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A CASE REPORT ON BRASH SYNDROME- METOPROLOL INDUCED

Pharma

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ABSTRACT

Metoprolol is one of the most commonly used Beta blocker, which work by blocking the effect of hormone epinephrine. Several adverse effects are reported with Metoprolol. In this report, we discuss one of the rare adverse effects of Metoprolol – BRASH syndrome. Cases on Metoprolol induced junctional bradycardia-hyperkalemia are rarely reported. The use of Metoprolol is increasing worldwide, hence these life-threatening adverse effects of Metoprolol should be borne in mind.

KEYWORDS

Metoprolol, Junctional bradycardia-hyperkalemia, BRASH syndrome

INTRODUCTION

The **BRASH** describe a syndrome where the synergistic effects of AV nodal blockers and renal impairment lead to severe bradycardia and hyperkalaemia. The syndrome is a clinical pentad of: **B**radycardia, **R**enal Failure, **A**V nodal blockade, **S**hock, and **H**yperkalaemia. [1]

It involves the synergistic effect of AV nodal blockade and hyperkalemia resulting in severe bradycardia. The resulting reduction in cardiac output, in turn, leads to poor renal perfusion, therefore, worsening the acute kidney injury as well as the degree of hyperkalemia. If undiagnosed, this can progress to multi-system organ failure requiring hemodialysis. This vicious cycle is often initiated by an innocuous event such as recent illness or medication changes. [2]

An ECG is vital in determining BRASH syndrome from other causes of bradycardia. It is, however, commonly underwhelming as it does not typically demonstrate the stereotypical electrocardiographic changes seen with hyperkalemia. In isolated hyperkalemia, as the serum potassium levels elevate, the T waves begin to peak with PR interval prolongation followed by QRS widening and subsequent bradycardia; however, these morphologies are commonly absent in BRASH syndrome patients. The low pressure signifies the shock stage. [3]

The management includes medical interventions in mild BRASH to invasive therapies such as hemodialysis or transvenous pacing. [3]

Case Report

A 71-year-old male, who is known to have hypertension (for 7 years), type 2 diabetes mellitus (for 39 years) and CAD (for 4 years), was referred to emergency department for exertional dyspnoea, giddiness and loss of balance while walking. He also had complaints of central chest discomfort and diaphoresis. He was on antihypertensives (losartan, amlodipine, metoprolol, clonidine), hypoglycemic agents (insulin, metformin, glimepiride), antiplatelets (aspirin, clopidogrel), gabapentin-nortriptyline, duloxetine and atorvastatin. He was on metoprolol 25mg twice daily.

On the day of arrival at emergency department, his physical examination was remarkable for heart rate of 28/min, blood pressure of 96/60mmHg. The rest of his vital signs including temperature, respiratory rate and oxygen saturation were within normal limits. Blood and urine culture were sent to exclude the chances of sepsis, which later came up to be negative.

Later, his blood investigation showed creatinine of 2.39 mg/dl, blood urea of 73.5 mg/dl, bicarbonate of 15.7 mmol/L and potassium of 7 mmol/L. The ECG showed ST sagging and junctional bradycardia. The patient was admitted to Nephrology department with preliminary diagnosis of bradycardia related to hyperkalemia and beta-blocker, and he was given 25% dextrose infusion with 10 U insulin, Neb. Salbutamol 2.5 mg-2 respules every 4 hours and a 10 ml 10% calcium gluconate injection. The patient was transferred to the medical intensive care unit, for close monitoring. All his antihypertensive medications were stopped including metoprolol. Haemodialysis was initiated in view of hyperkalemia with bradycardia and renal dysfunction, via right temporary femoral dialysis catheter. Post hemodialysis, the patient was stable with HR raised to 70 bpm, blood pressure of 130/90mmHg and potassium level of 3.4 mmol/L. ECG showed resolution of junctional rhythm. His nebulisations were stopped as his potassium level improved.

The next day, his clinical course remained stable with blood pressure of 120/70 mmHg, heart rate of 72 beats/minutes and repeat potassium level of 4.33 mmol/L. He had GCS of E4V5M6 and ECG was normal. As patient had adequate urine output, his temporary femoral catheter was removed and shifted out from ICU. Later his AKI improved and his regular medications were optimized at discharge.

Table 1. BRASH characteristics of the patient from admission till discharge from the hospital

	Day 1	Day 2	Day 3
Potassium (in mmol/L)	7	4.33	4.29
HR (beats/minute)	38	72	76
BP (in mmHg)	96/60	120/70	130/90
Creatinine (in mg/dL)	2.39	1.25	1.22
ECG	ST sagging Junctional bradycardia		Normal

This table shows the features which points to BRASH syndrome-(potassium level, heart rate, blood pressure, creatinine level and ECG of the patient) on the days of his hospital stay. On first day, he had hyperkalemia, bradycardia, shock, acute kidney injury and ECG showed junctional rhythm. At the time of discharge, he had recovered with improvement of all parameters.

DISCUSSION

Beta-blockers are indicated and have FDA approval for the treatment of tachycardia, hypertension, myocardial infarction, congestive heart failure, cardiac arrhythmias and coronary artery disease. Metoprolol is a beta blocker which work by inhibiting adrenergic responses mediated through the beta receptors. Most common side effects of metoprolol are bradycardia, tiredness and shortness of breath.[4]

BRASH syndrome is typically due to the synergy between hyperkalemia and AV-nodal blocking medications, which leads to bradycardia. The reduction in cardiac output due to bradycardia causes impaired renal perfusion and renal dysfunction, which in turn exacerbates hyperkalemia. Concurrent use of AV-blockers increases the risk of AKI and hyperkalemia. [5]

BRASH syndrome is an uncommon but often a fatal condition, but this syndrome is not well documented in any medical literatures. The junctional bradycardia- hyperkalemia condition is not reported in Vigiaccess till date. Hence it is important to monitor and report this adverse event.

CONCLUSION

This case presents a unique incidence of BRASH syndrome caused by Metoprolol. Thus, if a patient on AV nodal blocking agent develops junctional bradycardia-hyperkalemia, the drug can be suspected as the possible offending agent after ruling out other possible causes of this condition in the patient. Haemodialysis can be performed as part of supportive therapy.

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Conflicts Of Interest

There are no conflicts of interest.

Abbreviations

- BP- Blood Pressure
- HR- Heart Rate
- ECG- Electrocardiogram
- CAD- Coronary Artery Disease
- AV- Atrioventricular
- GCS- Glasgow Coma Scale
- AKI- Acute Kidney Injury
- FDA- Food and Drug Administration
- ADR- Adverse drug reaction

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