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RESEARCH ARTICLE
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DOMPERIDONE INDUCED GALACTORRHOEA IN REPRODUCTIVE AGE GROUP FEMALES- A CASE SERIES

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Abstract

Background: Domperidone is a commonly utilized anti-emetic and combination drug with proton pump inhibitor. Galactorrhoea is a exceptional adverse effect of this drug.

Aim: To report the rare side effect of domperidone i.e. galactorrhoea.

Method: A hospital based case study of females taking domperidone presenting with galactorrhoea.

Result: The females of reproductive age group on domperidone showed galactorrhoea as an uncommon side effect.

Conclusion: Females displaying with galactorrhoea ought to be explored for prolactenemia and appropriate history of intake Domperidone.

Keywords: Domperidone, drug induced galactorrhoea, galactorrhoea, prolactin, reproductive age group females.

INTRODUCTION

Domperidone is, a peripheral and central dopamine receptor antagonist with gastro-prokinetic and antiemetic effects[1], it is a widely prescribed medication in clinical practice as fixed dose combination drug for vomiting, gastro-paresis and hiccoughs. It acts on D2 receptors present on upper gastrointestinal tract and regulates the motility of gastric and small intestinal smooth muscle and has been shown to have some effects on the motor function of the oesophagus[2].Common side effects of Domperidone are diarrhoea, stomach cramps, headache, constipation, mastalgia, xerostomia and rashes. Rarer side effects observed in few patients are galactorrhoea and hyper-prolactenemia in females of reproductive age group. This drug presents very low rates of extrapyramidal side effects due to its negligible penetration through the blood–brain barrier (BBB) We report 5 cases of Domperidone induced hyperprolactenemia and galactorrhoea in females of reproductive age group.

Case 1

A 32-year-old healthy multiparous female with no comorbidities presented with bilateral galactorrhoea for 1 week. She had no menstrual irregularities and thyroid dysfunction. She was on Domperidone and pantoprazole combination therapy for 2 weeks due to dyspeptic symptoms. She developed galactorrhoea after 1 week of treatment. She had no history of drug intake of antidepressants, antipsychotics, oral contraceptive pills and antihypertensives. Her serum prolactin level was 28ng/ml. We assumed Domperidone to be cause of galactorrhoea. Galactorrhoea resolved within 1 week of stoppage of Domperidone. She is followed up regularly for 1 month without any symptoms.

Case 2

A 29-year-old married nulliparous woman presented with recurrent headache and vomiting episodes. She was diagnosed with migraine. Other investigations like MRI, ophthalmic investigations are normal. She was prescribed combination therapy of naproxen and Domperidone. On 4^{th} day she presented with galactorrhoea. On examination, the patient had bilateral mastalgia with whitish breast discharge. She was advised for fluid discharge cytology. She had no history of taking other drugs like oral contraceptive pills, anti-depressants or anti-tubercular drugs. On investigations serum prolactin level was 58 ng/ml, TSH was 3 IU/ml. The drug combination was stopped immediately. Within a week galactorrhoea resolved. After 2 weeks prolactin level was repeated. It was found to be 22ng/ml.

Case 3

A 38-year-old female, school teacher, non-smoker, non-alcoholic, a known case of gastro-esophageal reflux disease was admitted for treatment. She was discharged on rabeprazole 20 mg with Domperidone 30 mg. After 8 days of the treatment she complained of painful enlargement of both breasts with moderate grade fever with chills, and galactorrhoea for 3 days. The patient had her menstrual cycle 8 days back and it was regular (every 28 days for 5 days). She gave no history of taking any other drugs like oral contraceptive pills, antidepressants, or anti-tubercular drugs. On examination, the patient had tenderness of both breasts with oozing of milk from both nipples with a mass on palpation. Her secondary sexual characters and external genitalia found to be normal. She was advised to go for b/l breast discharge cytology. On investigation, the patient's hemoglobin was 12 gm. / dl; total leukocyte count: 12,800 /cu ml; differentials: N-82, L-17, M-1; urine routine and microscopy, LFT, and RFT were normal. Chest X-ray and ultrasound abdomen was normal. The patient's hormone levels (TSH, LH, FSH, Prolactin, Oestradiol, and Testosterone) were normal. On further evaluation, she was diagnosed to be a case of Domperidone induced galactorrhoea. Then Domperidone was discontinued. After 7 days of stopping Domperidone galactorrhoea, fever, pain subsided.

Case 4

A 40 –year-old female patient, known case of fibroid uterus and had undergone TLH+B/L Salpingectomy. She complained of intermittent giddiness, nausea, dyspepsia, and unilateral headache subsequently. She was started on tab. Amitriptyline 10mg, tab flunarizine 10mg, tab pantoprazole 20mg and Domperidone 30 mg . However, the patient observed spontaneous discharge of whitish fluid from the right breast / nipple (Galactorrhea) and advised for discharge fluid cytology. On investigation serum prolactin level 137 ngm/ml. No visual defects, no other significant clinical feature suggestive of microadenoma was detected. The offending drugs that may cause hyperprolactenemia were stopped like tab amitriptyline, tab flunarizine, and combination of tab pantoprazole and Domperidone. After stopping these medications the patient's serum prolactin levels showed a significant reduction to 44ngm/ml and galactorrhea was stopped.

Case 5

A 39 year-old-lady with diabetes mellitus on metformin and glipizide therapy complained of fullness of stomach, abdominal discomfort, nausea after taking food. She was advised rabeprazole and domperidone for 15 days. She developed milky discharge from both nipples after 8 days of taking the treatment and advised for discharge fluid cytology. On investigation her prolactin level was 23 ng /ml, her thyroid profile was normal, RFT, LFT was normal, LH, FSH, Testosterone and Estradiol level was normal. She had regular menstrual cycle (5 days every 30 days). After stoppage of combination medication of rabeprazole and Domperidone galactorrhoea subsided after 3 days.

Discussion

Galactorrhoea, the inappropriate of milk from the breast, is considered abnormal if present for longer than 6 months after child birth or after discontinuation of breast feeding[3]. It can be physiological as in pregnancy, lactation, chest wall stimulation, sleep, stress or pathological as in tumors (craniopharyngioma, prolactinoma), trauma, acromegaly, hypothyroidism, cirrhosis of liver& chronic renal failure. It can be drug induced as in phenothiazine, chlorpromazine, perphenazine, haloperidol, metoclopramide, α –methyldopa, opiates, ranitidine, amitriptyline, amoxapine, fluoxetine, verapamil, oestrogens an indigenous drugs like red cloves, blessed thistle, fennel, fenugreek seeds.

Domperidone is a D2 antagonist, very poorly crosses the blood brain barrier so that it has minimal CNS side effects as compared to metoclopramide. It has CNS side effects like galactorrhoea, gynaecomastia, impotence, menstrual irregularities. The side effects occur mainly due to elevated prolactin level. Other side effects like abdominal cramps, dizziness, constipation, dysuria, extra pyramidal side effects, diarrhea, hot flushes, heart burn, mastalgia, leg cramps, pruritus, rash, stomatitis, urinary frequency, QT prolongation/L breast fluid cytology showed only cyst macrophages.

In our study all 5 cases presented with galactorrhoea with the history of intake of Domperidone. Galactorrhoea might be due to surplus prolactin release or enhanced prolactin sensitivity within the breast tissue. One of the first reports on domperidone induced galactorrhea was from Great Britain in 1983[4] . Another was from India in 1991[5] .

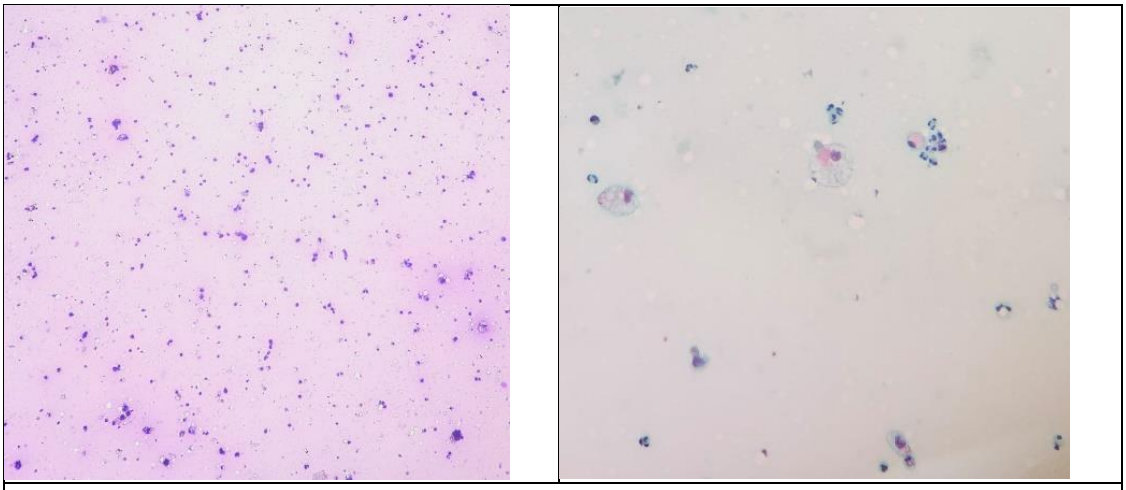

Figure 1, 2: (Gimesa, Pap) – Cytosmears show multiple scattered macrophages, no duct epithelial cells in fatty background and RBCs.

Treatment of galactorrhea depends upon its cause. Drug-induced galactorrhea generally responds to discontinuation of the offending drug. As mentioned in our case report, the patient responded well to the discontinuation of the drug. Sometimes, the addition of dopamine agonist (bromocriptine or cabergoline) may be required for the management of galactorrhea.

CONCLUSION

These case reports showed that Domperidone may cause galactorrhea without an obvious rise in the serum prolactin concentration. In these cases presented here, symptoms reversed after withdrawal of Domperidone. Domperidone is a frequently used drug on a daily basis as an antiemetic[6]. Galactorrhea is an uncommon adverse drug reaction encountered. Hence, physicians should be aware of such unusual side effects of a common drug to avert unnecessary worry and investigations.

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