Haloperidol As A Treatment Of Opioid Induced Hyperalgesia

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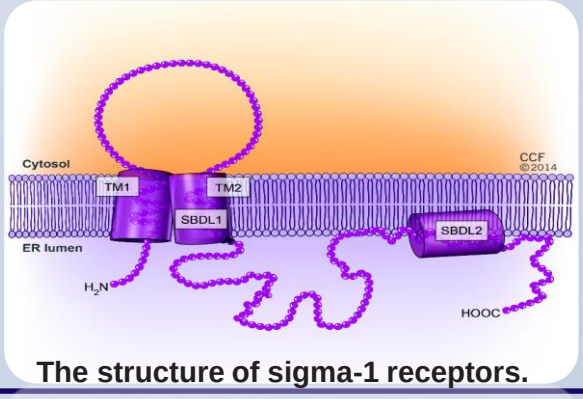
INTRODUCTION

•Opioid-induced hyperalgesia (OIH) is a state of nociceptive sensitization paradoxically caused by exposure to opioids.

•Paradoxical increased response to certain painful stimuli on opioids.

•Sigma-1 Receptors (S-1R) expressed in the central and peripheral nervous system on mitochondrion associated membranes of the endoplasmic reticulum are activated by cellular stress.



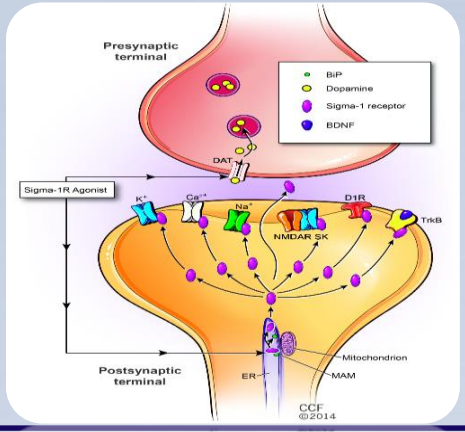
The structure of sigma-1 receptors.

CASE DESCRIPTION

A 67 years old male with a bone marrow biopsy proven myelofibrosis with a neoplastic clone consistent with MDS/MPN and was started on azacitidine. After the first does he developed weakness, fever and pancytopenia. He was admitted with a febrile illness and placed on antibiotics. His pancytopenia persisted despite azacitadine. A repeat bone marrow biopsy revealed transformation to AML. He was started on fludarabine, cytarabine and G-CSF which he did not tolerate. Post chemotherapy he started experiencing worsening generalized pain. Subsequently, patient's family opted for hospice and comfort measures. He was discharged to nursing home on hospice with hydromorphone PCA 0.3 mg/hr basal and 0.3 mg Q30 min PCA dose. Patient developed worsening pain which intensified with an increased basal dose to 0.6 mg to 1 mg/hr and increase PCA dose to 0.6 mg Q30 min to 0.6mg Q10min. OIH was considered for his worsening pain. He was started on oral haloperidol 1mg Q1H PRN. Pain was relieved after first dose of haloperidol.

DISCUSSION

•S-1R are chaperone proteins which interact with multiple receptors and ion channels.
•Opioids can activate S-1R.
•Receptors release neurotransmitters, reduce intracellular Ca^{2+} currents through voltage gated Ca^{2+} channels, modulate Na^{+}, K^{+} and ligand-activated ion channels and activate multiple kinases and nitric oxide synthase.
•Receptors inhibit G-protein interactions with Mu receptors and directly facilitate NMDA receptor activation and indirectly kinases causing pronociception and hypersensitivity.
•Haloperidol is potent S-1R blocker.
•S-1R activation is coupled to pain facilitation and inhibition of opioid antinociception, haloperidol inhibits pain hypersensitivity and "releases the brake" on opioid antinociception enabling effective analgesics.



Sigma-1 receptors synaptic pathways.

CONCLUSIONS

Haloperidol is potent S-1R blocker.

This patient history illustrates the balance between treating pain with opioids and the adverse effect, opioids induced hyperalgesia.

Haloperidol rebalances the equation.

REFERENCES

1- Davis MP. Sigma-1 receptors and animal studies centered on pain and analgesia. *Expert Opinion on Drug Discovery.* 2015;10(8):885-900.

2- Barrett, James E, S. J Enna, and Lynn Lecount. *Pharmacological Mechanisms And The Modulation Of Pain*. 1st ed. Cambridge, MA: Academic Press/Elsevier, 2016. Print.