

## The Man Who Saw Things on Carvedilol

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**The newer generation non selective vasodilating beta adrenergic blocking agent Carvedilol, also has an alpha 1 adrenoceptor antagonistic effect and is widely used in treating various cardiovascular diseases. It is a selective alpha and non-selective beta blocker. Its side effects are vast and not limited to any particular organ system, the neuropsychiatric adverse effects include; somnolence, nervousness, sleep disorder, aggravated depression, vivid dreams, delirium, psychosis, impaired concentration, abnormal thinking, paroniria, and emotional lability. Hallucinations are rarely reported and as far as we know the only reported couple of cases were on metoprolol and propranolol, none has been reported with Carvedilol.**

**Key words: Carvedilol, beta blockers, hallucinations, visual hallucinations**

### INTRODUCTION

Carvedilol is a newer generation non selective vasodilating beta adrenergic blocking agent, with an alpha 1 adrenoceptor antagonistic effect and widely used in congestive heart failure, hypertension and post myocardial infarction [1]. It is popularly referred to as a selective alpha and non-selective beta blocker [1, 2]. Side effects are vast and not limited to any particular organ system, neuropsychiatric adverse effects include; somnolence, nervousness, sleep disorder, aggravated depression, vivid dreams, delirium, psychosis, impaired concentration, abnormal thinking, paroniria, and emotional lability [1-4]. Hallucinations are rarely reported and as far as we know the only reported couple of cases were with metoprolol and propranolol, none has been reported with Carvedilol. We present a patient with vivid visual hallucinations on Carvedilol with detailed description of his report.

### CASE PRESENTATION

M.K. is a 67-year-old male with a history of diabetes mellitus, hypertension, hyperlipidemia, Mild Cognitive Impairment, status post prostate cancer and myocardial infarction. Hypertension was poorly controlled on Amlodipine/Benazepril combination, Carvedilol was added for better control of blood pressure and status post myocardial infarction. Within a few days of starting Carvedilol, patient began complaining of seeing people by his bedside especially at night. These people and odd looking animals would sit by his bedside talking to themselves and watching him. Reported seeing these figures walking with him "step by step" sometimes. Also reported seeing the fire hydrant wave at him and move around. He has seen people come out of the picture on the wall of his bedroom and watch him lay in bed. Also reported people with blurry faces

and rats in clothing, which was the scariest for him. This went on for over 10 months before he reported these symptoms. Visual hallucinations occurred on most days and tends to last throughout the day, but appeared to worsen as the day goes by. He was started on Quetiapine at 25 mg at bedtime which did help him sleep but visual hallucinations persisted. His other medications included aspirin, pravastatin, vitamin D<sub>3</sub>, saxagliptin, glimepiride and alfuzosin. Full neurological and laboratory work up including drug screen were negative. The decision was made to taper him off of Carvedilol leading to a decrease in frequency and intensity of the visual hallucinations. After Carvedilol was stopped visual hallucinations continued to improve over the following 2-3 weeks before it finally abated. There was no change in any other medication and did not go up on the dose of Seroquel because of his age and comorbid medical illnesses.

### DISCUSSION

Central Nervous System [CNS] side effects are reported commonly among the very lipophilic [enhanced CNS drug penetration] beta blocking agents like propranolol and metoprolol, but to the best of our knowledge none has been reported with newer agents like Carvedilol [2]. We now know that lipophilicity is just one of several factors that determines CNS effects [4]. Incidence in patients on propranolol could be as high as 14.3% to 17.5% [2]. It was initially thought that the newer lipophilic beta blockers like Carvedilol have a lower risk of CNS side effects based on speculated properties like structural details and changes in plasma catecholamine and melatonin levels [2]. CNS side effects is believed to be due to beta blockers' actions on beta adrenoceptors in the CNS, antagonistic effect on brain serotonergic receptors and some membrane stabilizing effects [4]. It is not clear why some symptoms are

reported mostly before or just after sleep [hypnagogic or hypnopompic state] as was sometimes seen in our patient also. We believe this side effect is probably underreported for various reasons, mostly patient factors. There has been reports of beta blocker induced delirium especially in the elderly with cognitive impairment [2, 4]. Symptoms tend to begin shortly after starting the medication as seen in our patient, it however took a few weeks after discontinuing Carvedilol before his visual hallucinations abated. The Naranjo score [causality probability] in our patient is 8, the progression however is completely different from what has been reported with other lipophilic beta blockers like metoprolol and propranolol where symptoms abate few days after stopping the drug. The reason for this is not well understood, but we postulate that it could be because Carvedilol was tapered off in the first place or because it has a fairly longer half-life compared to propranolol or metoprolol. Carvedilol, unlike other lipophilic beta blockers doesn't appear to have any effect on nocturnal melatonin release or taken up, stored and released from adrenergic cells alongside noradrenalin, though these are special features that improves its overall efficacy while reducing other side effects, it could contribute to its prolonged CNS effects unlike previously thought. It is also possible that this patient is more prone to CNS side effects because of a possible underlying organicity that may be causing a Mild Cognitive Impairment.

The pathophysiology of visual hallucinations from beta blockers could be as a result of serotonergic blockade or an extrapolation of the pathophysiology of delirium with use of beta blockers. Though our patient described some confusion after waking up in the morning there was no clouding of consciousness or an abnormal Mini Mental Status Exam on examination.

It was initially thought that visual hallucination is rare and unlikely with the newer lipophilic beta blockers like Carvedilol, this might not be the case and relevant study is warranted to elucidate this further.

#### CONFLICT OF INTEREST

None to report

#### SPONSORSHIP

None

#### REFERENCES

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