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Fingolimod-induced asthma deterioration in a patient with relapsing–remitting multiple sclerosis

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Dear Editor,

Fingolimod prevents egress of lymphocytes from lymph nodes by modulating the sphingosine-1-phosphate (S1P) receptor. Compared with placebo, it improves relapse rate, disability progression and magnetic resonance imaging (MRI) findings in multiple sclerosis (MS).¹

S1P regulates diverse functions including contraction of human airway isolated smooth muscle cells. Even though mild dose-dependent reduction in the mean force expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) have been described in patients with MS,² several recent reports suggest that fingolimod is safe in patients with asthma.^{3,4} We here present a 43-year-old female who was diagnosed with relapsing–remitting MS (RRMS) in 2007. Due to disease breakthrough and side effects under glatiramer, interferon-beta-1b, subcutaneously and interferon-beta-1a intramuscularly, fingolimod was started in May 2013.

Bronchial asthma was diagnosed in 2004 and several asthma exacerbations which have had to be treated with systemic corticosteroids have been reported since. From 2009, the patient's asthma had been completely stable with a combined inhaled corticosteroid and long acting beta2-agonist (formoterol-budesonide 200/6 mcg twice daily). Pre-treatment spirometry showed a FEV1 of 3.06 L (100% predicted), FVC 3.98 L (118%), and FEV1/FVC of 73%. Reversibility in FEV1 was 7% (200 ml). CO diffusion capacity and total lung capacity (TLC) were normal.

After 6 weeks of fingolimod, the patient was experiencing increased shortness of breath with complaints of wheezing and nocturnal dyspnea. Spirometry

showed a decrease in pulmonary function: FVC of 3.56 L (106% pred.), FEV1 2.52 L (88% pred.) and FEV1/FVC of 71%.

During a period of 7 weeks, the dose of formoterol-budesonide was doubled, and beclomethason twice daily 200 ug, montelukast 10 mg and nasal inhalation steroids were added, but did not induce any improvement.

Spirometry 12 weeks after start of fingolimod showed further deterioration of pulmonary function with a FVC of 3.41 L (102% pred.), FEV1 2.29 L (79% pred.), and FEV1/FVC of 67%. Treatment with systemic corticosteroids (prednisolone 20 mg once daily) was initiated without any effect.

As respiratory symptoms persisted despite maximal asthma treatment, and in the absence of evidence for any other cause of dyspnea, fingolimod was discontinued after a total treatment duration of 3 months.

Four weeks after discontinuation of fingolimod, pulmonary function stabilized, showing FVC 3.58 L (107%), FEV1 2.72 L (94%), FEV1/FVC 76%.

In this MS patient with bronchial asthma, pulmonary function was stable for many years before the start of fingolimod. After initiation of fingolimod, a significant increase of refractory asthma symptoms and deterioration of pulmonary function was observed, which clearly improved after cessation of fingolimod, suggesting a causal relationship.

Few data have been reported about asthma in patients using fingolimod. However, meeting abstracts suggest that fingolimod is safe to use in moderate

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asthma.⁵ Our case, however, does not confirm these findings.

It is important to keep in mind that asthma deterioration can be provoked by fingolimod. We suggest to perform at least spirometry before initiation of fingolimod in every asthma patient, and to monitor patients in close cooperation with the pulmonologist.

References

1. Kappos L, Radue EW, O'Connor P, et al. A placebo-controlled trial of oral fingolimod in relapsing multiple sclerosis. *N Engl J Med* 2010; 362: 387–401.
2. Kappos L, Antel J, Comi G, et al. Oral fingolimod (FTY720) for relapsing multiple sclerosis. *N Engl J Med* 2006; 355: 1124–1140.
3. Trifilieff A and Fozard JR. Sphingosine-1-phosphate-induced airway hyper-reactivity in rodents is mediated by the sphingosine-1-phosphate type 3 receptor. *J Pharmacol Exp Ther* 2012; 342: 399–406.
4. Voldsgaard A, Koch-Henriksen N, Magyar M, et al. Cardiac and pulmonary effects related to initiation of fingolimod treatment. (Oct 4, 2013).
5. Slade A et al. Effects of oral fingolimod (FTY720) on pulmonary function tests in patients with moderate asthma. *Neurology* 2010; 74(number 9, supplement 2).

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