

Successful Clonidine Withdrawal in Patients receiving Cardio-selective Beta-blockers and Beta-blockers with Alpha-blocking Activity

Mostafa Ibrahim ElAwady^{1*}, Wasim Akram², Mohamed Sherbash¹, Noorudeen Kaladi Kunnunmal², Hanadi Al Hamad²

¹Clinical Pharmacy Department, Hamad Medical Corporation, Rumailah Hospital, Doha, Qatar; ²Geriatric and Long term Department, Hamad Medical Corporation, Rumailah Hospital, Doha, Qatar

ABSTRACT

Introduction: Clonidine U.S. prescribing information recommends discontinuation of beta blockers several days prior to clonidine withdrawal to reduce the risk of rebound hypertension. In the three cases clonidine was successfully stopped while the patients were receiving Bisoprolol, Carvedilol and Labetalol without rebound hypertension in two months follow up period.

Methods: Three cases developed Clonidine induced urinary retention, and it was needed to stop it, but the three cases were receiving Labetalol, Carvedilol and Bisoprolol, so it was decided by multidisciplinary team to stop the Clonidine and as the patients' heart rate was on the higher side, so it was decided to continue on the beta blockers, continue on the other antihypertensive medications, and follow up the patients for rebound hypertension.

Results: It was succeeded to stop the Clonidine, during the two months follow up period, the three patients didn't develop rebound hypertension, and there was no more urine retention.

Conclusion: Clonidine can be safely withdrawn while the patient is still receiving Beta-Blocker with Alpha-Blocking Activity e.g. Labetalol and Carvedilol or cardio-selective beta-blocker such as Bisoprolol especially if the patient is getting other antihypertensive medications.

Keywords: Clonidine; Cardio Selective Beta-Blockers; Beta-Blocker with Alpha-Blocking Activity

INTRODUCTION

Role of clonidine in hypertension

Clonidine is an Alpha₂-Adrenergic Agonist that can be used for chronic hypertension as an additional therapy for resistant hypertension [1]. Clonidine stimulates alpha-adrenoceptors in the brain stem [1,2]. This action results in reduced sympathetic outflow from the central nervous system and in decreases in peripheral resistance, renal vascular resistance, heart rate, and blood pressure [1,2].

Beta-blockers

Beta-blockers are drugs that bind to beta-adrenoceptors and thereby block the binding of norepinephrine and epinephrine to

these receptors. This inhibits normal sympathetic effects that act through these receptors. Therefore, beta-blockers are sympatholytic drugs [3].

The first generation of beta-blockers was non-selective, meaning that they blocked both beta-1 (β_1) and beta-2 (β_2) adrenoceptors. Second generation beta-blockers are more cardio-selective in that they are relatively selective for β_1 adrenoceptors. This relative selectivity can be lost at higher drug doses. Finally, the third-generation beta-blockers are drugs that also possess vasodilator actions through blockade of vascular alpha-adrenoceptors [3].

Rebound hypertension mechanism

Clonidine is an Alpha₂-Adrenergic Agonist, which upon initiation it will suppress centrally the release of circulating

*Correspondence to: Mostafa Ibrahim ElAwady, Clinical Pharmacy Department, Hamad Medical Corporation, Rumailah Hospital, Doha, Qatar, Tel: +97477881690; E-mail: MELawady@hamad.qa

Received: January 10, 2020; Accepted: February 28, 2020; Published: March 05, 2020

Citation: ElAwady MI, Akram W, Sherbash M, Kunnunmal NK, Al Hamad H (2020) Successful Clonidine withdrawal in patients receiving Cardio-selective Beta-blockers and Beta-Blockers with Alpha-Blocking Activity. J Drug Metab Toxicol 11: 244. doi: 10.35248/2157-7609.20.11.244

Copyright: © 2020 ElAwady MI, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Catecholamines [1,2], so upon discontinuation the concentration of Circulating Catecholamines will increase [1,2], in the presence of beta2-receptor blockade, the vasoconstrictor properties of the Catecholamines on the peripheral blood vessels will be unopposed, resulting in the exaggerated hypertensive response [1,2]. As a result, it was recommended by the manufacturer to discontinue beta blockers several days prior to clonidine gradual withdrawal to reduce the risk of rebound hypertension [1,2].

In this study, the decision to stop Clonidine while patients were on a beta blocker was due to clonidine-induced urine retention. We went against manufacturer's recommendation that is to stop beta-blockers first, to maintain control over heart rate.

Despite that, and interestingly, clonidine was safely tapered down and stopped while our patients were still using Beta blockers (selective and non-selective with alpha-receptors blocking activity) along with other antihypertensive agents with no rebound hypertension noted. Therefore, we wrote about the 3 cases of our patients to report to the medical community our findings that are on contrary to manufacturer recommendation, of safe tapering of Clonidine without discounting beta-blockers beforehand.

METHODS

Study design

This is a case series study with a retrospective design, in Long term care facility, Rumailah Hospital in the State of Qatar.

Clonidine tapering

The Clonidine tapering was done over six days to avoid withdrawal adverse effects [1,4,5], and because of half-life of Clonidine is 12-16 hours [1,5], a washout period of 7 days was allowed after complete discontinuation. Foley's catheter was then removed, and bladder scanning continued for 2 days.

Follow-up period

Blood pressure was followed regularly for at least 2 months after Clonidine discontinuation, and all readings were within the normal range the same as before Clonidine tapering started.

Patient information and treatment course

Case No. 1: 57 Years old, male patient, a case of Right Paramedian pontine stroke with medical history of Diabetes Mellitus Type 2, Hypertension.

Upon admission to long-term facility he was in vegetative state, with spontaneous eyes opening, bed bound, but he is already initiated to sit on wheel chair with Occupational therapist

supervision, on Nasogastric tube, Foleys catheter and Tracheostomy.

The patient was started on trial for Foley's catheter weaning. After Foley's, removal bladder scan is done during the next days, but he showed retention with residual volume >300 milliliter. A straight catheter was put each time for >3 days, Clonidine-induced urine retention was suspected, so it was needed to be stopped but the patient was receiving other medications including (Amlodipine 10 mg daily, Bisoprolol 7.5 mg daily, Clonidine 0.45 mg every 8 hours, Hydralazine 100 mg every 8 hours, Lisinopril 10 mg daily, Hydrochlorothiazide 25 mg daily, Aspirin 75 mg daily, Atorvastatin 40 mg daily and Insulin). His renal and liver functions are normal.

Case No. 2: 58 Years old, male patient, a case of Intra Cerebral Hemorrhage with medical history of Diabetes Mellitus Type 2, Hypertension, ischemic CVA. Upon admission to long-term facility he was bedridden with poor neurological recovery, on Nasogastric tube, Foleys catheter and Tracheostomy.

The patient was started on trial for Foley's catheter weaning. After Foley's, removal bladder scan is done during the next days, but he showed retention with residual volume >300 milliliter. A straight catheter was put each time for >3 days, Clonidine-induced urine retention was suspected, so it was needed to be stopped but the patient was receiving other medications including (Amlodipine 10 mg daily, Labetalol 100 mg every 8 hours via Nasogastric tube, Lisinopril 20 mg every 12 hours, Clonidine 0.15 mg every 8 hours, Hydralazine 100 mg every 8 hours and Insulin). His renal and liver functions are normal.

Case No. 3: 50 Years old, male patient, a case of prolonged out hospital cardiac arrest led to severe hypoxic brain injury, with past medical history of hypertension on multiple anti-HTN drugs with poor compliance, Type II Diabetes mellitus with poor compliance with his treatment, Chronic Kidney Disease Stage III. Upon admission to the long-term facility he was bedridden with severe hypoxic brain injury, on Nasogastric tube, Foleys catheter, and Tracheostomy.

The patient was started on trial for Foley's catheter weaning. After Foley's removal bladder scan is done during the next days but he showed retention with residual volume >300 milliliter. A straight catheter was put each time for >3 days, Clonidine-induced urine retention was suspected, so it was needed to be stopped but the patient was receiving other medications including (Amlodipine 10 mg daily, Aspirin 75 mg Daily, Carvedilol 25 mg every 12 hours, Clonidine 0.15 mg every 8 hours and, Hydralazine 75 mg every 8 hours).

Follow-up and outcomes: The Foley's catheter was successfully removed without any urine retention after Clonidine discontinuation, and none of the three patients developed rebound hypertension during the 2-months follow-up period.

Blood pressure measurements before and after Clonidine tapering for the three cases were as follows (Table 1):

Table 1: Blood Pressure measurements before and after Clonidine tapering.

Case number	Blood Pressure (mm Hg)	
	Before	After
1	SBP (140-150)	SBP (130-140)
	DBP (90-100)	DBP (80-90)
2	SBP (130-140)	SBP (130-140)
	DBP (85-95)	DBP (85-95)
3	SBP (125-135)	SBP (125-135)
	DBP (80-90)	DBP (80-90)

DISCUSSION

This case series study is specifying the conditions of Clonidine and beta blockers drug-drug interaction.

This is the first study to report safe tapering of clonidine while patients are still on beta-blocker without developing rebound hypertension. Our results are in contrast with previously published case reports which describe this drug-drug interaction. One case report tapered clonidine dose of 0.3 mg four times a day over 4 days period while patient was on propranolol, yet patient developed severe hypertension (290/170 mm Hg) on third tapering day [6]. Second case of a patient where clonidine was gradually reduced from 0.4 mg to none during a four-day period. At this point, therapy with propranolol hydrochloride, 160 mg; hydrochlorothiazide, 50 mg; and triamterene, 100 mg in divided daily doses, was also stopped. After 48 hours, patient was admitted to emergency with a soaring blood pressure reaching (250/140 mm Hg) [4].

Propranolol blocks both beta1- and beta2-adrenergic receptors without any alpha- receptors blockage activity, but in our cases

Bisoprolol which is Selective inhibitor of beta1-adrenergic receptors [5], Carvedilol which is having nonselective beta-adrenoreceptors and alpha-adrenergic blocking activity [7], and Labetalol which blocks alpha1-, beta1-, and beta2-adrenergic receptor sites [8], were used.

CONCLUSION

Therefore, we suggest that Clonidine can be safely tapered down and stopped while the patient is still using either cardio-selective Beta blockers such as Bisoprolol or Beta-Blockers with Alpha-Blocking Activity such as Labetalol and Carvedilol especially if the patient is using other categories of antihypertensive medications, rather than using a non-selective beta-blocker agent with no alpha-blocking activity such as propranolol.

ACKNOWLEDGEMENTS

We thank the Pharmacy and Medical staff in Rumailah Hospital for their support in collecting the required data to publish this case series.

REFERENCES

1. <https://docs.boehringer-ingenelheim.com/Prescribing%20Information/Pis/Catapres%20TTS/CatapresTTS.pdf>
2. <https://www.medicines.org.uk/emc/product/6538/smpc>
3. <https://www.cvpharmacology.com/cardioinhibitory/beta-blockers>
4. Strauss FG, Franklin SS, Lewin AJ, Maxwell MH. Withdrawal of antihypertensive therapy. Hypertensive crisis in renovascular hypertension. JAMA. 1977; 238(16): 1734-1736.
5. https://www.accessdata.fda.gov/drugsatfda_docs/label/2007/019982s014lbl.pdf
6. Cairns SA, Marshall AJ. Clonidine withdrawal. Lancet. 1976;1(7955):368.
7. [Accessdata.fda.gov/drugsatfda_docs/label/2005/020297s013lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/020297s013lbl.pdf)
8. https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/020297s013lbl.pdf