# Rebound Hypertension After Clonidine Withdrawal in a Pediatric Intensive Care Unit : A Case Report


## Abstract

Clonidine abrupt cessation may cause a rebound hypertension. Diagnosis can be confirmed with clinical findings and an increase in noradrenaline urinary levels.

We present the case of a patient who presented hypertension and tachycardia after clonidine withdrawal, with no increase in noradrenaline urinary levels, but with an increase in urinary dopamine levels, which is normally not increased significantly. We successfully treated hypertension with the reintroduction and progressive weaning of clonidine, after a therapeutic test with a dopamine antagonist.

All catecholamines should be tested in the event of suspected rebound hypertension after clonidine withdrawal.



## Key words

Rebound Hypertension, Clonidine, Dopamine, Pediatric Intensive Care Unit, Case report


## Introduction

Clonidine is a centrally acting antihypertensive drug. It is gaining more interest in the intensive care setting, including sedation and analgesia for ventilated patients[1,2]. Its prescription is linked to the risk of rebound hypertension[3].

We present the case of a patient whose diagnosis of rebound hypertension after clonidine withdrawal was made based on an increase in urinary excretion of dopamine without an increase in urinary levels of other catecholamines.

## Case report

**Patient information :** We admitted an 11 months female infant to the pediatric intensive care unit of Children's hospital of Rabat. She was transferred from the pediatric intensive care unit of another hospital for the management of a post infectious bronchiolitis obliterans. The patient is immunocompromised due to a defect in HLA class II expression.

She was sedated with fentanyl, midazolam and clonidine, and under mechanical ventilation for the management of a pediatric acute respiratory distress syndrome. She received immunoglobulins, with no improvement.

At her arrival in our unit, clonidine was discontinued. Three days later, she developed hypertension with tachycardia.

**Clinical finding :** The patient presented with a heart rate of 190 beats per minute, blood pressure of 223/112 mmHg with no difference in the four members. No signs of shock nor right heart failure were found. Cardiac auscultation was unremarkable. Femoral pulses were found and symmetrical. Urine output was 2.16 cc/kg/h. Abdominal auscultation found no arterial bruit. The patient wasn't sweating.

Pulmonary auscultation found crackles, with an oxygenation index at 21 in a ventilated patient under sedation with a comfort B score of 9.

**Timeline :** Figure 1

**Diagnostic assessment :** We ruled out hypercapnia and the presence of bladder globe. Sedation was optimized. An abdominal CT scanner with angiography was carried out and found no tumor or vascular anomaly. Blood cortisol, urinary free cortisol and TSH tests came back normal. Transthoracic echocardiography ruled out any cardiopathy or aortic malformation.
Urinary catecholamines and their metabolites test analysis were done in France, as no laboratory in Morocco were able to perform these tests. Results came back after two weeks in favor of an increase in urinary dopamine levels (Table 1). Given the family's lack of resources, we could not test the catecholamine's blood levels.

**Diagnosis :** Our final diagnosis was rebound hypertension secondary to clonidine withdrawal.

**Therapeutic interventions :** We first introduced propranolol (6 mg/8h) and captopril (2 mg/8h) orally before the results of urinary catecholamines tests came back. The patient showed no improvement with these drugs (Table 2). They were discontinued.
We then introduced domperidone, a dopamine antagonist, in an oral route, at 0.25 mg/kg/8h for three days. As the patient showed a decrease in blood pressure, we then introduced clonidine at 0.02 mg/8h orally.

**Follow-up and outcome of interventions :** The patient showed a decrease in heart rate and blood pressure. We started a progressive reduction in clonidine doses until we stopped it after 2 months. The patient didn't present hypertension after this progressive weaning.
A transthoracic echocardiography found a hypertrophy of the left atrium.
The patient stayed in our unit for the management of the post infectious bronchiolitis obliterans.

## Discussion

Our patient developed high blood pressure following cessation of clonidine. After eliminating rapidly reversible causes, we followed the guidelines regarding the etiological diagnosis of secondary hypertension[4]. Given the absence of renal and endocrine causes or a pheochromocytoma, we measured urinary catecholamines.
We found an increase in urinary excretion of dopamine without an increase in other urinary catecholamines.

We needed to link hypertension with a rise in dopamine plasma levels, and we don't have the resources in our hospital to test dopamine blood levels.
Domperidone is a dopamine antagonist which does not modify the action of the renin angiotensin aldosterone system, the excretion of electrolytes and catecholamines and which has no hypotensive action[5,6]. The duration of administration was reduced to avoid side effects. We observed a decrease in blood pressure and heart rate.
We subsequently reintroduced clonidine, a drug whose antihypertensive effects are positively correlated with the reduction in plasma release of dopamine[7].
A gradual reduction in the dose allowed us to completely wean off this drug, without occurrence of tachycardia or hypertension.

Our case is unique in that rebound hypertension secondary to clonidine is characterized by increased levels of urinary norepinephrine excretion, with a non-significant increase in dopamine[8,9].

The limitation of our study lies in the lack of arguments behind the administration of domperidone and it's real effects against the rise of dopamine.

## Conclusion

Clonidine is a centrally acting antihypertensive drug whose abrupt cessation can lead to an increase in circulating catecholamines. The current expansion of its indications in the ICU must lead us to respect its prescription rules, and the monitoring of the adverse effects of its sudden cessation.

In this sense, the dosage of all urinary catecholamines, including dopamine, and their metabolites, is of considerable interest.

**Références :**


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| **Table 1:** Biological findings of interest | | | |
|---|---|---|---|
| Test | Level | Unit | Normal range |
| Urinary adrenaline | 0.012 | µmol/24h | < 0.018 µmol/24h |
| Urinary noradrenaline | 0.056 | µmol/24h | < 0.075 µmol/24h |
| Urinary dopamine | 3.99 | µmol/mmol* | < 2.00 µmol/mmol* |
| Urinary normetanephrine | 0.81 | µmol/24h | 0.4 - 2.10 µmol/24h |
| Urinary metanephrine | 0.28 | µmol/ 24h | 0.2 - 1.00 µmol/ 24h |
| *µmol of dopamine per mmol of creatinine | | | |

**Table 2:** Timeline of the mean systolic and diastolic blood pressure

| Date | Drug Used | Dosage | Mean systolic and diastolic blood pressure(mmHg) |
|---|---|---|---|
| **08/11/2023** | Propanolol<br>Captopril | 6 mg/8h<br>2 mg/8h | 193/105 |
| **09/11/2023** | Propanolol<br>Captopril | 6 mg/8h<br>2 mg/8h | 158/95 |
| **10/11/2023** | Propanolol<br>Captopril | 6 mg/8h<br>2 mg/8h | 174/112 |
| **11/11/2023** | Domperidone | 1 mg/8h | 122/96 |
| **12/11/2023** | Domperidone | 1 mg/8h | 128/83 |
| **13/11/2023** | Domperidone | 1 mg/8h | 128/81 |
| **14/11/2023** | Clonidine | 0.02 mg/8h | 119/74 |
| **15/11/2023** | Clonidine | 0.02 mg/8h | 126/88 |
| **16/11/2023** | Clonidine | 0.02 mg/8h | 119/78 |

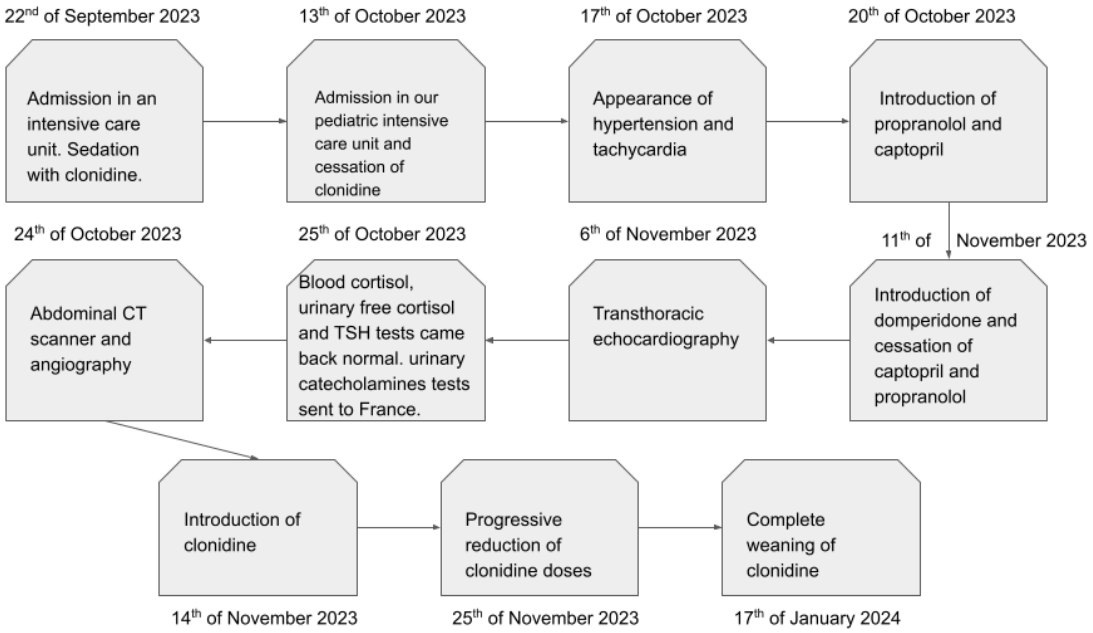


**Figure 1 :** Timeline of events