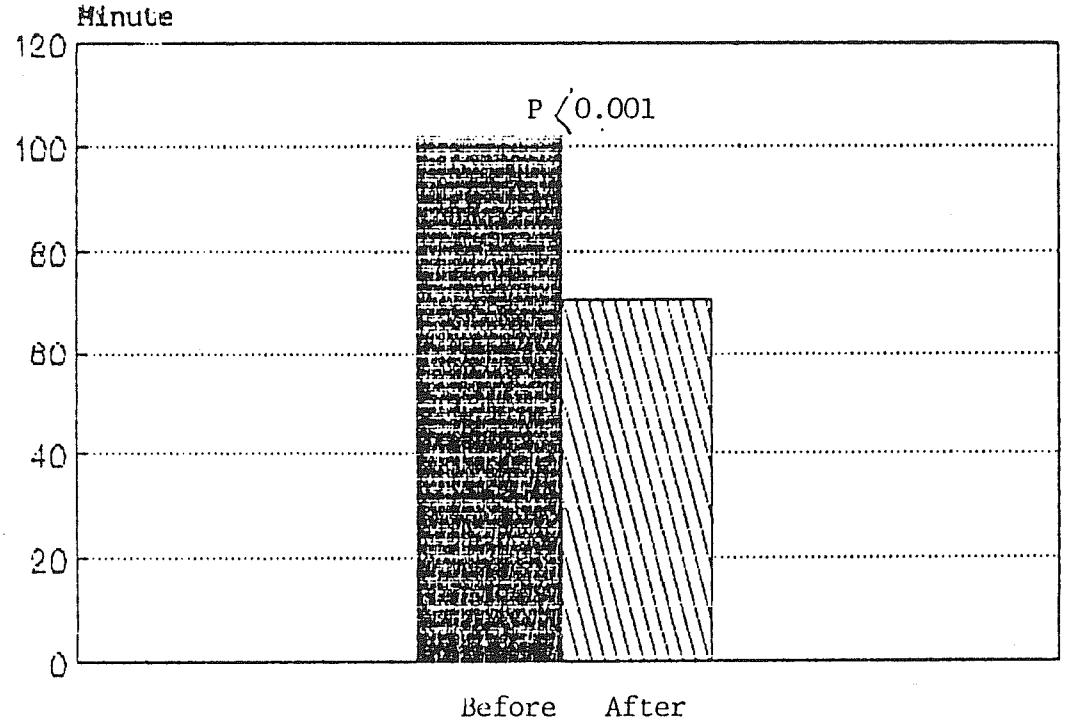

Figure 1: Gastric emptying time after and before domperidon

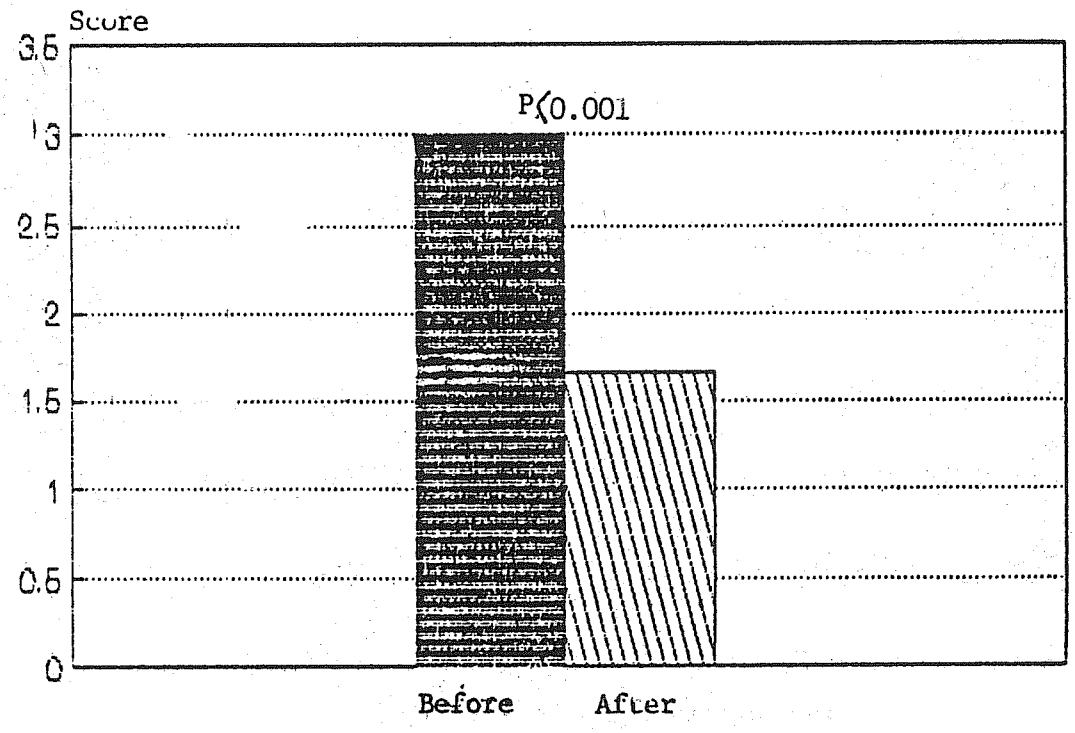

Figure 2: Symptoms score after and before domperidon

CONCLUSION

In our study domperidon treatment decreased gastric emptying time and improved the symptoms in diabetic patients with gastroparesis. As domperidon has rare central effects, we can accept its superiority over other dopamin antagonists and suggest that it should be the first drug to be chosen for the treatment of gastroparesis in diabetic patients.

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REFERENCES

1. Malagelada J-R: Gastric emptying: Clinical significance and treatment. Drugs 1982; 243: 353–359.
2. Valenzuale JE: Dopamine as a possible neurotransmitter in gastric relaxation. Gastroenterology 1976; 71: 1019–1022.
3. DeCarle DJ, Christensen J: A dopamine receptor in esophageal smooth muscle of the opossum. Gastroenterology 1976; 70: 216–219.
4. Pinder RM: Metoclopramide: A review of its pharmacological properties and clinical use. Drugs 1976; 12: 81–131.
5. Laduran PM, Leysens JE: Domperidone, a specific in vitro dopamine antagonist, devoid of in vivo central dopaminergic activity. Biochem Pharmacol 1979; 28: 2161–2165.
6. Brogden RN: Domperidon: A review of its pharmacological activity pharmacokinetics and therapeutic efficacy in the symptomatic treatment of dyspepsia and as an antiemetic. Drugs 1982; 24: 360–400.
7. Eyre-Brook IA, Smallwood R, Johnson AG: Human antroduodenal motility, pyloric closure, and domperidone. Scand J Gastroenterol 1984; 19 (suppl 92): 4–7.
8. Weihrauch TR, Ehl W: Effect of domperidone on the motility of antrum pylorus and duodenum in man. Scand J Gastroenterol 1981: 16 (suppl 67): 195–198.
9. Broekaert a: Effect of domperidone on gastric emptying and secretion. postgrad Med J 1979; 55 (suppl 1): 11–14.
10. Heer M: Diabetic gastroparesis: Treatment with domperidone a double blind, placebo controlled trial. Digestion 1983; 27: 214–219.
11. Heer M: Diabetic gastroparesis and colonic dilatation treated with domperidone. Lancet 1980; 2: 1145–1146.
12. Isserstedt GA, Mathematics and Statistics, Bernier DR, Christian PE, Langan JK, Wells LD (Editors). Nuclear Medicine Technology and Techniques, St Louis, Toronto, Baltimore 1989;P:1-56.
13. Reynolds JC, Putnam PE: Prokinetic agents. Gastroenterol ClinNorth Am 1992; 21: 567–596.
14. Brogden RN, Carmine AA, Heel RC, et al: Domperidone: A review of its pharmacological activity, pharmacokinetics and therapeutic efficacy in the symptomatic treatment of chronic dyspepsia and as an antiemetic. Drugs 1982; 24: 360–400.
15. Sowers JR, Share B, Mc callum RW. Effects of domperidone, an extracerebral inhibitor of dopamine receptors, on thyrotropin, prolactin, renin, aldosteron, and 18–hydroxycorti-costerone secretion in man. J Clin Endocrinol metab 1982; 54: 869–871.