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Case report

Long-term exposure to inhaled capsaicin: Can it induce or worsen asthma?

Exposition prolongée à la capsaïcine : peut-elle induire ou aggraver un asthme ?

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Abstract

Capsaicin, the pungent extract of red chilli peppers, is widely used in experimental cough models. We report two cases in which repeated exposure to red peppers led to asthma. The first patient was a 69-year-old non-atopic man who had worked in a grocery shop where he was exposed to red peppers for 5 years. He was first seen complaining of dyspnea and rhinorrhea. On clinical examination, he was wheezing and had sibilant rhonchi. Spirometry revealed a reversible obstructive defect. A realistic provocation test with red peppers was positive. Assessment after medical treatment and a change in employment revealed significant clinical improvement. The second patient was a 40-year-old atopic woman with a 30-year history of allergic asthma, who presented to our hospital because her asthma had worsened. Medical history revealed chronic exposure to dry red pepper powder at home. Spirometry demonstrated a reversible obstructive defect. Clinical improvement occurred after medical treatment and avoidance of exposure to peppers in the first patient, allowing him to stop treatment within 18 months. However, the second patient's asthma was worse, in spite of definite avoidance of red peppers and continued medical treatment. Capsaicin stimulates unmyelinated slow C fibers of the sensory nervous system, inducing reflex cough and sneezing. Recurrent exposure to this substance may lead to neurogenic inflammation resulting in increase of airway responsiveness. It is therefore possible that prolonged exposure to capsaicin can induce asthma and/or worsen pre-existent asthma.

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Keywords: Asthma; Capsaicin; Inflammation

Résumé

La capsaïcine est un extrait piquant du poivre rouge largement utilisé dans les modèles expérimentaux de la toux. Nous rapportons deux cas où l'exposition répétée à la capsaïcine a entraîné un asthme. Le premier patient était un homme de 69 ans non atopique qui avait travaillé dans une épicerie où il était exposé au poivre rouge depuis cinq ans. Il consulta d'abord pour une dyspnée avec rhinorrhée. À l'examen clinique il présentait un wheezing et des râles sibilants. La spirométrie révéla un syndrome broncho-obstructif réversible. Un test de provocation bronchique réaliste avec le poivre rouge fut positif. Après traitement médical et changement de poste de travail, l'évaluation montra une amélioration clinique significative du patient. La seconde patiente était une femme âgée de 40 ans, souffrant d'asthme depuis 30 ans, mais qui consulta à notre hôpital pour une aggravation de sa maladie. L'interrogatoire révéla une exposition chronique à la poudre de poivre rouge à son domicile. La spirométrie objectiva un syndrome broncho-obstructif réversible. Chez le premier patient, l'amélioration clinique se manifesta après la cessation de son exposition au poivre rouge associée à un traitement médical antiasthmatique, ce qui lui permit d'arrêter son traitement au bout de 18 mois. En revanche, la seconde patiente, dont l'asthme était plus sévère, fut obligée de poursuivre le traitement malgré l'arrêt de l'exposition au poivre rouge. La capsaïcine stimule les fibres C lentes non myélinisées du système nerveux sensitif, entraînant une inflammation neurogène et une hyperréactivité bronchique. Il est donc possible que l'exposition prolongée à la capsaïcine puisse provoquer un asthme ou aggraver un asthme préexistant.

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1. Introduction

Capsaicin, the pungent extract of red pepper, is widely used in clinical research as an essential component for experimental cough models [1]. However, bronchopulmonary effects of recurrent natural exposure to capsaicin resulting in asthma have not previously been reported.

We present two clinical cases and discuss the underlying mechanisms of this disorder.

1.1. Case 1

A 69-year-old non-atopic male smoker (32 pack-years), who had been employed in a grocery store where he was exposed to red chilli peppers during the previous 5 years, presented to our hospital with a 4-year history of paroxysmal sibilant dyspnea occurring mainly during the daytime. His symptoms had become more severe over the previous two years, with more frequent dyspnea and repeated emergency room visits. He also complained of rhinorrhea, sneezing and watery eyes during working hours. These symptoms were diminished when he was absent from work. On clinical examination, his temperature was 37.2 °C, pulse rate 92 beats/minute and respiration rate 28 breaths/minute. The chest examination revealed sibilant rhonchi in both lung fields and a normal heart. Blood arterial gases were as follows: pH of 7.33, PaO₂ of 79 mmHg, PaCO₂ of 33.2 mmHg and SaO₂ of 94.4%. Chest radiography showed thoracic distension. Spirometry revealed a reversible obstructive defect with FVC = 2.13 l (69% of predicted value [PV]), FEV₁ = 1.49 l (61% of PV) and FEV₁/FVC = 70%. After 7 days of corticosteroid therapy, the spirometry values were: FVC = 2.41 l (78% of PV), FEV₁ = 1.88 l (77% of PV) and FEV₁/FVC = 78%. Skin prick tests (SPT) with a standard series of inhalant allergen extracts were negative, as was a SPT with an extract of natural red pepper. A realistic provocation test with red pepper powder/dust was positive, with sneezing, dyspnea and sibilant rhonchi. On re-examination after medical treatment, which had included an inhaled corticosteroid and a short-acting inhaled β_2 agonist as well as changing his employment, the patient was markedly improved, requiring less medication and fewer emergency room visits. The treatment was reduced progressively and then stopped completely at the 18-month follow-up visit, when the patient reported total recovery.

1.2. Case 2

A 40-year-old non-smoking woman with a 30-year history of allergic asthma presented to our hospital with a history of worsening asthma, coughing and rhinorrhea and more frequent emergency room visits over the previous 8 years. She reported chronic exposure at home to dry red pepper powder (grinding red peppers and sieving the powder). On clinical examination, her temperature was 37.2 °C, pulse 92 beats/minute and respiration rate 20 breaths/minute. Chest examination revealed sibilant rhonchi in both lung fields. Chest radiography showed thoracic distension. Spirometry revealed an obstructive defect

with initially: FVC = 2.62 l (75% of PV), FEV₁ = 1.62 l (61% of PV) and FEV₁/FVC = 61%. After β_2 agonist inhalation, her FVC was 2.8 l (80% of PV), FEV₁ = 1.98 l (74% of PV) and FEV₁/FVC = 70%. SPT were positive to house dust mite and negative to an extract of natural red pepper. Re-examination after medical treatment, which included an inhaled corticosteroid, a short-acting inhaled β_2 agonist and avoidance of exposure to red pepper showed significant clinical improvement with stabilisation of her asthma. A follow-up visit revealed worsening of the patient's asthma due to re-exposure to red pepper. In spite of total avoidance of red pepper at home, there had been no clinical improvement. She continued to have frequent attacks of asthma even though she used a long-acting inhaled β_2 agonist as well as frequently taking an oral corticosteroid.

2. Discussion

To our knowledge, prolonged inhalation of airborne capsaicin-containing red pepper particles leading to the onset or worsening of asthma has not been reported previously. The clinical data in our first patient strongly suggested the hypothesis that inhaled capsaicin had induced his asthma: absence of personal or familial history of atopy, occupational exposure to a natural source of capsaicin, a positive red pepper provocation test and relief of symptoms during absence from work. Furthermore, capsaicin could also act as an airway irritant and thus worsen pre-existent asthma, as in our second patient.

Regarding the efficacy of avoidance, our first patient had very satisfactory regression of all his asthma symptoms within 18 months after changing his employment, whereas in the second case, even though she had stopped grinding red peppers, her asthma was even worse when she was seen some weeks/months. The difference in the clinical course of the two patients might be explained as follows: long-term exposure to capsaicin in the first case did not trigger a chronic inflammatory airway reaction, probably due to the patient's non-atopic status; his asthma symptoms totally regressed when he was no longer exposed to red peppers. However, in the second case, even after definitive avoidance, capsaicin might have had a long-lasting pathogenic effect due to the patient's atopic status.

Capsaicin (8-methyl-N-vanillyl-6-nonenamide) is the active component of red chili peppers that accounts for the hot sensation associated with their consumption. Pure capsaicin is a hydrophobic colorless and odorless crystalline-to-waxy compound. Capsaicin inhalation is considered to be a safe research tool, notably for measuring cough reflex sensitivity. According to a recent review of 122 published studies (evaluating 4833 subjects undergoing a capsaicin cough challenge test), no serious adverse reactions to capsaicin inhalation challenge have been reported [2]. However, a handful of cases of asymptomatic bronchoconstriction, as measured by FEV₁ but without clinically-evident bronchospasm or exacerbation of existing asthma, have been observed [3–6]. In fact, most of the published studies dealing with capsaicin examined either the acute effects of inhaled capsaicin on the airways or the short-term impact of

repeated capsaicin challenge test [2]. Only a few studies have specifically examined the long-term respiratory effects of occupational exposure to capsaicin and they found no significant difference in terms of pulmonary function indexes between exposed workers and healthy controls. Nevertheless, it was reported that occupational exposure to red pepper resulted in a significant increase of complaints of chronic cough [5,7,8].

Based on our two cases, we raise the possibility that inhalation of capsaicin can induce new asthma or exacerbate pre-existent asthma. If this is so, then the possible underlying mechanism (or mechanisms) of its action is still unclear [9]. It is known that capsaicin stimulates unmyelinated slow C fibers of the sensory nervous system [10,11] and acts at a receptor that is either tightly coupled to, or indeed is, a relatively non-selective cation channel. Binding of capsaicin to this receptor allows both sodium and calcium (and possibly potassium) ions to flow down their concentration gradients, causing initial depolarization and neurotransmitter release, including the calcitonin gene-related peptide (CGRP) and tachykinins [11,12]. CGRP produces vasodilatation with mucosal oedema and cellular infiltration [13], whereas the tachykinins, especially substance P, neurokinin A and neurokinin B, induce mucus hypersecretion [14], leucocyte chemotaxis and bronchoconstriction [9]. Prolonged exposure to capsaicin produces subsequent desensitization or neuroinhibition. The latter may lead to loss of responsiveness to all stimuli and is probably associated with the neurotoxic effect of this agent [11], resulting in neurogenic inflammation. The mediators of neurogenic inflammation trigger mast cell degranulation and mast cell mediators stimulate peripheral nerves. This "bidirectional regulatory circuit" therefore entertains airway inflammation [15].

3. Conclusion

Recurrent exposure to red chilli peppers, which are natural sources of capsaicin, may induce new asthma or aggravate pre-existing asthma. The pathogenesis of capsaicin-induced asthma has not yet been investigated but may be similar to that induced

by other airway irritants. We suggest that capsaicin inhalation might be used as a model to investigate the mechanism by which inhaled environmental chemicals provoke a disorder in the regulation of neurogenic inflammation, leading to asthma or asthma-like disorders.

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