**Case Reports in Clinical Medicine, 2015, 4, 193-196**
Published Online May 2015 in SciRes. http://www.scirp.org/journal/crcm
http://dx.doi.org/10.4236/crcm.2015.45039

# Propranolol-Induced Epistaxis in a Woman with Multiple Obstetric Complications: Case Report

**Jesse Abiodun Otegbayo[1*], John Osaigbovoh Imaralu[2], Bamikole Tosin Osibowale[1]**

[1]Department of Internal Medicine, Babcock University Teaching Hospital, Ilishan-Remo, Nigeria
[2]Department of Obstetrics and Gynaecology, Babcock University Teaching Hospital, Ilishan-Remo, Nigeria
Email: [*]otegbayoa@comui.edu.ng

Received 23 April 2015; accepted 22 May 2015; published 27 May 2015



## Abstract

**Epistaxis is a common complaint which is rarely life-threatening, as most cases are self-limited and as such unreported. However, it may be a significant cause for concern if it becomes recurrent. Although a number of medications including topical antihistamines and non-steroidal anti- inflammatory drugs are known aetiological factors for epistaxis due to their antiplatelet effects, beta blockers are not being widely reported as a possible cause. This report presents the case of a 34-year-old G2P0+1, who was diagnosed with hyperthyroidism in pregnancy and subsequently reported epistaxis twice at different occasion and different hospital settings when propranolol was introduced for her treatment, with resolution of epistaxis after withdrawal of propranolol. The report aims to highlight and sensitize physicians to the possible risk of bleeding in patients placed on beta blockers especially propranolol for a wide range of medical condition due to its thrombocytopathic effect.**

## Keywords

**Epistaxis, Thrombocytopathy, Propranolol, Pregnancy**

## 1. Introduction

Beta adrenergic blockers have been of multiple clinical applications in medicine for ages, and they have a relatively good safety profile in terms of side effects and the development of adverse drug reactions. The two broad classifications are selective and non-selective beta adrenergic blockers. A prominent member of the non-selec-

[*]Corresponding author.

**How to cite this paper:** Otegbayo, J.A., Imaralu, J.O. and Osibowale, B.T. (2015) Propranolol-Induced Epistaxis in a Woman with Multiple Obstetric Complications: Case Report. *Case Reports in Clinical Medicine*, **4**, 193-196.
http://dx.doi.org/10.4236/crcm.2015.45039

tive group is propranolol, which has been found to be useful in various fields of medicine such as neurology for essential tremors [1] and migraine [2], cardiovascular for angina, systemic hypertension, portal hypertension, palpitations and cardiac arrhythmias [3]; glaucoma [4] in ophthalmology and in endocrinology for thyrotoxicosis among other uses.

In 1966, Stephen [5] reported 3 classifications of unwanted side effects of propranolol in American Journal of Cardiology, and divided them into: effects common to many drugs such as nausea, vomiting and rashes; undesirable effects relating specifically to the pharmacologic actions of the drug such as bradycardia, cardiac failure and hypotension; and biochemical abnormalities. Apart from non-thrombocytopaenic purpura documented among the 5000 patients evaluated for side effects of propranolol by Stephen, a review of propranolol literature did not reveal any blood dyscrasia or epistaxis as a side effect. The British National Formulary (BNF) [6] listed the side effects of propranolol as bradycardia, heart failure, hypotension, conduction disorders, bronchospasm, peripheral vasoconstriction (including exacerbation of intermittent claudication and Raynauds phenomenon), gastrointestinal disturbances, fatigue, sleep disturbances, rarely rashes, dry eyes and exacerbation of psoriasis. No reference was made in the BNF to the thrombocytopathic effect and possibility of epistaxis with the use of propranolol.

This report of a G2P0+1 with propranolol-induced epistaxis and turbulent pregnancy is being reported to sensitize healthcare givers to the possible occurrence of epistaxis as a side effect of propranolol hydrochloride.

## 2. Case Report

Mrs. JPA, an unbooked 34-year-old G2P0+1, presented to the obstetrics emergency unit at an estimated gestational age of 28 weeks with a 12 hour history of drainage of liquor. At 10 weeks gestational age in this index pregnancy, she was diagnosed with severe hyperthyroidism at another specialist hospital where she presented; with features of a thyroid storm. She was then placed on propylthiouracil (PTU). Due to subsequent unavailability of PTU, she was placed on oral propranolol, after which she developed epistaxis, which abated after discontinuation of propranolol. She had no history of nose-picking or use of non-steroidal anti-inflammatory drugs (NSAIDs).

There was no associated bleeding par vaginam or from any other orifice in her body. She had no history suggestive of a bleeding disorder and had never bled in the index pregnancy prior to presentation. There was also no history suggestive of labour pain. She had a similar episode of drainage of liquor 10 years earlier which occurred at 24 weeks gestational age; she expelled a live well formed baby that died a few hours after.

Clinical examination revealed a young, anxious profusely sweating woman who was talkative and had warm wet and red palms. She had a regular pulse rate of 128 beats per minute and a blood pressure of 120/60 mmHg. Her temperature was 36.3˚C and a respiratory rate of 20 cycles/min. She had a hyperactive precordium with the apex beat in the 5$^{th}$ left intercostal space mid-clavicular line, no murmur was heard. Her abdomen was gravidly enlarged and the liver, spleen and kidneys were not palpable. The height of fundus corresponded with a 27 week gestation and fetal heart tone heard with a sonicaid was regular. Sterile speculum examination revealed pooling of clear fluid in the posterior fornix and egress of fluid from the cervical os confirming preterm pre-labour rupture of membranes.

She was admitted into the antenatal ward for conservative management; intramuscular Dexamethasone 12 mg was administered twice 12 hours apart and oral erythromycin 500 mg 6 hourly was commenced and administered until delivery. She was also re-commenced on oral propranolol which was increased from 40 mg twice daily to 40 mg thrice daily. The possibility of hydatidiform mole was considered on account of which a repeat uterine ultrasound and serum quantitative $\beta$-HCG were requested. The patient was monitored closely for early signs of chorioamnionitis or worsening thyrotoxicosis.

She, however, complained of spontaneous epistaxis 2 days after recommencement of propranolol which had to be withdrawn. The epistaxis abated and no further episode occurred again. She was commenced on that same day on PTU after reviewing the results of thyroid function tests which revealed markedly elevated thyroid hormones; T3 = 4.0 ng/mL (0.6 - 1.85 ng/mL), T4 = 15.2 µg/dL (4.8 - 12.0 µg/dL) and reduced thyroid stimulating hormone (TSH) level. TSH = 0.2 µIU/mL (0.4 - 6.0 µIU/mL). The results of clotting profile, complete blood count and serum $\beta$-HCG were all within normal limits. Ultrasound scanning of the thyroid gland revealed an enlarged thyroid with a volume of 25.3 mls and diffuse heterogeneous echogenicity suggestive of toxic goiter.

She made steady improvement in her clinical state until the 23$^{rd}$ day of admission when she developed pla-

cental abruption for which she had emergency caesarean section and was delivered of a preterm live female baby that was transferred to the neonatal ward. Mrs. JPA's condition further improved after delivery with disappearance of palpitations, cessation of hyper-defaecation, and resolution of the tachycardia with maintenance of normal pulse throughout the 8 days of observation post delivery.

Repeat thyroid function tests revealed normal levels of thyroid hormones and thyroid stimulating hormones. Placental histology was also found to be normal in addition to a repeat serum $\beta$-HCG which was also normal. Thyroid function tests for the baby also revealed a normal finding. She was then discharged home to be seen in the postnatal and medical out-patient follow up clinics.

## 3. Discussion

Pregnancy, though a physiological state, is often attended by some complications which may be life-threatening atimes. Some life-threatening complications of pregnancy may be associated with coagulopathy leading to bleeding diathesis. Among the complications associated with bleeding tendencies are: pre-eclampsia and eclampsia with resultant; haemolysis, elevated liver enzymes, low platelets syndrome (HELLPS) [7] among others.

Our patient had a turbulent pregnancy that was complicated with premature rupture of membranes (PROM) thyrotoxicosis with symptomatic tachyarrhythmia, (for which she had to be on bed rest for proper monitoring), placental abruption (for which she had emergency lower segment caesarian section), and eventually had a pre-term baby. The occurrence of epistaxis on two different occasions after being placed on propranolol, and the resolution of nosebleeding after withdrawal of the drug strongly suggests a causal effect.

Thyrotoxicosis is a known occurrence in molar pregnancy and has been known to occur in 7% of complete molar pregnancies due to the homology of $\beta$-HCG with thyroid stimulating hormone [8]. However, two uterine ultrasonography by different operators did not reveal a likelihood of hydatidiform mole. More convincingly, histopathological examination of the placenta after delivery revealed a normal placenta. This finding made it difficult to pin down the aetio-pathogenesis of thyrotoxicosis in this patient who had no previous symptoms or family history suggestive of thyroid dysfunction to molar pregnancy. Similarly the absence of eye signs such as exophthalmos, and absence thyroid gland tenderness as well as absence of thyroid nodule on ultrasonography make the possibility of autoimmunity unlikely, while not absolutely excluding it. We were, however, unable to do serum levels of thyroid autoantibodies which may have been helpful.

The resolution of thyrotoxic symptoms and return to normal results of thyroid function tests in the post-partum period would, however, strongly suggest that the thyroid problem was pregnancy-related.

Propranolol is a relatively safe common drug of high therapeutic index and with quite a number of therapeutic uses in clinical medicine. Some of its uses include its use in systemic hypertension, portal hypertension, anti-arrhythmia, anti-migraine and as an adjunct in the treatment of thyrotoxicosis among other uses. This case report is the first, to the best of our knowledge, to associate epistaxis with propranolol in pregnancy. It therefore calls for caution and close monitoring of pregnant women placed on the drug to prevent any disastrous bleeding, especially in this part of the world where prevalence of anaemia in pregnancy is high [9].

Thrombocytopaenic and thrombocytopathic properties of propranolol are not commonly highlighted as side effects in literature, however, a recent search revealed that as far back as 1966, these effects had been listed as unwanted side effects of propranolol [1], similarly, in 1977, Weksler *et al.* in New York had in their study concluded that anti-platelet effect of propranolol was due to modulation of platelet membrane function by propranolol and did not involve beta-adrenergic blockade; they posited that propranolol might alter platelet reactivit by interfering with internal shifts of calcium ions at intracellular sites [10]. More recently, in 1995, Dash and Rao found in their study that propranolol inhibited activation of the enzymes protein kinase C and phospholipase C which were required in platelet function, thus affecting platelet function without thrombocytopaenia [11]. It is obvious therefore from the foregoing and other studies that the antiplatelet effect of propranolol is actually a class effect and not limited to propranolol, as a study on platelet aggregation in essential hypertension showed propranolol to inhibit platelet aggregation better than atenolol [12]. It is also plausible that the antiplatelet effects of drugs such as aspirin, dipyridamole, ticlopidine and clopidogrel could be enhanced with propranolol combination, and therefore calls for closer monitoring of patients for bleeding whenever they are placed on such combination therapy.

The platelet count in our patient was within the normal limits on different occasions, suggesting that the epi-

staxis was due to thrombocythopathic effect and not of thrombocytopaenic effect of propranolol.

## 4. Conclusion

In view of this effect of propranolol, it might be tempting to recommend it as a drug of choice in elderly patients with hypertensive atheroscelosis to prevent ischaemic stroke on the one hand, and to de-emphasize its use for portal hypertension in cirrhotic patients who are prone to thrombocythopathy and thrombocytopaenia due to hypersplenism. We recommend that patients on propranolol be watched and asked for possible epistaxis, and the drug should be withdrawn forthwith if there is evidence of epistaxis.

## Acknowledgements

We appreciate all the nursing and laboratory staff who participate in the management of the patient.

## Conflict of Interest

No conflict of interest declared.

## Authors' Contributions

JAO initiated the publication, wrote the discussion and edited the manuscript. IJO wrote the Case presentation. BO wrote the Abstract. All authors read the manuscript.

## References

[1] Rajput, A.H. and Rajput, A. (2014) Medical Treatment of Essential Tremor. *Journal of Central Nervous System Disease*, **6**, 29-39. http://dx.doi.org/10.4137/JCNSD.S13570

[2] Pringsheim, T., Davenport, W., Mackie, G., Worthington, I., Aubé, M., Christie, S.N., Gladstone, J., Becker, W.J. and Canadian Headache Society Prophylactic Guidelines Development Group (2012) Canadian Headache Society Guideline for Migraine Prophylaxis. *Canadian Journal of Neurological Sciences*, **39**, S1-S59.

[3] Akbar, S. and Alorainy, M.S. (2014) The Current Status of Beta Blockers' Use in the Management of Hypertension. *Saudi Medical Journal*, **35**, 1307-1317.

[4] Ohrström, A., Kättström, O., Polland, W., Mortensen, J. and Stenström, B. (1984) Oral and Topical Adrenergic Beta-Receptor Blockers in Glaucoma Treatment. A Multicenter Study. *Acta Ophthalmologica*, **62**, 681-695. http://dx.doi.org/10.1111/j.1755-3768.1984.tb05795.x

[5] Stephen, S.A. (1966) Unwanted Effects of Propranolol. *The American Journal of Cardiology*, **18**, 463-472. http://dx.doi.org/10.1016/0002-9149(66)90071-3

[6] British Medical Association (2002) British National Formulary, Royal Pharmaceutical Society of Great Britain. 77-78.

[7] Salako, B.L., Odukogbe, A.T., Olayemi, O., Adedapo, K.S., Aimakhu, C.O., Alu, F.E. and Ola, B. (2003) Serum Albumin, Creatinine, Uric Acid and Hypertensive Disorders of Pregnancy. *East African Medical Journal*, **80**, 424-428.

[8] Hershman, J.M. (1992) Role of Human Chorionic Gonadotropin as a Thyroid Stimulator. *The Journal of Clinical Endocrinology and Metabolism*, **74**, 258-259.

[9] Omigbodun, A.O. (2004) Recent Trends in the Management of Anaemia in Pregnancy. *Tropical Journal of Obstetrics and Gynaecology*, **21**, 1-3.

[10] Weksler, B.B., Gillick, M. and Pink, J. (1977) Effect of Propranolol on Platelet Function. *Blood*, **49**, 185-196.

[11] Dash, D. and Rao, K. (1995) Effect of Propranolol on Platelet Signal Transduction. *Biochemical Journal*, **309**, 99-104.

[12] Punda, A., Polić, S., Rumboldt, Z., Bagatin, J., Marković, V. and Lukin, A. (2005) Effects of Atenolol and Propranolol on Platelet Aggregation in Moderate Essential Hypertension: Randomized Crossover Trial. *Croatian Medical Journal*, **46**, 219-224.