International Journal of Biological and Pharmaceutical Sciences Archive

ISSN: 0799-6616 (Online)

Journal homepage: https://ijbpsa.com/

(RESEARCH ARTICLE)

Evaluating the effect of domperidone syrup on prolactin levels and its relationship to side effects in female patients with gastroesophageal reflux disease

Nibras abdulazizi Hamood [1,*] and Asmaa abdulhaq Mohammed [2]

[1] *Department of Biology, Collage of Education Pure science, University of Samarra.*
[2] *Northern Technical University Aldour Technical Institute,Salahaddin, Iraq.*

International Journal of Biological and Pharmaceutical Sciences Archive, 2026, 12(01), 083–088

Publication history: Received on 17 June 2026; revised on 24 July 2026; accepted on 27 July 2026

Article DOI: https://doi.org/10.53771/ijbpsa.2026.12.1.0072

Abstract

Background: Domperidone (Motilium) is a dopamine antagonist primarily used to treat vomiting associated with gastroesophageal reflux disease (GERD) and to stimulate gastrointestinal motility. Domperidone works by inhibiting dopamine receptors in the brain and digestive tract, leading to faster contractions of the smooth muscles in the digestive tract, increased gastric emptying, and relief of symptoms associated with digestive disorders such as nausea, vomiting, heartburn, and GERD.

Aim of the study: The present study aimed to evaluated level of white blood cell (WBC), Red blood cell (RBC), prolactin, and Dopamine in female patients with gastroesophageal reflux disease after taking domperidone.

Materials and methods: The sample included thirty female patients with gastroesophageal reflux disease after taking domperidone, and five control.

Result: The results demonstrated that oral domperidone administration induced significant hematological and hormonal changes throughout the study period. No significant difference in RBC count was observed at baseline, whereas WBC count was significantly higher in the treated group. After 4 weeks, RBC count decreased significantly, while WBC showed no significant change. By 8 weeks, significant alterations in both RBC and WBC counts were observed compared with the control group ($P < 0.05$). Regarding hormonal parameters, prolactin levels did not differ significantly at baseline, whereas dopamine levels were significantly lower in the treated group. Following 4 and 8 weeks of treatment, prolactin levels increased markedly, accompanied by a significant reduction in dopamine levels compared with the control group ($P = 0.0001$).

Conclusion: The present findings indicate that prolonged oral administration of domperidone significantly alters both hematological and hormonal parameters.

Keywords: Domperidone (Motilium); Gastroesophageal reflux disease; Prolactin hormone; Dopamine receptor antagonists

1. Introduction

Domperidone is a type II dopamine receptor antagonist that increases the speed of gastrointestinal contractions. It is used as an antiemetic and anti-fullness medication because it increases gastric emptying[1]. It is a drug developed by Janssen Pharmaceuticals, Belgium. Domperidone does not normally cross the blood-brain barrier. Its antiemetic effect is due to a combination of actions: it acts on dopamine receptors in the chemoreceptor stimulation zone (CTZ), which

* Corresponding author: Nibras abdulazizi Hamood

lies outside the physiological blood-brain barrier, and on D2 receptors at the gastroesophageal junction, thereby blocking dopamine action associated with nausea of any cause[2]. Domperidone should be used with extreme caution, especially in the elderly and those with pre-existing or recent heart disease, as an increased risk of ventricular arrhythmias and sudden cardiac death has been reported in several studies[2].

Domperidone is rapidly absorbed after oral administration, with absorption occurring in approximately 30–60 minutes from a fasting state. Its low oral bioavailability (approximately 13–17%) is likely to be around 15%, due to poor absorption by the gastrointestinal tract and significant hepatic metabolism. Maximum plasma levels of 21 ng/mL were attained 90 minutes following two weeks of daily oral intake of 30 mg, about equivalent to 18 ng/mL observed after the initial dose. Domperidone exhibits a binding affinity of 91–93% to plasma proteins. Research indicates a broad distribution in tissues with minimal amounts in the brain, and it is present in breast milk[3]. Domperidone is subject to swift and comprehensive hepatic metabolism by hydroxylation and N-dealkylation. In vitro metabolic studies utilising diagnostic inhibitors demonstrated that CYP3A4 is the predominant cytochrome P-450 isoform responsible for the N-dealkylation of domperidone, whilst CYP1A2 and CYP2E1 participate in the aromatic hydroxylation of domperidone[4]. Urinary elimination constitutes 31% and faecal elimination represents 66% of an oral dosage. The percentage of the drug eliminated in its original form is roughly 10% in faeces and 1% in urine. The plasma half-life following a solitary oral administration is 7–9 hours in healthy subjects, although it is extended in persons with significant renal dysfunction[5].

Domperidone is a selectively peripheral D2-D3 dopamine receptor antagonist that does not clinically interact with D1 receptors. The medication alleviates nausea by inhibiting D2 receptors in the chemoreceptor trigger zone, located in the floor of the fourth ventricle of the brain. Domperidone modestly enhances upper gastrointestinal motility and amplifies the reduction in oesophageal sphincter pressure by inhibiting dopamine receptors in the gastric and duodenal lining. It obstructs dopamine receptors in the anterior pituitary gland, resulting in heightened prolactin release. Domperidone might confer advantages for certain individuals while posing risks for others based on genetic predispositions[6, 7].

Domperidone induces hyperprolactinemia as a result of dopamine receptor inhibition. Hyperprolactinemia may inhibit the release of FSH-LH hormones from the brain, leading to hypogonadism and an imbalance in testosterone levels [8][9]. Tissue culture studies suggest that almost one-third of human breast tumours rely on prolactin. Consequently, meticulous attention must be paid while prescribing Domperidone to those with a familial predisposition to breast cancer [10]. The dopamine molecule features a catechol framework (a benzene ring accompanied by two hydroxyl substituents) with a single amino group linked through an ethyl chain. Dopamine is the most basic of the catecholamines, a group that include the neurotransmitters adrenaline and norepinephrine [11]. Dopamine is a natural alkaloid. The ionic variant exhibits significant solubility in aqueous solutions and demonstrates considerable stability. To augment the stability and aqueous solubility of the ionic variant, dopamine is synthesised for chemical or medicinal applications as dopamine-A hydrochloride. The quantity of dopaminergic neurones (neurones that produce dopamine) is very limited, at 400,000 in the human brain. Dopamine receptors influence several outcomes not alone by G protein coupling but also through associations with diverse proteins (dopamine-interacting proteins)[12]. These receptors play a crucial role in various neurological functions, such as motivation, pleasure, perception, memory, learning, and precise motor control. It additionally regulates neuroendocrine signalling. A minimum of five subtypes of dopamine receptors exist (D1, D2, D3, D4, and D5)[13]. D1 and D5 belong to the D1-like dopamine receptor family, whereas D2, D3, and D4 are categorised under the D2-like receptor family. There exists some evidence indicating the presence of novel receptors, D6 and D7, however their universal identification remains inconclusive, D1 receptors exhibit extensive distribution over the brain[14].

Prolactin is produced by the lactotropic cells in the anterior lobe of the pituitary gland[15]. These cells respond to estrogen. It is characterized by its protein structure and is considered one of the hormones with high molecular weights. In females, this hormone stimulates lactation, which in turn leads to the formation and secretion of milk[8]. Prolactin contains 198 amino acids and a molecular weight of 24,000 Daltons. The amount of the hormone in the gland is 2% of the growth hormone in it[16]. Prolactin-secreting cells constitute 10-25% of the pituitary gland cells in humans, and these cells are located in the lateral parts of the pituitary gland. Prolactin is secreted in episodes lasting up to 75 minutes, occurring between 7 and 20 times a day [17]. A decrease occurs during the menstrual cycle, particularly in the first half of the follicular phase, while it increases in the second phase, the luteal phase. Measuring its concentration in the blood is used in the diagnosis of epilepsy because prolactin levels rise after an epileptic seizure[18]. Dopamine (the neurotransmitter) plays a significant role in controlling prolactin secretion; it inhibits its release, while inhibiting dopamine leads to increased prolactin secretion in the body [19]. Prolactin, in turn, inhibits the secretion of luteinizing hormone and inhibits the effect of the luteinizing hormone-releasing hormone on the pituitary glandular cells, and the effect of gonadotropin on the ovary remains, which leads to inhibition of the ovulation process and thus the cessation of ovarian activity and a decrease in estrogen and progesterone[20].

2. Material and methods

Samples were collected directly by drawing venous blood from 35 female and divided to two groups as:

- **Group1 (Control Group):** This group consist of five female, free of disease and received no supplements other than a healthy diet.
- **Group 2 (Drug Group):** This group consist of thirty female received oral domperidone in tablet form at a concentration of 10 mg/kg, three times daily before meals, for 60 days.

2.1. Blood sample collection

Blood samples were collected at a rate of three draws during the experimental period: The first draw on day zero, the second draw after 4 weeks, and the third draw after 8 weeks. The sample volume taken was (5 cc) per woman per draw. The sample was divided into two parts: (2 cc) was placed in an EDTA K3 (ethylene diamine tetraacetic acid) tube to prevent clotting and to measure the blood parameters (WBCs, RBCs), and (3 cc) was placed in a gel tube for centrifugation at 5000 rpm for (15) minutes. The samples were then stored at a temperature of (-20)°C in an Eppendorf tube until hormonal analyses were performed.

2.2. Assessment of WBC and RBC

The Auto Analyzer is a multi-measurement analyzer designed for diagnostic tests in clinical laboratories. This device features flow cytometry technology, meaning that cells are measured by being suspended in a stream of reagents and passed through an electronic detector.

2.3. Determination of prolactin hormone concentration

Prolactin hormone is estimated by following the steps included with the kit and according to the manufacturer's instructions for the ELISA technique. The basic principle of measuring prolactin in serum is based on the immunoassay of the enzyme-binding protein, which forms a sandwich complex of antibody and antigen. This complex results from the binding of antibodies to the prolactin hormone present in the sample, which is considered a foreign substance or antigen (Ag), thus forming a sandwich complex. This method is one of the most sensitive and specific methods for the quantities of molecules in the sample, as it requires two antibodies (Ab) that are specific to the substance to be measured and are required to detect the antigen (Ag). This reaction is direct, meaning that the absorbance increases as the concentration of the hormone in the sample increases [21].

2.4. Determination of concentration dopamine in serum

It is an immunological measure for determining the amount of dopamine, a flexible testing system for various types of biological samples, and was done according to the instructions for the ready-made kit from Demeditec Germany. Dopamine is extracted by means of a specific, dedicated gel located in the Wells base of the test plate. The competitive ELISA technique uses a Microtiter format, where the antigen binds to the Microtiter unit and the samples, controls, and standards compete for a specific number of antibody binding sites. After binding occurs, free antigens and free antibody complexes are removed by washing. The antibody bound by means of rabbit anti-IgG conjugation is detected using TMB as a substrate and measured at a wavelength of 450 nm.

3. Result

The results presented in the table (1) demonstrated changes in RBC and WBC counts in females treated with domperidone compared with the control group over the study period. At day 0, no significant difference was observed in RBC count between the drug-treated and control groups ($P = 0.201$). In contrast, the WBC count was significantly higher in the drug-treated group than in the control group ($P = 0.01$). After 4 weeks of treatment, the RBC count in the drug-treated group decreased significantly compared with the control group ($P = 0.027$). However, no significant difference was observed in WBC count between the two groups ($P = 0.166$). At 8 weeks, the RBC and WBC count significantly lower in the drug-treated group than in the control group ($P<0.05$).

Table 1 Comparison of serum prolactin and dopamine concentrations between the domperidone-treated and control groups at baseline, 4 weeks, and 8 weeks

Groups Parameter	Mean ± SD		P-value
	Control	Patients	
RBC/ 0 day	4.578±0.825	4.124±0.703	0.201
WBC / 0day	4.506±0.880	5.732±0.934	0.01*
RBC/ 4 weak	4.578±0.825	3.930±0.538	0.027*
WBC / 4 weak	4.506±0.880	5.046±0.776	0.166
RBC/ 8 weak	4.578±0.825	3.954±0.435	0.014*
WBC / 8 weak	4.506±0.880	5.365±0.644	0.013*

The results in Table (2) demonstrated that oral administration of domperidone produced marked changes in serum prolactin and dopamine levels throughout the study period.At day 0, no significant difference was observed in serum prolactin levels between the patient and control groups (P = 0.061). In contrast, serum dopamine levels were significantly lower in the patient group than in the control group (P = 0.02).

After 4 weeks of domperidone administration, serum prolactin levels increased dramatically in the patient group compared with the control group, with a highly significant difference (P = 0.0001). Conversely, dopamine levels decreased markedly in the patient group compared with the control group, also showing a highly significant difference (P = 0.0001). At 8 weeks, prolactin concentrations increased in the patient group, while dopamine levels declined slightly. Both parameters remained significantly different from those of the control group (P = 0.0001).

Table 2 Comparison of serum prolactin and dopamine concentrations between the domperidone-treated and control groups at baseline, 4 weeks, and 8 weeks

Groups Parameter	Mean ± SD		P-value
	Control	**Patients**	
Prolactin/ 0 day	1.136±0.470	1.862±0.807	0.061
Dopamine/ 0 day	0.460±0.472	0.206±0.146	0.02*
Prolactin/ 4 weak	1.136±0.470	40.286±5.123	0.0001*
Dopamine/ 4 weak	0.460±0.472	0.022±0.013	0.0001*
Prolactin/ 8 weak	1.136±0.470	59.436±4.521	0.0001*
Dopamine/ 8 weak	0.460±0.472	0.015±0.005	0.0001*

4. Discussion

The results showed a significant increase (P≤0.05) in prolactin concentration in the second group (the domperidone group) in the fourth and eighth weeks of the study compared to the control group. The highest increase in the second group was in week (8). The reason for the increase in prolactin in the drug group is that domperidone has the ability to affect dopamine receptors across the barriers of the central nervous system (pituitary gland). Since dopamine is an inhibitor of prolactin, the relationship between them is inverse, meaning that the drug's ability to inhibit dopamine leads to an increase in prolactin release[22]. In a study conducted on female infertility, it was shown that one of the important reasons for infertility is related to high levels of prolactin, as it works to suppress the ovulation cycle and then works to prevent the secretion of follicle-stimulating hormone (FSH) and the gonads. Another study confirmed an increased risk of cancer among people with elevated PRL.

As for the prolactin hormone, the results showed a significant increase compared to the control group at a significant level (P≤0.05). The results of this study are consistent with [12]. The reason for the increase in prolactin hormone in

the drug group is that domperidone has the ability to affect dopamine receptors across the barriers in the central nervous system (pituitary gland). Since dopamine is an inhibitor of prolactin hormone, the relationship between them is inverse, i.e., the drug's ability to inhibit dopamine leads to an increase in prolactin release [4].

The results showed a significant decrease (P≤0.05) in dopamine concentration in the second group at all times compared to the control group. Dopamine is one of the most important physiological factors for inhibiting prolactin, and domperidone is one of the drugs that inhibit it, and thus its inhibition leads to an increase in prolactin release in the body.

The results showed no significant change in the levels of red blood cells (RBC) and white blood cells (WBC) in the second group compared to the control group at a significant level (P≤0.05). However, regarding dopamine, the results showed a significant decrease in dopamine concentration in the second group compared to the control group at a significant level (P≤0.05). These results are consistent with those of [23, 24], as dopamine is one of the most important physiological factors for prolactin inhibition, and domperidone is one of the drugs that inhibits it. Consequently, its inhibition leads to an increase in prolactin release in the body. As for prolactin, the results showed a significant increase compared to the control group at a significant level (P≤0.05). These results are consistent with those of[12]. The increase in prolactin levels in the drug group is due to the fact that domperidone has the ability to affect dopamine receptors across the barriers of the central nervous system (pituitary gland). Since dopamine is an inhibitor of prolactin, the relationship between them is inverse, i.e., the drug's ability to inhibit dopamine leads to an increase in prolactin release [4].

5. Conclusion

The present findings indicate that prolonged oral administration of domperidone significantly alters both hematological and hormonal parameters.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study."

References

[1] Asztalos, E.V., et al., Enhancing human milk production with domperidone in mothers of preterm infants: results from the EMPOWER trial. Journal of Human Lactation, 2017. **33**(1): p. 181-187.

[2] Leelakanok, N., A. Holcombe, and M.L. Schweizer, Domperidone and risk of ventricular arrhythmia and cardiac death: a systematic review and meta-analysis. Clinical drug investigation, 2016. **36**(2): p. 97-107.

[3] Poovathingal, M.A. and R. Bhat, Domperidone induced galactorrhea: an unusual presentation of a common drug. Indian Journal of Pharmacology, 2013. **45**(3): p. 307-308.

[4] Travi, B.L. and G. Miró, Use of domperidone in canine visceral leishmaniasis: gaps in veterinary knowledge and epidemiological implications. Memórias do Instituto Oswaldo Cruz, 2018. **113**(11): p. e180301.

[5] Reddymasu, S.C., I. Soykan, and R.W. McCallum, Domperidone: review of pharmacology and clinical applications in gastroenterology. Official journal of the American College of Gastroenterology| ACG, 2007. **102**(9): p. 2036-2045.

[6] Sakamoto, Y., et al., Effects of domperidone on gastric emptying: a crossover study using a continuous real-time 13C breath test (BreathID system). Hepato-gastroenterology, 2011. **58**(106): p. 637-641.

[7] Athukuri, B.L. and P. Neerati, Enhanced oral bioavailability of domperidone with piperine in male wistar rats: involvement of CYP3A1 and P-gp inhibition. Journal of Pharmacy & Pharmaceutical Sciences, 2017. **20**: p. 28-37.

[8] Goel, P., et al., Evaluation of serum prolactin level in patients of subclinical and overt hypothyroidism. Journal of clinical and diagnostic research: JCDR, 2015. **9**(1): p. BC15.

[9] Sabanegh Jr, E.S. and K. Siddiqi, Surgical Reconstructions for Obstruction, in Male Infertility: Problems and Solutions. 2010, Springer. p. 89-98.

[10] Kadam, A.B., S.S. Havele, and S.R. Dhaneshwar, Validated HPTLC method for simultaneous estimation of Lafutidine and Domperidone in bulk drug and formulation. Int J Pharm Pharm Sci, 2012. **4**(4): p. 221-225.

[11] Bor, S., et al., A meta-analysis on the cardiac safety profile of domperidone compared to metoclopramide. United European gastroenterology journal, 2018. **6**(9): p. 1331-1346.

[12] Hurley, M. and P. Jenner, What has been learnt from study of dopamine receptors in Parkinson's disease? Pharmacology & therapeutics, 2006. **111**(3): p. 715-728.

[13] Ellenbroek, B.A., et al., Alexander Rudolf Cools (1942–2013). Psychopharmacology, 2014. **231**(11): p. 2219-2222.

[14] Arana, A., et al., Risk of out-of-hospital sudden cardiac death in users of domperidone, proton pump inhibitors, or metoclopramide: a population-based nested case-control study. Drug safety, 2015. **38**(12): p. 1187-1199.

[15] Ahmed, H., The relationships between serum prolactin level and semen analysis parameters among patients attended the reproductive health center, Khartoum 2016–2017. Sudan Medical Monitor, 2017.

[16] Brown, R.S., et al., Acute suppression of LH secretion by prolactin in female mice is mediated by kisspeptin neurons in the arcuate nucleus. Endocrinology, 2019. **160**(5): p. 1323-1332.

[17] Sato, Y., et al., Prolactin upregulates female-predominant P450 gene expressions and downregulates male-predominant gene expressions in mouse liver. Drug Metabolism and Disposition, 2017. **45**(6): p. 586-592.

[18] Guyton, A.C., Text book of medical physiology. 2006: China.

[19] Bronstein, M.D., Disorders of prolactin secretion and prolactinomas. Endocrinology: adult and pediatric, 2016: p. 104-128. e6.

[20] Bhandari, P., et al., Status of Prolactin and Thyroid Hormone Level among Primary Infertility Patients Visiting Tertiary Care Hospital, Nepal. International Journal of Medical Research & Health Sciences, 2019. **8**(1): p. 109-114.

[21] Maddox, P.R., D.L. Jones, and R.E. Mansel, Basal prolactin and total lactogenic hormone levels by microbioassay and immunoassay in normal human sera. European Journal of Endocrinology, 1991. **125**(6): p. 621-627.

[22] Borri, C., et al., Polylysine as a functional biopolymer to couple gold nanorods to tumor-tropic cells. Journal of Nanobiotechnology, 2018. **16**(1): p. 50.

[23] Abdelhalim, M.A.K. and B.M. Jarrar, The appearance of renal cells cytoplasmic degeneration and nuclear destruction might be an indication of GNPs toxicity. Lipids in Health and Disease, 2011. **10**(1): p. 147.

[24] Colville, T.P. and J.M. Bassert, Clinical anatomy and physiology for veterinary technicians. 2015: Elsevier Health Sciences.