

## Case study

### **Pantoprazole-Domperidone Induced Hyperprolactinemia and Galactorrhea in a Chronic Kidney Disease Patient on Dialysis**

#### **Abstract**

Pantoprazole-Domperidone fixed-dose combinations are commonly used in End Stage Renal Disease (ESRD) patients on dialysis. The medication helps in control of drug induced gastritis that can occur due to several medications including oral calcium and iron supplements. Besides this the pantoprazole-domperidone combination helps in treatment of uremic gastritis, peptic ulcer disease, and gastroesophageal reflux disease.

Rarely, pantoprazole and domperidone may induce galactorrhea. We report a case of a female patient on dialysis who developed drug induced hyperprolactinemia and galactorrhea due to therapeutic dose of a fixed-dose combination of pantoprazole (40mg) and domperidone (30mg), used for treatment of gastritis- the duration of therapy being 4 months. Galactorrhea subsided after discontinuation of pantoprazole-domperidone.

*Keywords: hyperprolactinemia, galactorrhea, pantoprazole, domperidone; pantoprazole + domperidone combination*

#### **Introduction**

Hyperprolactinemia and galactorrhea may be caused by several factors in nonpregnant females and males. The etiological factors include (but not limited to) pituitary tumors including prolactinomas, Cushing's disease, Addison's disease, hypothyroidism, renal disease, and drug induced. Both pantoprazole and domperidone may induce hyperprolactinemia and galactorrhea, though this is rare.<sup>1,2</sup> Some investigators have shown that domperidone may cause galactorrhea even without

elevation of serum prolactin levels.<sup>3-5</sup> Here we are reporting a case of pantoprazole and domperidone fixed-dose combination induced hyperprolactinemia and galactorrhea in a female patients on maintenance dialysis. In this case, once the offending agents were discontinued, serum prolactin levels became normal, and galactorrhea stopped.

### Case report

A 39 year old non-pregnant female with Chronic Interstitial Nephritis (CIN) post obstructive uropathy, chronic kidney disease (CKD), and End Stage Renal Disease (ESRD) on maintenance hemodialysis was started with pantoprazole (40mg) and domperidone (30mg) fixed-dose combination for treatment of gastritis. The other drugs she was taking are enlisted here:

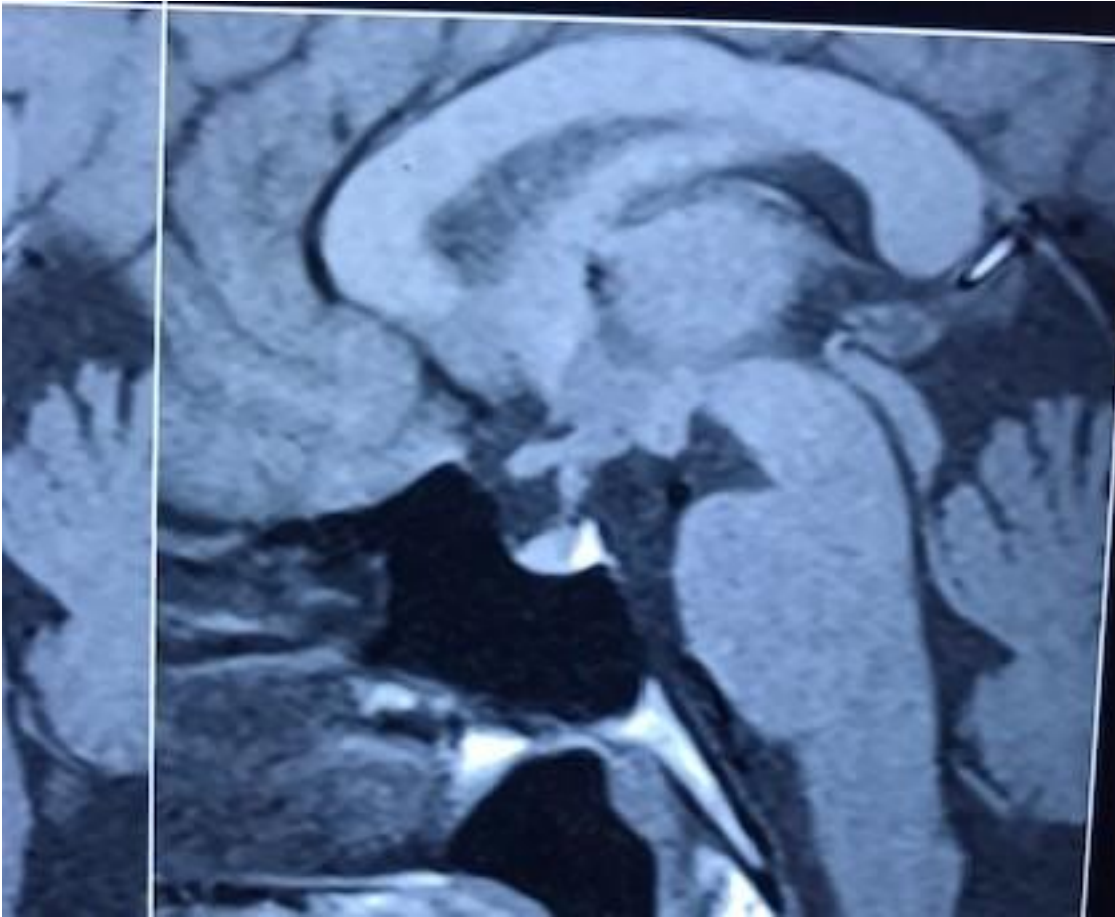
- Clinidipine 10mg once a day
- Metoprolol 50mg, twice a day
- Vitamin supplements, twice a day
- Calcium supplements, twice a day
- Probiotics, twice a day
- Erythropoietin alpha, 4000 units, twice a week, IV during dialysis.

She was apparently alright for 5 months after which started experiencing discomfort in her breasts, which appeared to be swollen and itching. After a few weeks she noticed white discharge from her breast nipples (galactorrhea).

Investigations revealed elevated fasting serum prolactin level (470 ng/ml) (normal range: 2.8-29.2 ng/mL in non-pregnant females).

Plain Magnetic resonance imaging (MRI) screening of sella turcica (given below) ruled out any pituitary lesions or other pathology.

Image : Plain Magnetic resonance imaging (MRI) screening of sella turcica



As there was no other probable cause, we attributed galactorrhea due to pantoprazole and domperidone as the most probable causative agents and stopped the medication, since to our knowledge and based on the literature, none of the other long-term medications have been linked to an effect on prolactin secretion.

Two weeks after stopping the medication, fasting serum prolactin level returned to normal (21.07ng/mL) accompanied with resolution of galactorrhea. This indicates that galactorrhea was induced by the pantoprazole plus domperidone fixed dose combination.

### **Discussion**

Hyperprolactinemia is sustained increase in serum prolactin levels (fasting level of >20ng/ml in men, and >25 ng/ml in women).<sup>6</sup> Galactorrhea can be seen in less than half the cases of hyperprolactinemia.<sup>7</sup> Besides pregnancy, hyperprolactinemia may occur due to several factors including stress, pituitary disorders, pituitary tumors, Cushing's disease, Addison's disease,

hypothyroidism, renal disease, and drug induced.<sup>1,7</sup> The drug induced hyperprolactinemia may occur with use of antidepressants (monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, tetracyclic antidepressants), antihypertensives (methyldopa, reserpine, verapamil, enalapril), antipsychotics, H2 receptor antagonists, anti-androgens, estrogens, proton pump inhibitors, metocloperamide and domperidone.<sup>1</sup> Several investigators have reported occurrence of hyperprolactinemia and galactorrhea with use of omeprazole, esomeprazole, lansoprazole, rabeprazole, and also domperidone.<sup>1,2,4,8-12</sup> Some investigators have reported domperidone induced galactorrhea without elevated serum prolactin levels.<sup>3-5</sup>

Renal dysfunction may cause hyperprolactinemia. In ESRD patients, prevalence of hyperprolactinemia ranges from 35% to 60% in both males and females.<sup>13</sup> This could be due to reduced clearance of prolactin, and/or increased secretion of prolactin from the pituitary due to blunted dopaminergic inhibition (lactotrophic resistance).<sup>13</sup>

In this patient, there was a gradual decline in renal function, and it did not appear to cause any discomfort in the breasts or galactorrhea. Moreover, once we stopped the pantoprazole plus domperidone fixed-dose combination (offending agents), patients symptoms subsided, and serum prolactin levels returned to normal. This shows that hyperprolactinemia and galactorrhea were due to the offending agents (pantoprazole and domperidone), and renal dysfunction may not have caused hyperprolactinemia and galactorrhea in this patient.

This patient was not on any other medication known to cause galactorrhea. She was on clindipine and metoprolol for hypertension that are not known to cause hyperprolactinemia. The other drugs included vitamin supplements, calcium supplements, erythropoietin alpha and probiotics- none of these are known to cause hyperprolactinemia and/or galactorrhea.

## **Conclusion**

In non-pregnant females and males, hyperprolactinemia may occur due to several factors including, but not limited to, stress, prolactinoma, Cushing's disease, Addison's disease, hypothyroidism, renal disease, and medications. Some medications that can induce hyperprolactinemia are antidepressants, antihypertensives (methyldopa, reserpine, verapamil, enalapril), antipsychotics, H2 receptor antagonists, anti-androgens, estrogens, proton pump inhibitors, metocloperamide and domperidone. Review of literature shows that both pantoprazole and domperidone may rarely induce hyperprolactinemia and galactorrhea: this is rare, and only a few reports have been published so far. In this case report we have presented a case of pantoprazole plus domperidone fixed-dose combination induced hyperprolactinemia and galactorrhea in a non-pregnant female on dialysis. Patient complained of breast discomfort and milky discharge from nipples after 5 months of starting the offending drug combination. Investigations revealed hyperprolactinemia. After ruling out other causes, diagnosis of drug induced galactorrhea was made. Serum prolactin level returned to normal, and galactorrhea stopped and patient started feeling better after discontinuing the offending agent.

**Disclaimer regarding Consent and Ethical Approval:**

As per university standard guideline, participant consent and ethical approval have been collected and preserved by the authors

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