PAPERS AND SHORT REPORTS

Effect of aspirin on nasal resistance to airflow

A S JONES, J M LANCER, A A MOIR, J C STEVENS

Abstract

The effect of aspirin on nasal resistance to airflow was investigated by rhinomanometry in 25 healthy subjects before and after ingestion of aspirin or vitamin C in a double blind crossover trial.

Aspirin caused a significant increase in nasal resistance compared with vitamin C. The effect of aspirin may be due to its inhibition of the synthesis of prostaglandins.

Introduction

For many years it has been suspected that ingestion of aspirin can cause nasal obstruction in certain subjects. Long term ingestion of aspirin may be one of the causes of the nasal obstruction syndrome of vasomotor rhinitis.[1] Few patients with this syndrome have the classical symptoms of intolerance to aspirin, and in most cases nasal obstruction is the only side effect. The changes in nasal resistance to airflow induced by aspirin may be small, and until recently there was no accurate method of measuring nasal resistance. In recent years the measurement of nasal resistance by rhinomanometry has developed to such an extent that quantitative studies of factors that may alter this resistance can now be carried out. Nasal resistance varies in response to many physiological factors. Although the resistance of each individual nasal passage varies, the total nasal resistance is relatively constant.[2,3] We studied 25 subjects, thereby reducing the overall variation of nasal resistance to airflow due to physiological factors.

Subjects and methods

We studied 25 healthy subjects (14 women and 11 men) aged between 22 and 33. None of the patients had a history of intolerance to aspirin or noticed nasal obstruction when they took aspirin. A double blind crossover trial was conducted with soluble aspirin as the active drug and soluble vitamin C as the placebo. An alternate technique of allocation dictated which drug was given first. A Mercury Electronics NR1 rhinomanometer was used to measure the nasal resistance to airflow in all subjects before and 45 minutes after ingestion of the drug. The method of active anterior rhinomanometry was used as recommended by a report on standardisation of rhinomanometry.[4] This entailed measuring simultaneously the airflow through one nasal cavity and the pressure gradient across this nasal cavity at each breath. Nasal resistance was derived from the mean of 15 readings. The calibration and use of the rhinomanometer have been described previously.[5,6]

Physiological factors that affect nasal resistance to airflow include stress, exercise, and changes in temperature, illumination, and the concentration of inspired oxygen and carbon dioxide.[7] A strict experimental protocol was therefore observed. The method of rhinomanometry and the experiment was fully explained to each subject, who was then seated in a quiet room for 30 minutes before the experiment started. Factors such as the temperature of the room, humidity, illumination, and the level of noise were kept constant throughout the experiment. For the duration of the study the temperature of the room was kept at 18 (± 2)°C and the relative humidity at 50 (± 5)%. After nasal resistance had been measured each subject was given orally either 900 mg soluble aspirin or 1000 mg soluble vitamin C dissolved in 200 ml water. Neither the investigator nor the subject was told which drug had been administered. After 45 minutes nasal resistance was measured again. Two days later the experiment was repeated using the other drug.

Statistical analysis was carried out using the t test. The two sample t test was used to identify significant changes in the nasal resistance of individual subjects after ingestion of each drug. When comparing the changes in resistance in the 25 subjects as a whole the matched pairs two sided t test was used (a parametric test of significance was used because the resistance values approximated to a normal distribution).

Results

Figures 1 and 2 show the effects of aspirin and vitamin C on nasal resistance to airflow. A significant ($p < 0.05$) increase in nasal resistance was seen after ingestion of aspirin, but there was no significant change after ingestion of vitamin C. The change in resistance after aspirin was significantly greater ($p < 0.02$) than the change after vitamin C (fig 3). As 15 measurements of nasal resistance were taken it was possible to determine if there had been any significant change in resistance within each subject. Values of nasal resistance before and after the drug was taken were compared (table). Aspirin caused an increase in nasal resistance in most subjects (17), whereas vitamin C produced no

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such effect. The observation that significant changes occurred in subjects who had taken the placebo was compatible with the usual variation of normal nasal resistance to airflow with time.[3] None of the subjects felt any subjective change in nasal patency after taking either aspirin or vitamin C.

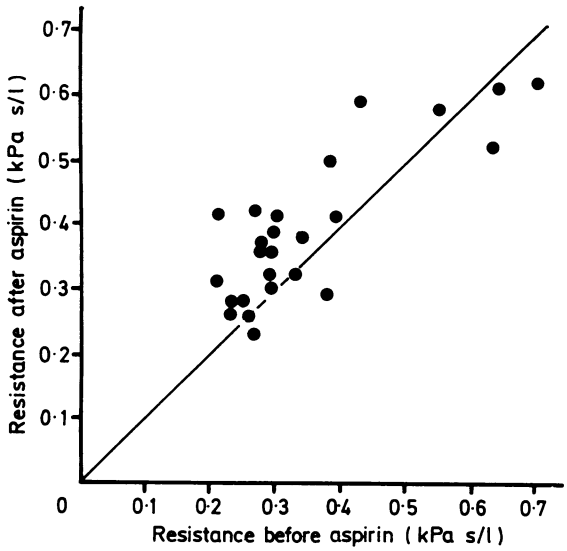

FIG 1—Effect of aspirin on nasal resistance to airflow in 25 subjects.
Conversion: SI to traditional units—Resistance: 1 kPa s/l= 10·3 cm H_2O s/l.

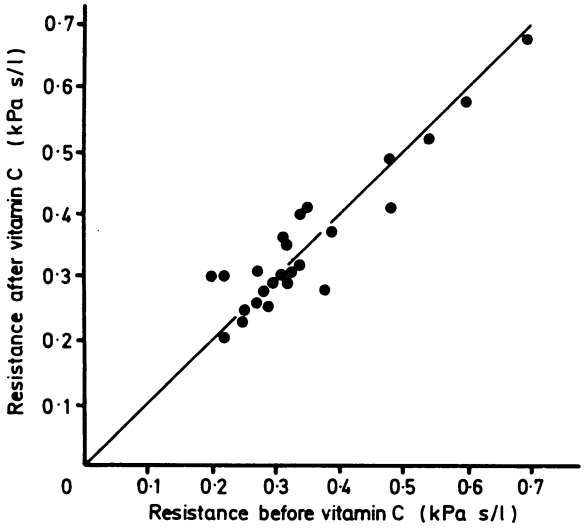

FIG 2—Effect of vitamin C (placebo) on nasal resistance to airflow in 25 subjects.
Conversion: SI to traditional units—Resistance: 1 kPa s/l= 10·3 cm H_2O s/l.

Discussion

Our results showed that aspirin caused an increase in nasal resistance in 17 of the 25 subjects studied. This effect may have been due to the action of aspirin on the metabolism of prostaglandins. Aspirin is a potent inhibitor of synthesis of prostaglandins by virtue of its effect on cyclo-oxygenase.[8] When aspirin is given to subjects who are sensitive to aspirin bronchoconstriction occurs, and this has been related to a reduction in the plasma concentration of prostaglandin $F_{2\alpha}$.[9] In these patients the plasma prostaglandin $F_{2\alpha}$ concentration is usually raised compared with that in the normal population.[10]

Porcine nasal mucosa can synthesise the E series prostaglandins[11] and contains enzymes that can inactivate these compounds.[12] Prostaglandins E_2 and D_2 cause a reduction in nasal resistance when injected into the nasal arterial blood supply of the pig,[13] and prostaglandins E_1, E_2, and $F_{1\alpha}$ cause a similar reduction when administered topically in man.[14] Thus considerable circumstantial evidence suggests that prostaglandins are

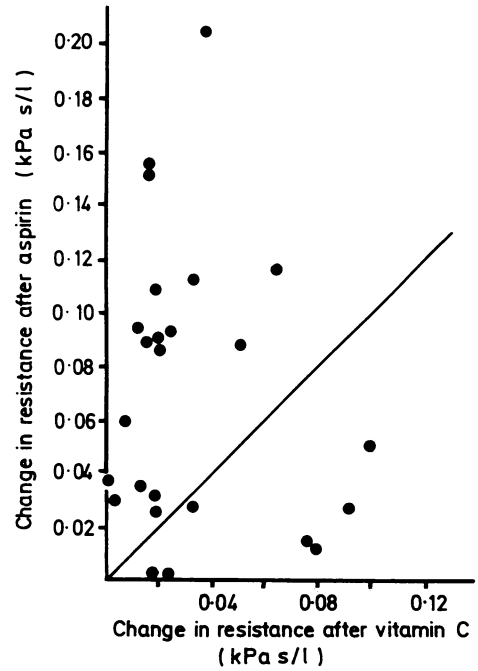

FIG 3—Change in nasal resistance to airflow after aspirin compared with change in resistance after vitamin C in 25 subjects.
Conversion: SI to traditional units—Resistance: 1 kPa s/l= 10·3 cm H_2O s/l.

Changes in nasal resistance to airflow in 25 healthy subjects taking aspirin and vitamin C

Change in nasal resistance ($p < 0.05$)	Drug	
	Aspirin	Vitamin C
Increase	17	8
Decrease	4	10
No significant change	4	7

important in regulating resistance in the airways. The ability of aspirin, a potent inhibitor of prostaglandins, to increase nasal resistance in normal subjects suggests that protaglandins are important in maintaining nasal patency.

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Comparison of the antiemetics metoclopramide and promethazine in labour

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Abstract

A double blind trial was conducted in 477 mothers in labour to compare the antiemetics metoclopramide 10 mg and promethazine 25 mg and placebo when added to the first dose of pethidine. Metoclopramide and promethazine were equally effective, and both better than placebo, in reducing the incidence of nausea and vomiting after the administration of pethidine. Seventy seven per cent of mothers were drowsy, and 8% slept in the hour after the pethidine injection, with no difference between the groups. The sedative effect was more persistent in the promethazine group, 66% of whom were still drowsy after delivery. One third of the mothers in each group needed further analgesia, with 77% of these ultimately requesting an epidural. The reduction in pain half an hour and one hour after pethidine, assessed by a visual analogue scale, were, respectively, 22% and 22% for placebo; 26% and 23% for metoclopramide; 13% and 9% for promethazine.

Analgesia after metoclopramide was significantly better than that after promethazine in terms of pain score, duration of first injection, and need for Entonox. Metoclopramide is therefore to be preferred to promethazine as an antiemetic in labour.

Introduction

Mothers being delivered at St Thomas's Hospital are offered a choice of analgesia, and although over 40% receive an epidural, 40% initially choose pethidine. In centres where epidurals are not available round the clock pethidine is used more extensively, often combined with a phenothiazine derivative to counteract emesis. A combination of promethazine and pethidine has been popular for many years as a premedicant[1] and in labour.[2,3] Trials in other types of patients, however, have shown promethazine to be a profound and long acting sedative[4,5] with an antianalgesic effect.[6] Metoclopramide has been used as a postoperative antiemetic since the 1960s.[7] Many clinical trials in labour have investigated its effects on gastric emptying,[8-10] but only one formally studied its antiemetic effect in comparison with perphenazine, with no investigation of its antinauseant properties.[11] We examined the incidence of nausea and vomiting, sedation, and analgesia after metoclopramide, promethazine, and placebo given intramuscularly with the first dose of pethidine in a double blind trial in labour.

Methods

Patients requiring pethidine in labour, who gave their verbal consent, were included in the trial. Those with severe fetal abnormalities or intrauterine death diagnosed before delivery were excluded. With the first dose of pethidine (100-150 mg) each patient was given a randomly coded ampoule containing either metoclopramide 10 mg, promethazine 25 mg, or saline (2 ml) intramuscularly. This was termed the first injection. Any patient who needed further analgesia was given either pethidine alone or an epidural, as requested (the second injection). The occurrence of nausea, vomiting, and drowsiness or sleep was recorded by the midwife in the hour preceding the injection and in each subsequent hour until delivery or the next injection. Pain relief was assessed using the visual analogue pain score before and half an hour and one hour after the injection. The need for nitrous oxide plus oxygen (Entonox), oxytocin, or a further injection of antiemetic was also recorded.

A questionnaire relating to analgesia, sedation, and emesis was presented to the patient shortly after delivery.

The results were examined using χ^2 test for numerical data; the standard error of each proportion was calculated from the formula:

$$\mathrm{SE}\left(\frac{r}{n}\right)=\sqrt{\frac{1}{n}\left[\frac{r}{n}\times\left(1-\frac{r}{n}\right)\right]}$$

the significance of the difference between proportions was calculated using the formula:

$$\left(\frac{r_1}{n_1}-\frac{r_2}{n_2}\right)\Big/\sqrt{\frac{r_1+r_2}{n_1+n_2}\left(1-\frac{r_1+r_2}{n_1+n_2}\right)\left(\frac{1}{n_1}+\frac{1}{n_2}\right)}$$

where r = number of positive responders. Student's t test was used to compare pain score.

Results

A total of 600 coded ampoules were used, but because of the mistaken inclusion of mothers who had already received antiemetics, delivery within an hour of the injection, or shortcomings in data collection, only 477 patients took part in the trial (metoclopramide 157, placebo 161, promethazine 159).

There was no significant difference between the groups in age,

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