

Asthma relieved by aspirin and by other cyclo-oxygenase inhibitors

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Some patients with bronchial asthma report that aspirin decreases their shortness of breath. We describe an asthmatic patient in whom airways obstruction could be reversed effectively by aspirin and by several other cyclo-oxygenase inhibitors, that is, analgesics that suppress the generation of prostaglandins (PG), thromboxane A₂ (TXA₂), and prostacyclin (PGI₂) in the tissues.

Case report

A 62-year-old man had been well until 10 years previously when he experienced a first attack of dry cough. Coughing continued and four years before admission, after a flu-like illness, attacks of breathlessness and wheezing began to occur. Though treated with bronchodilators and prednisone he noticed that aspirin relieved his symptoms and began to take it regularly. The frequency and severity of attacks of cough and dyspnoea diminished, and the steroid dose could be reduced by half. Diabetes and extrapyramidal tremor, diagnosed a few years before admission, were controlled well by diet and trihexyphenidyl respectively. Two years before admission, prednisone was replaced by triamcinolone and petechiae over the forearms appeared.

The patient was a dyspnoeic man with petechiae over both forearms, vitiligo on the forehead and abdomen, and signs of pulmonary overinflation. Routine laboratory test results were within normal

limits. Skin tests with common aeroallergens gave negative results. His airways obstruction was partially reversed by isoprenaline. The tourniquet test result was positive. Bleeding, clotting, prothrombin, partial thromboplastin, and euglobulin lysis times, as well as platelet count, fibrinogen, and fibrin degradation product levels, were all within the normal range. Results of the following platelet function studies, performed as described previously (Szczeklik *et al*, 1978) were normal: aggregation thresholds both to arachidonic acid and ADP, generation of thromboxane A₂ by platelet-rich plasma, and inhibition of aggregation by aspirin and nictindole.

Six non-steroidal anti-inflammatory drugs and placebo were taken in gelatin capsules, and clinical symptoms and peak expiratory flow rate (PFR) were checked every 60 min over the following eight hours. Only one drug or placebo was given on any one day. The initial PFR values during the tests were in the range of 30-50% of predicted. Aspirin (600 mg), indomethacin (40 mg), fenoprofen (200 mg), and mefenamic acid (75 mg) all increased PFR values by 40-75%. These effects occurred about one hour after ingestion of the drug, lasted several hours, and were accompanied by a considerable relief of dyspnoea and decrease of wheezes heard over the lungs. Salicylamide (1.0 g), benzydamine (1.0 g), and placebo had no effect on either PFR or clinical symptoms. The detailed studies of the influence of aspirin on lung

Table Effect of aspirin on lung function. Measurements were taken initially and 90 min after placebo. Then 1.2 g aspirin was taken and pulmonary function tests were recorded 90 and 135 minutes later

| Pulmonary tests | 1000 (Initial values) | 1130 (After placebo) | 1300 (After 1.2 g aspirin) | 1345 | Predicted values |
|------------------------------|--------------------------|-------------------------|-------------------------------|------|------------------|
| FEV ₁ /FVC% | 65 | 60 | 70 | 76 | 70 |
| Raw (hPa/l s ⁻¹) | 15.4 | 14.4 | 2.9 | 2.8 | 1.8 |
| SRaw (hPa · s) | 107.6 | 92.2 | 14.0 | 13.0 | 7.5 |
| PFR (l/s) | 3.0 | 2.72 | 4.55 | 5.3 | 9.6 |
| MEF ₅₀ (l/s) | 0.8 | 0.8 | 2.3 | 1.9 | 4.4 |
| MEF ₂₅ (l/s) | 0.35 | 0.4 | 0.85 | 0.6 | 2.1 |

FEV₁/FVC% = Forced expiratory volume 1 second in per centage of forced vital capacity; Raw = Airway resistance; SRaw = Specific airway resistance; PFR = Peak expiratory flow rate; MEF₅₀ = Maximal expiratory flow at 50% of vital capacity; MEF₂₅ = Maximal expiratory flow at 25% of vital capacity; 0.98 × hPa = cm H₂O.

function are presented in the table. The patient was restudied four months later, and the results with analgesics were very much the same.

Comment

Airways obstruction was strikingly relieved by aspirin in the patient studied. Similar beneficial effects were produced by three other cyclo-oxygenase inhibitors, that is, by indomethacin, mefenamate, and fenoprofen, but not by two remaining analgesics—salicylamide and benzydamine—which do not inhibit PG biosynthesis (Vane, 1976; Szczeklik *et al.*, 1977). It was, therefore, logical to assume that the pharmacological removal of a product of arachidonic acid (AA) cyclo-oxygenation from his respiratory tract helped our patient to overcome the airways obstruction. Perhaps this product was a bronchoconstrictor $\text{PGF}_{2\alpha}$, TXA_2 , or other as yet unknown metabolite. Whatever the metabolite was, it could not have been a physiological one, since we have found that bronchodilator PGI_2 and PGE_2 are two major products of AA transformation in the lungs (Gryglewski *et al.*, 1978).

In our patient the suspected abnormality in arachidonate metabolism was restricted to the respiratory system. Detailed platelet function studies, particularly those related to arachidonic pathway, failed to show any differences from the normal. The transient petechiae were most likely due to increased vascular fragility secondary to triamcinolone administration.

The number of asthmatic patients who might benefit from aspirin is not known. Trial of aspirin treatment might seem warranted in asthma, since it could allow the steroid dose to be reduced, as in our case. Great care, however, would be necessary at the beginning of such treatment, and the

initial dose of aspirin should not exceed 20–40 mg, as the same cyclo-oxygenase inhibitors, which proved to be so efficient in relieving bronchoconstriction in our patient, may produce bronchoconstriction in other asthmatics suffering from so-called aspirin-induced asthma (Szczeklik *et al.*, 1975; 1977). Thus two opposite reactions can be caused in asthmatics by the same specific inhibitors. This indicates that different mediators, even derived from the same precursor, might play a different role in various types of asthma.

Discussion

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Corrections

- Warren, C P W *et al.* Mechanical properties of the lung in extrinsic allergic alveolitis. *Thorax*, 1978, **33**, 315–321.
The caption to figure 1 should show (a) four weeks and (b) one week.
- Battesti, V P *et al.* Chronic cor pulmonale in pulmonary sarcoidosis. *Thorax*, 1978, **33**, 76–84.
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