SHORT ACTING BETA AGONIST INDUCED MUSCLE CRAMPS

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Although Beta agonist induced muscle cramps in asthmatic patients is widely studied in literature, it is often missed by the internist.

Case Presentation :-

- A 50-year old female presented with two days of progressively worsening of shortness of breath, cough and muscle cramps in the lower limbs. On examination, She had wheeze at both the lung bases. CVS examination was normal. On careful questioning the patient told that She used 8 to 10 times a day the rescue inhaler containing xopenex in the past three days.

Table-1: Patient Vitals

BP - 110/68
Pulse - 90bmp
Temp - 98.2 F (recorded orally)
RR - 24/min
SpO2 -94%

Table-2: Patient Lab values

WBC - 10.8 x 10^3 Neutrophils: 52% Lymphocytes: 32% Monocytes: 6% Eosinophils: 10% Basophils: 0%	**Serum Electrolytes :** Na - 140 K - 3.3 Ca - 9.2 Cl - 100 HCO3 - 22
CPK - 98 U/L	
BUN - 24	
Creatinine – 1.1	

- On doing diagnostic workup, EKG showed normal sinus rhythm. Chest X-ray showed non-specific findings related to obstructive lung disease. Peak flow meter readings were low. Ankle brachial index score of 1.2, arterial Doppler lower extremities showed no abnormalities. All the above workup revealed no abnormalities except increased Eosinophil count and low potassium levels.

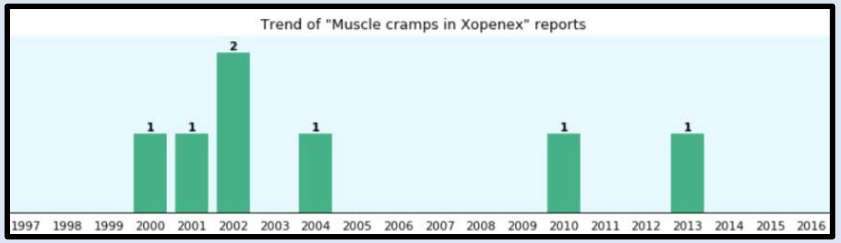
- Medication prescribed with starting dose of 40mg oral prednisone tapered in one week, Tudorza inhaler and asked her to hold the rescue inhaler (xopenex) and follow-up in 1 week. On her next visit, symptoms were subsided and lab values were normal.

Discussion :-

- Activation of β_2 adrenergic receptors on airway smooth muscle leads to the activation of adenylate cyclase and to an increase in the intracellular concentration of cyclic AMP. The increase in cyclic AMP is associated with the activation of protein kinase A, which in turn inhibits the phosphorylation of myosin and lowers intracellular Ca concentration, resulting in muscle relaxation. But researchers don't know yet why beta2 agonists cause muscle cramps.

- **Fact Sheet:** 6,074 people were selected who have side effects with Xopenex. Among them, 7 people (0.12%) have Muscle Cramps.

Pic 1: Number of reports submitted per year.



Pic 2: Adverse Reactions Reported in a 4-Week, controlled Clinical Trial in Adults and Adolescents ≥12 Years Old

Body System Preferred Term	Placebo (n=75)	Xopenex 1.25 mg (n=73)	Xopenex 0.63 mg (n=72)	Racemic albuterol 2.5 mg (n=74)
Body as a Whole				
Allergic reaction	1.3	0	0	2.7
Flu syndrome	0	1.4	4.2	2.7
Cardiovascular System				
Tachycardia	0	2.7	2.8	2.7
Musculoskeletal System				
Leg cramps	1.3	2.7	0	1.4

Pic 3: Mean Changes from Baseline HR, Glucose and Potassium at 1 Hour after First Dose (Day 1) in Adults.

Treatment	Heart Rate (bpm)	Glucose (mg/dL)	Potassium (mEq/L)
Xopenex 0.63 mg, n=72	2.4	4.6	-0.2
Xopenex 1.25 mg, n=73	6.9	10.3	-0.3
Racemic albuterol 2.5 mg, n=74	5.7	8.2	-0.3
Placebo, n=75	-2.8	-0.2	-0.2

- Xopenex may produce hypokalemia in some patients, possibly through intracellular shunting. The decrease is usually transient, not requiring supplementation.

Conclusion :-

Understand the side effects of the drugs of asthma. Although widely studied, recognize that short-acting beta agonist (SABA) in an inhaled quantity is an uncommon cause of muscle cramps. SABA causing muscle cramps should be suspected in a patient with decreased serum potassium levels, with no other known factors for lowering potassium and when rest of the workup is normal. This case illustrates that SABA even in inhaled amounts can cause muscle cramps mostly when taken more than six times a day and also the importance of detailed history taking.

References :-

- Full prescribing information XOPENEX® (Levalbuterol HCL)-Akorn Pharmaceuticals.
- Could Xopenex cause muscle cramps? from-ehealthme.com/ds/xopenex/muscle%20cramps/