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May cyproheptadine be a treatment choice for prophylaxis of PFAPA syndrome?

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Dear Editor,

Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA syndrome) is a common periodic fever syndrome in Turkey. PFAPA is an auto inflammatory syndrome characterized by periodic episodes of recurrent febrile episodes associated with aphthous stomatitis, pharyngitis and cervical adenitis. Febrile episodes last 3 to 6 days and recur about every 3-8 weeks. The syndrome causes fatigue, chills, and occasionally abdominal pain and headache, as well as fever, pharyngitis, aphthous ulcers, and lymphadenopathy. Children are healthy between episodes, and have normal growth and development

There is no specific treatment to cure PFAPA and the treatment is optional. Single dose prednisolone therapy during attack, and tonsillectomy are the treatment options [1]. Cyproheptadine (CH) was started for migraine patients with PFAPA. I observed that the attack intervals was prolonged. I also noticed that attacks of PFAPA was exacerbated if the CH was cessated. CH is known that serotonin increases the release of pro-inflammatory cytokines and CH is a potent antiserotonergic drug.

The pathogenesis of PFAPA is known to be related to proinflammatory cytokines. Interferon-ϒ (IFN-ϒ), tumor necrosis factor-α (TNF-α), IL-1b, IL-6, and IL-12 concentrations elevate during attacks in PFAPA [2, 3]. Serotonin is a neurotransmitter released by activated platelets. Functional studies showed that serotonin is a potent regulator of human dendritic cell unction, increase the release of pro-inflammatory cytokines such as IL-1beta, IL-6, IL-8/CXCL8, IL-12p40 and tumor necrosis factor-alpha (TNF-alpha) [4]. Cimetidine, a selective histamine-2 receptor antagonist was recommended to use for prophylaxis and reduce the attacks of PFAPA syndrome. It inhibits suppressor CD8+ T-lymphocyte activation and chemotaxis [5]. Histamine-2 receptor antagonist markedly decreased serotonin concentrations by the prolonged treatment. I observed that CH is particularly useful for prophylaxis of PFAPA.

My hypothesis is that "May serotonin be an important role of pathogenesis of PFAPA? May CH be a choice for prophylaxis of PFAPA? Serotonin may play an important role in PFAPA and serotonin antagonist drugs such as CH may be a treatment choice for prophylaxis of PFAPA. This new medical hypothesis must be confirmed with clinical observational studies. And also my hypothesis should be evaluated with studies related to serotonin levels in PFAPA.

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This article does not contain any studies with animals and human participants. This article contains a clinical observation based hypothesis.

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