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Sodium Salicylate Sensitivity in an Asthmatic Patient with Aspirin Sensitivity

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Non-acetylated salicylates have been recommended for use as alternatives to nonsteroidal anti-inflammatory drugs(NSAIDs) in aspirin and/or tartrazine-sensitive patients. We experienced a case of an aspirin-sensitive asthmatic patient who developed a broncho-obstructive reaction after taking 100 mg of sodium salicylate. The result of this study suggests that sodium salicylate may cross-react with aspirin in aspirin-and tartrazine-sensitive patients.

Key Words : *Aspirin-sensitive asthma sodium salicylate*

INTRODUCTION

Aspirin(ASA)-sensitive asthma is an acquired disease characterized by eosinophilic infiltration of the respiratory tract and progressive nasal and bronchopulmonary dysfunction(Mathison and Stevenson, 1983). The explanation for ASA-induced asthma has been postulated as being caused by shunting of arachidonic acid from the generation of prostaglandins to the biosynthesis of leukotrienes with their attendant effects on the airway(Vane, 1975 ; Szczeklik et al., 1975). Drugs, such as non-steroidal anti-inflammatory drugs(NSAIDs), which also inhibit cyclo-oxygenase, are known to regularly cross-react with ASA(Szczeklik et al., 1977 ; Stevenson, 1984). It has generally been accepted that non-acetylated salicylates such as sodium salicylate, salsalate, and choline magnesium trisalicylate are tolerated by ASA - sensitive patients(Stevenson, 1984 ; Stevenson and Mathison, 1985). We describe a patient with asthma and nasal polyp who developed bronchospastic reaction after adm-inistration of sodium salicylate, as well as aspirin and tartrazine.

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CASE REPORT

Our patient was a 52-year old woman who had suffered from asthma for 4 months. Four months prior to admission, her left forearm was injured by a fall. After taking some analgesics for pain, she began to feel asthmatic symptoms. Her asthma continued to be symptomatic despite treatment with a bronchodilator. The patient was first seen by us in March 1990, at which time she was found on physical examination to have nasal polyp on the right side and bilateral inspratory and expiratory wheezing. Aspirin-sensitive asthma was suspected on the basis of her asthma, nasal polyp, and a history that suggested aspirin sensitivity.

Laboratory studies included white blood cell count of 6200 per mm3 with 7% eosinophils. The total IgE level by PRIST was 241 IU per ml. Skin prick test exhibited all negative

responses except histamine. A pulmonary function test revealed a maximal mid-expiratory flow rate(MMEF) of 43% predicted, along with a forced expiratory volume in one second(FEV1)/functional vital capacity (FVC) of 73% predicted, consistent with a mild obstructive pattern. The methacholine bronchial challenge test showed a more than 20% decrease in FEVI after inhalation of 0.62 mg/ml of methacholine(PC20 : 0.55 mg/ml). A chest X-ray was normal. A Paranasal sinus view revealed moderate thickening of the mucosal lines in both maxillary sinuses, suggesting sinusitis.

METHODS

Bronchodilators and steroids, administered before the study to keep the disease stable, were continued during the challenges. The patient underwent single-blind oral challenges with tartrazine, sodium salicylate, and asprin over 7 days according to the methods described in the previous studies(Oh et al., 1988 ; Hong et al., 1989). The broncho-obstructive response was assessed by use of an autospirometer(Jaeger, West Germany). A decline in the FEV1 value of 20% or greater as compared with the baseline was considered to be a positive reaction. Progressively increasing doses of each agent used are shown in Table 1. As a placebo, lactose 1.0 gm was administered at the beginning of the daily test session. Pulmonary function testing was repeated at 30-minute intervals for 2 hours following the ingestion of the test dose. If no significant change in the FEV1 or MMEF occurred in 2 horus, the next larger dose was given. If the patient showed significant bronchoconstriction, the test

Table 1. Agents and Doses for oral provocation test.

Agent	Dosage
Acetyl-Salicylate	1, 3, 10, 30, 50mg
Tartrazine	10mg
Sodium Salicylate	1, 10, 100, 200, 500, 1000mg

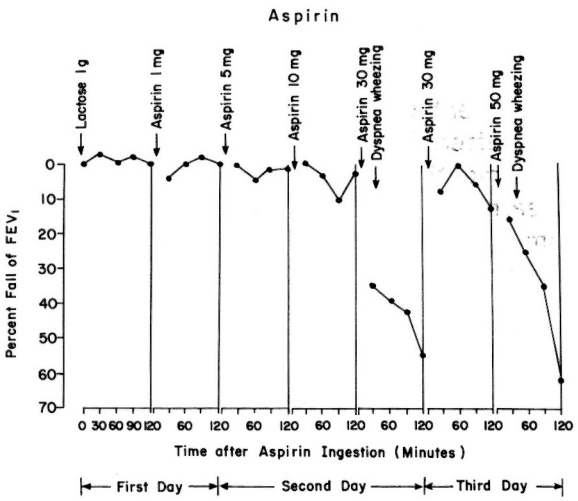

Fig. 1. Result of oral aspirin provocation test. On the second day, severe dyspnea developed after 30mg of aspirin ingestion. On the third day, there was no bronchoconstriction after 30mg of aspirin. Severe dyspnea was induced by 50mg of aspirin.

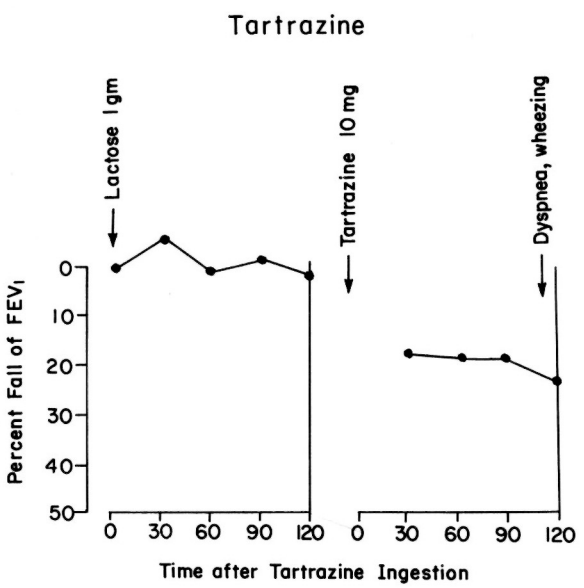

Fig. 2. Result of oral tartrazine provocation test Dyspnea developed after 10mg of tartrazine ingestion.

was terminated for that day.

RESULTS

Acetyl Salicylate Provocation Test: The patient started to take 3 mg of ASA as shown in Fig. 1. After the ingestion of 30 mg of ASA, she complained of dyspnea, and 36% of FEV1 was decreased on the pulmonary function test in 30 minutes. On the next day, there was on significant broncho-constriction with 30 mg of ASA. After taking 50 mg of ASA, severe dyspnea and wheezing were noted in 30 minutes. We gave up ASA desensitization.

Tartrazine Provocation Test: The patient was given 50 mg of tartrazine orally. Cough and dyspnea were developed in 30 minutes and 21% decrease in FEV1 was noted as shown in Fig. 2.

Sodium Salicylate Provocation Test: There was no changes in FEV1 after taking lactose, 1mg and 10mg of sodium salicylate, When the patient received 100mg of sodium salicylate orally, severe dyspnea and biphasic wheezing was noted in 60 minutes and a 26% decrease in FEV1 was noted. On next day, there was no significant broncho-constriction with taking 100mg of sodium salicylate. On the same day, there was no bronchoconstriction after taking 200mg, 500 mg, and 1.0 g of sodium salicylate.

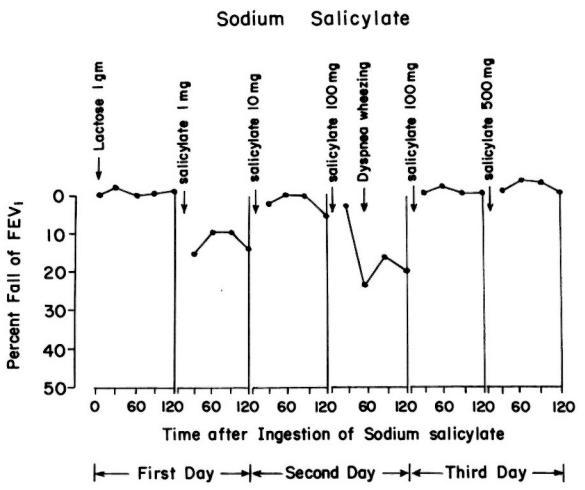

Fig. 3. Results of oral sodium salicylate provocation test On the second day, dyspnea developed after 100mg sodium salicylate ingestion. On next day, there was no more bronchoconstriction with 100mg and 500mg of sodium salicylate.

DISCUSSION

The prevalence of ASA sensitivity has been reported in 1.4 percent of chronic rhinitis patients(Settipane et al., 1974), 14 to 22 percent of persons with nasal polyps(Settipane, 1974; Slepian, 1985), In Korea, Hong et al. (1989) reported that 13(36.1%) subjects among 36 asthmatics showed a positive response to the oral ASA provocation test. The positive rate on oral ASA provocation test was higher in patients with a history of hypersensitivity to aspirin or NSAIDs than in those without history. Four Subjects(11.1%) among them developed asthmatic attacks with tartrazine.

Concerning the mechanism of aspirin hypersensitivity, there are seve al hypotheses. In some patients, the clinical symptoms are of an anaphylactic type and suggest an allergic pathogenesis. Acetylated proteins(Farr, 1970) or aspirin anhydride impurities(De Weck, 1971) have been proposed as possible antigens. In the early 1980s, it became apparent that arachidonic acid could be diverted from the cyclooxygenase pathway to the 5-lipoxygenase pathway, if the former enzyme was inhibited. The leukotriene(LK) products would provide potent mediation of neutrophil influx into the tissue via the action of LT B4 and also provide potent stimulation for broncho-constriction, increased mucosal permeability with edema formation, and mucus secretion by the activation of LT C4, LT D4, and LT E4(Stevenson, 1987). Besides, several groups (Vargaftig et al., 1980; Kauer et al., 1981; Morley et al.,1984) have demonstrated a broncho-constricting substance in the supernatants of activated platelets, It has been speculated that a defect in their functional response to cycooxygenase-inhibiting durgs accounts for the release of bronchoconstrictors that produce ASA-induced respiratory reactions. Recently, Szczeklik (1988) suggested that aspirin-induced

asthma could result from chronic viral infection. Further studies are needed to clarify the mechanism of ASA-induced asthma.

Cross-reactivity between aspirin and tartrazine in aspirin-sensitive patients has also been described(Juhlin et al., 1972 ; Settpane, 1983 ; Stevenson and Simon, 1988). Since it is known that non-acetylated salicylate does not cross-react with ASA at all or does not cross-react in the usual therapeutic dosages, the use of non-acetylated salicylates has been recommended for therapy in patients who are sensitive to aspirin and/or tartrazine(Stevenson and Simon, 1988). Recently, Stevenson et al.(1988) noted that salsalate occasionally could cross-react with ASA in susceptible patients. Shudwin et al.(1986) reports one case of aspirin-sensitive asthma who showed a urticarial and bronchospastic reaction after choline magnesium trisalicylate and salicylsalicylic acid. The patient described here developed bronchospastic reaction on oral challenge with sodium salicylate. On next day, there was no bronchoconstriction with same dose(100㎎) of sodium salicylate, which was caused by desensitization, Since there was no more bronchoconstriction with 1g of sodium salicylate per day, it was considered to be a desensitized state. Another 5 aspirin-sensitive asthmatic patients in our laboratory showed no bronchoconstrictive response with the ingestion of sodium salicylate.

The mechanism of sensitivity to sodium salicylate in ASA-sensitive patients is unknown. The experience with our patient emphasizes that caution should be used in the routine substitution of non-acetylated salicylate for aspirin-sensitive patients.

REFERENCES

Chudwin DS, Strub M, Golden HE, Frey CDO, Richmond GW, Luskin T : *Sensitivity to non-acetylated salicylates in a patient with asthma, nasal polyps and rheumatoid arthritis. Ann Allergy 57 : 133—4, 1986.*

De Weck AL : *Immunological effects of aspirin anhydride, a contaminant of commercial acetylsalicylic acid preparations. Int Arch allergy Appl Immunol 41 : 393—5, 1971.*

Farr RS : *The need to reevaluate acetylsalicylic acid(aspriin). J Allergy 45 : 321—5, 1970.*

Hong SP, Park HS, Lee MK, Hong CS : *Oral provocation tests with aspirin and food additives in asthmatic patients. Yonsei Med J 30:339—345, 1989*

Juhlin L, Michaelsson G, Zettestrom O : *Urticaria and asthma induced by food-and - drug additives in patient with aspirin hypersensitivity. J Allergy Clin Immunol 50 : 92—8, 1972.*

Knauer KA, Lichtenstein LM, Adkinson .NF, Fish JE : *Platelet activation during antigen-induced airway reactions in asthmatic subjects. N Eng J Med 304 : 1404—6, 1981.*

Mathison DA, Stevenson DD : *Aspirin sensitivity in rhinosinusitis and asthma. J Immunol Allergy Prac 5 : 17—23, 1983.*

Morley J, Sanjar S. Page CP : *The platelet in asthma. Lancet 2 : 1142—4, 1984.*

Oh SH, Part HS, Lee MK, Hong CS : *Clinical experiences of the aspirin challenge test and desensitization in asthmatic patient. Kor J Intern Med 35 : 105—11, 1988.*

Settipane GA : *Aspirin and allergic diseases : a review. Am J Med 74 : 102—9, 1983.*

Settipane GA, Chafee FH, Klein DE : *Aspirin intolerance Ⅱ. A prospective study in an atopic and normal population. J Allergy Clin Immunol 53 : 200—4, 1974.*

Slepian IK, Mathews KP, Mc Lean JA : *Aspirin-sensitive asthma. Chest 87 : 386—91, 1985.*

Stevenson DD : *Diagnosis, prevention and treatment of adverse reactions to aspirin and non-steroidal anti-inflammatory drugs. J Allergy Clin Immunol 74 : 617—22, 1984.*

Stevenson DD and Mathison DA : *Aspirin sensitivity in asthmatics : when may this drug be safe, Postgrad Med 78 : 111, 1985.*

Stevenson DD : *Proposed mechanisms of aspirin sensitivity reaction. J Allergy Clin Immunol 80 : 788—90, 1987.*

Stevenson DD, Schrank PJ, Hongham AJ, Goldlust MB, Wilson RR : *Salsalate cross sensitivity in aspirin-sensitivie asthmatics. J Allergy Clin Immunol 81 : 181, 1988 (abstract).*

Stevenson DD, Simon RA : *Aspirin sensi-*

tivity : Respiratory and cutaneous manifestations. Allergy, Third Ed, Mosby Co., St. Louis, p.1537—54, 1988.

Szczeklik A : *Aspirin-induced asthma as a viral disease. Clin Allergy 18 : 15—20, 1988.*

Szczeklik A, Gryglewski RJ, Czerniawska-Mysik G : *Relationship of prostaglandin biosynthesis by analgesics to asthma attacks in aspirin-sensitive patients. Br Med J 1 : 67—9, 1975.*

Szczeklik A, Gryglewski RJ, Czerniawska-Mysik G : *Clinical patterns of hypersensitivity to non-steroidal anti-inflammatory drugs and their pathogenesis. J Allergy Clin Immunol 60 :276 34, 1977*

Vane JR : *Inhibition of prostaglandin syn-thesis as a mechanism of action of aspirin-like drugs. Nature 231 : 232—5, 1971.*

Vargaftig BB, Lefort J, Chignard M, Benveniste J : *Platelet-activating factor induces a platelet-dependent broncho-constrictor unrelated to the formation of prostaglandin derivatives. Eur J Pharmacol 65 : 185—9 1980.*