

Effectivity of Flunarizine in controlling acidosis induced headache

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Case Report

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Abstract

In my previous case report, I mentioned about the connection between metabolic acidosis and other diseases. Headache is one of the diseases mentioned in a female patient. For the patient, it was observed that acidosis is the indicator. Acidosis takes place first.

There can be many reasons for metabolic acidosis.

For this patient it was seen that, food is the trigger. With consistent disbalance in pH level in body it exhibits many symptoms like palpitations, altered mental status such as severe anxiety due to hypoxia, nausea, abdominal pain, altered appetite and weight gain, muscle weakness, bone pain, and joint pain.

In acidosis the arterial carbon dioxide tension increases, and it can cross the blood-brain barrier and changes extravascular pH. Headache is trigger.

Patient was treated with Pregabalin, Amitriptyline and Duloxetine combination.

Frequency of headache was less but it was not stopped. Then patient was treated with CGRP receptor blocker subcutaneous injection but was not able to get rid of the throbbing head pain.

On using Flunarizine (Sibelium 10 mg) the headache was stopped on 2 days of medicine taking. It helped in reducing allergy-like symptoms too.

The effectivity of Flunarizine in controlling acidosis related headache is well proved.

Background

Metabolic acidosis happens when,

1. Body's acid production increases
2. Kidney not being able to excrete enough acid.
3. Bicarbonate loss.
4. Body's bicarbonate buffer is low.

After long observation it was found that the patient is showing below symptoms along with the primary complaint of headache,

1. Gas, acid, bloating, nausea.
2. Muscle pain, stiffness in back neck.
3. Weak muscle.
4. Shortness of breath.

5. Fast heart rate.
6. Constipation.
7. Low appetite.
8. Mood swing.
9. Anxiety & Depression.
10. Food craving.
11. Shivering, tremor sensation.

Case Presentation

Carbon dioxide (CO₂) is a gas that is produced as a normal by-product of our body's energy production. As per the normal body's process, CO₂ diffuses into bloodstream so that it can be exhaled from lungs. When CO₂ level become elevated, the signal reaches brain. Brain, then sends signal to the respiratory system to control CO₂ level, to decrease the level. Lung starts working heavily, it tries to exhale elevated CO₂. So, a deep and faster breathing continues until the oxygen & carbon dioxide levels are balanced again.

In acidosis the arterial carbon dioxide tension increases, and it can cross the blood-brain barrier and changes extravascular pH. This imbalances pH level of CNS. Blood vessels get dilated. This triggers excitatory neurotransmitter release.

Once released, they travel to the outer layer of brain, the meninges. Which results in inflammation and swelling of blood vessels, causing an increase in blood flow around the brain. This makes the inflammation of the blood vessels resulting in throbbing pain.

Patient was initially treated with Pregabalin, Amitriptyline and duloxetine combination. The combination worked for some time, but headache was not stopped completely, only the frequency was less.

Patient took Ibuprofen (600mg) in SoS basis.

Later patient was given Aimovig (CGRP receptor inhibitor) subcutaneous injection. After taking the injection patient was able to be without headache for 7 consecutive days but after that headache again started.

Unavailability of Flunarizine in the locality was the cause patient was not able to take flunarizine.

Once started with Flunarizine (Sibelium 10mg) patient was able to get rid of the headache. This implies Flunarizine has the capability to decrease carbon dioxide tension in CNS.

Discussion

Pregabalin works as a selective calcium channel blocker (CCB). This medication is used to treat neuropathic pain, fibromyalgia, restless leg syndrome, and generalized anxiety disorder.

Amitriptyline inhibits serotonin transporter (SERT) and norepinephrine transporter (NET). Amitriptyline additionally acts as a potent inhibitor of the serotonin 5-HT_{2A}, 5-HT_{2C}, the α _{1A}-adrenergic, the histamine H₁. It is a non-selective blocker of multiple ion channels voltage-gated sodium channels.

Duloxetine is used to treat fibromyalgia, and neuropathic pain. It is a serotonin–norepinephrine reuptake inhibitor.

Erenumab targets the calcitonin gene-related peptide receptor (CGRPR) for the prevention of migraine.

Flunarizine is a selective calcium antagonist. Other actions include,

- Antihistamine
- Serotonin receptor blocking
- Dopamine D₂ blocking activity.
- It has been theorised that it may act not by inhibiting calcium entry into cells, but rather by an intracellular mechanism such as antagonising calmodulin.
- It readily passes the blood–brain barrier.

In research, it has been found that flunarizine can decrease the carbon dioxide tension in CNS. So, for acidosis induced headaches, flunarizine is the best.

As flunarizine has antihistamine property, it should be able to stop allergy induced headaches.

It has been observed in the patient that, calcium channel blocker drugs help in reducing symptoms of allergy.

It may happen that CCB drugs restrict the degranulation of the mast cells.

Now,

To get rid of allergy there are two ways,

1. Drug that inhibits histamine H₁ receptor. In that case the other mediators' receptors are not inhibited. And it is not possible to restrict downstream action of all mediators.
2. Stopping the unnecessary degranulation of mast cells.

Pregabalin can help in reducing the mast cell granulations. So, it contributes to allergy induced acute headaches. That is why use of pregabalin can lower the acute headache frequency.

Amitriptyline has the property of several receptor blocker. This helps to inhibit the receptors when the degranulation has already taken place, and mediators are playing and contributing to acute headache trigger.

That is why the combination of medicines Pregabalin, and Amitriptyline can lower the frequency of acute headache but cannot stop them.

It has been seen that during migraine headache CGRP, calcitonin gene-related peptide is released around the brain. When CGRP is released, it causes intense inflammation in the coverings of the brain (the meninges) and starts the headache. CGRP also contribute to linger the headache up to several hours.

The next question comes, why does CGRP release take place in brain?

Let us draw a sequence diagram.

Let us identify the ways to stop migraine trigger

CGRP receptor blocking is the 4th Layer. Flunarizine (Sibelium) may have the property of decreasing CO₂ tension in CNS. That is how it controls opening the ASIC3 channels. So, CGRP is not released, and no mast cell degranulation happens. As a result, no histamine release.

Conclusion

From the discussion flunarizine is very effective in acidosis induced acute headaches. We have seen that the other medicines are not working at the root cause level.

Abbreviations

CGRP

Calcitonin gene-related peptide

CNS

Central Nervous System

ASIC3

Acid Sensing Ion Channel 3

CCB

Calcium Channel blocker

Declarations

- Ethics approval and consent to participate: Not applicable
- Consent for publication: Written informed consent was obtained from the patient for publication of this
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Figures

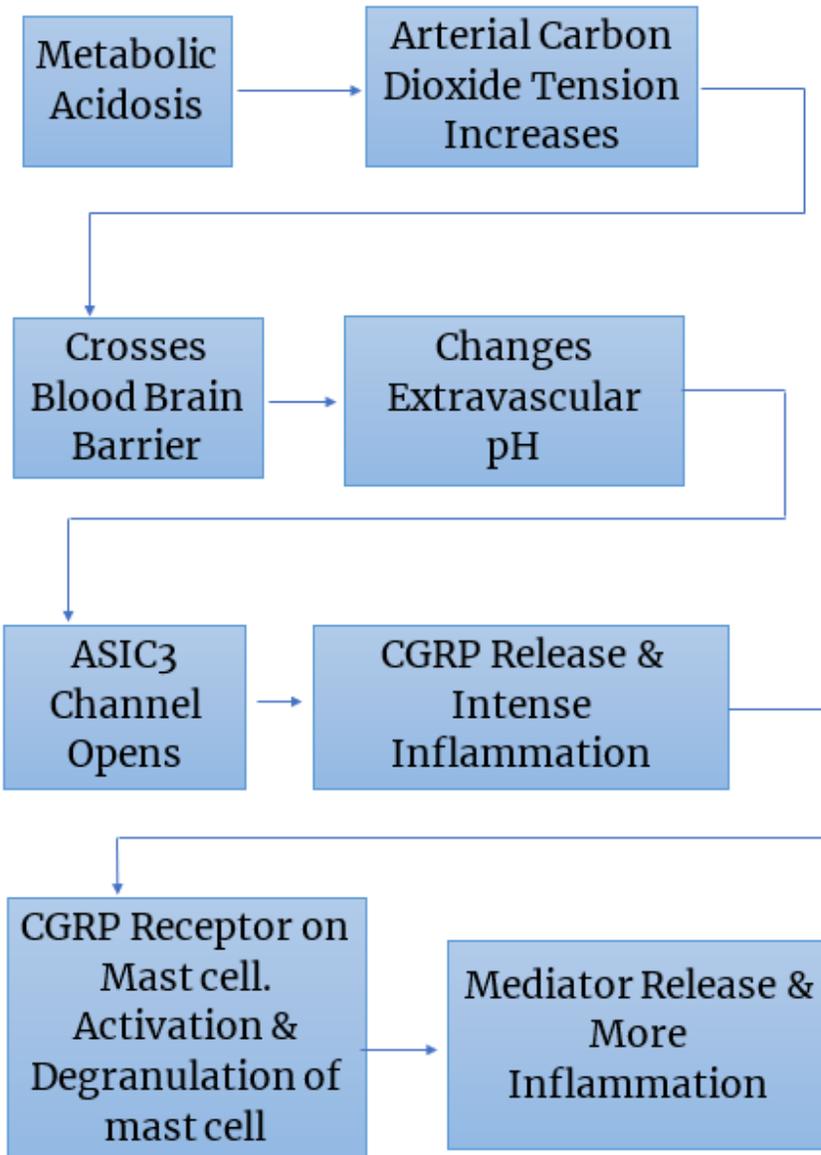


Figure - 1

Figure 1

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Let us identify the ways to stop migraine trigger

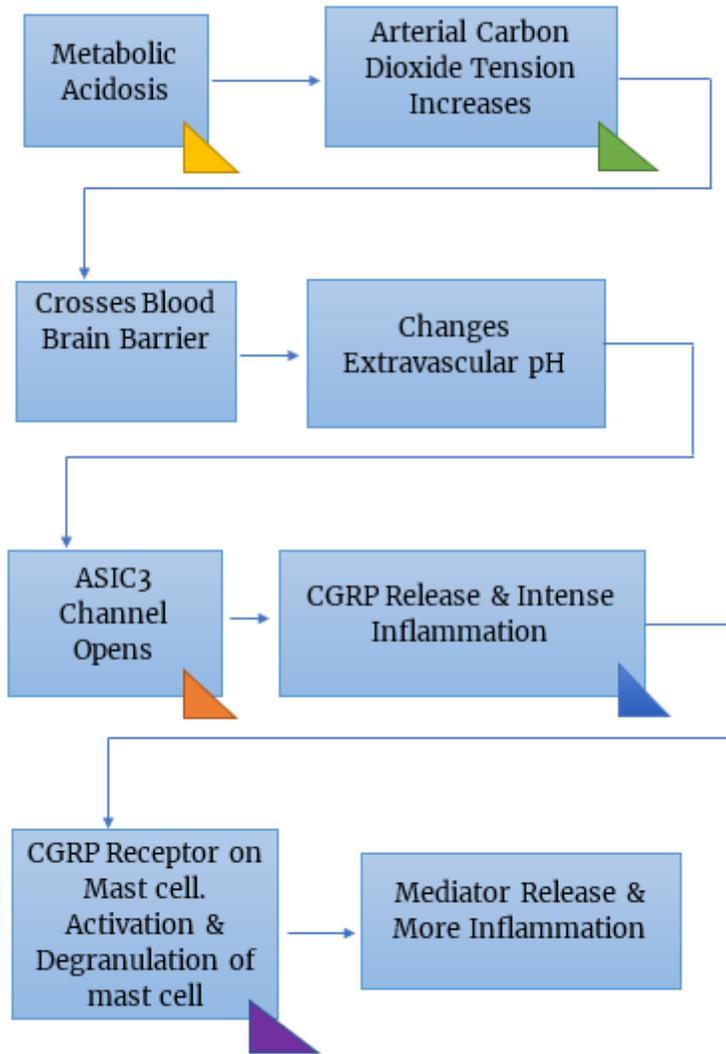


Figure – 2

Figure 2

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To get rid of acute headache	
	Electrolytes, Decreasing CO ₂ Tension
	Increase Bicarbonate Level (Carbonated Water)
	ASIC3 Channel Inhibitor
	CGRP Receptor Inhibitor, CCB
	H1 Receptor Inhibitor, CCB
	Pain already triggered, Painkiller

Figure – 3

Figure 3

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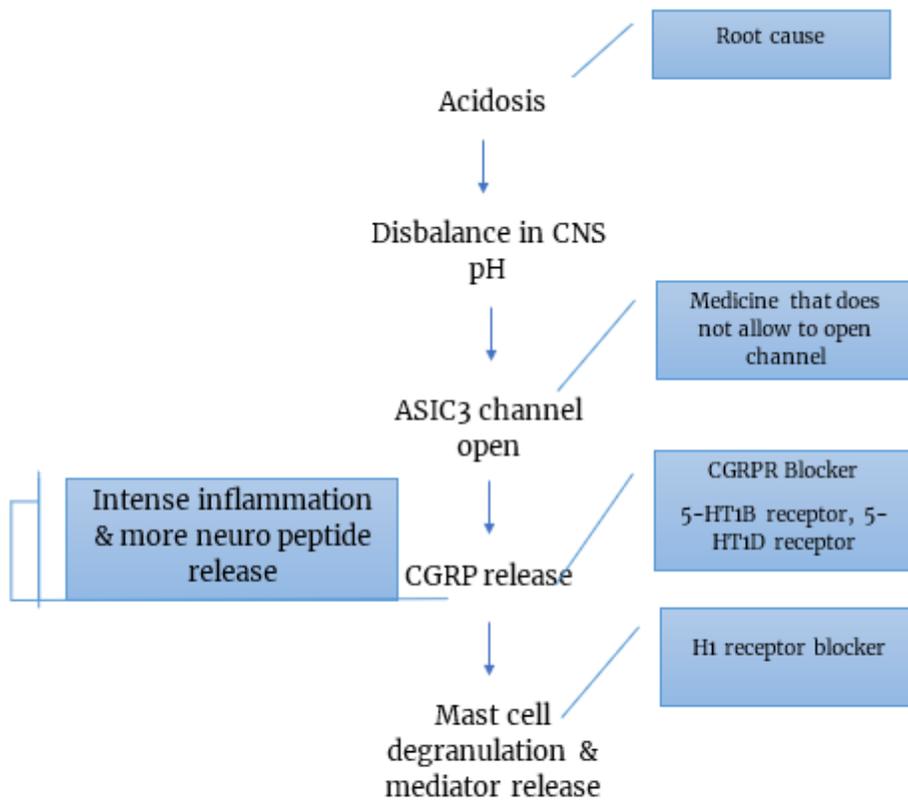


Figure – 4

Figure 4

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