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Nasal symptoms in pseudoallergic reactions

G. Loewe and J. Slapke, Berlin, German Democratic Republic

SUMMARY

In a retrospective investigation 469 pseudoallergic reactions (analgesics asthma reactions) that emerged in 197 patients with analgesics intolerance have been analysed. Besides mostly severe asthma-attacks 26.5% of the reactions were sneeze-attacks and in 37.5% nasal secretion was found. 86% of the reactions emerged within a maximum of 45 minutes after oral application of the analgesic. About a third of the analgesics-asthma reactions occurs together with reactions of the nose mucous membrane. So the connection of analgesics-asthma and chronic hyperplastical changes of the mucous membrane of the upper respiratory tract is also reflected in the course of the pseudoallergic intolerance reaction.

INTRODUCTION

Pseudoallergic reactions have increasingly been studied in recent years by various teams of research workers. This is mainly the result of a better understanding of the pathophysiology of drug side effects imitating the clinical picture of an allergic reaction although these side effects cannot be attributed to any of the established immunologic mechanisms. Pseudoallergic reactions may be caused by analgesics, antibiotics, anaesthetics, dextran, globulines and other substances. Clinical manifestations are various; parts that may be affected include the mucosa of the respiratory tract, the skin, the kidney, the thyroid, the lungs, and other organs; haematologic syndroms are described as well. We have come across pseudoallergic reactions occurring upon administration of analgesics for some years now. Since acetylsalicylic acid is most frequently the medicament which induces such a reaction and asthma is the first apparent symptom, this intolerance reaction has been called "aspirin-induced asthma" since the beginning of our century. However, we prefer to use the more comprehensive term "analgesics intolerance" because not only other analgesics can act as noxae inducing such a reaction but also because asthma is not the only symptom that may occur. We have previously reported about the incidence of this disease and about the

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coincidence of intolerance to analgesics, affections of the paranasal sinuses and chronic rhinitis (Loewe et al., 1984; Slapke et al., 1982). Two-thirds of the analgesics-induced asthma patients we examined suffered from such an affection of the upper respiratory tract. We performed this study to investigate in which way and how often the mucosa of the upper respiratory tracts is involved in acute intolerance reactions.

PATIENTS AND METHODS

In a retrospective case control study of 197 asthmatic patients (57 male and 140 female) with unambiguous information as to the presence of analgesics intolerance, 469 pseudoallergic reactions were found following the administration of analgesics. The devision in age of the patients is shown in Table 1.
We maintained a record of the symptoms, the analgesics ingredients, the interval between the administration as well as the time at which the reactions became apparent for the first time and the duration and degree of complaints.

Table 1. Age of asthmatic patients with analgesics intolerance (n = 197).

age group	%
< 30 years	13.0
31–45 years	54.2
> 45 years	32.8

RESULTS

In our patients analgesics containing pyrazolone were found to be the main agent inducing pseudoallergic intolerance reactions, whereas acetylsalicylic acid preparations were of less significance (Table 2).
This observation also reflects the use of analgesics in the German Democratic

Table 2. Pseudoallergic reactions to analgesics in 197 patients.

causative drugs	incidence in %
noramidopyrininemethanesulfonate-sodium	42
phenacetin/acetylsalicylic acid*	37
amidopyrine	35
amidopyrine/phenacone*	20
phenacone/phenacetin*	15

* compound preparation.

Table 3. Pseudoallergic reactions after receiving analgesics (n = 469 reactions in 197 patients).

symptom	incidence in %
asthma	100
rhinorrhoea	37.5
sneeze-attacks	26.5
angioedema	31.4
urticaria	27.3

Republic: in 1980 consumption of analgesics containing pyrazolone was about 60% and of drugs containing acetylsalicylic acid about 30% of the total consumption.

Apart from the attack of asthma nasal symptoms such as sneezing and secretion occurred in more than one-third of the cases. The skin was involved just as frequently (Table 3).

Of the 469 reactions 86% took place within 45 minutes after the administration of analgesics; the complaints persisted for several hours in 84% (Tables 4 and 5). The seriousness of 53% of the intolerance reactions was such that medical treatment was necessary and 59 patients even had to be hospitalized.

Table 4. Interval between analgesics-application and reaction of intolerance (n = 469 reactions in 197 patients).

interval	%
1–15 minutes	41
15–45 minutes	45
> 45 minutes	14

Table 5. Duration of complaints (n = 469 reactions in 197 patients).

duration	%
< 1 hour	13.2
1–3 hours	44.6
3–6 hours	24.3
> 6 hours	15.1
unknown	2.8

DISCUSSION

The striking connection between analgesics-induced asthma and affections of the upper respiratory tract in the form of chronic hyperplastic mucosal changes is a well-known fact (Delaney, 1972; Moloney et al., 1977) and only a few authors deny it (Speer et al., 1981). We too were able to confirm this connection in a large number of patients (Loewe et al., 1985). The results in this study also show this connection in case of pseudoallergic intolerance reactions. These reactions are characterized as follows:

- reaction starts with a short delay (less than 45 minutes on average);
- serious asthmatic dyspnoea;
- reactions often in connection with rhinorrhoea, sneezing, Quincke's oedema, urticaria;
- duration up to six hours and more;
- treatment required in more than half of the cases.

The involvement of the mucosa of the upper respiratory tract in one third of the intolerance reactions, as determined anamnestically, was also confirmed by an oral test in a small number of patients who were exposed to analgesics.

In conformity with references in the literature (Samter et al., 1968) we were able to prove an above-average occurrence of reactions of intolerance to alcoholic beverages in our patients as well (in about one-third of the cases). A striking fact is

the high percentage of alcohol-induced affections of the upper respiratory tract. One-fourth of our analgesics-sensitive patients were first affected after they had been given an analgesic. This, at least for part of the affections, queries the assumption that the clinical syndrome develops only on the basis of infectious ("intrinsic") bronchial asthma.

Apparently, there is a causal relationship between the intolerance to analgesics and both acute and chronic affections of the respiratory tract. This is suggested by the above connection which is based on clear statistical evidence. However, the pathologic evidence for this connection is still unclarified. If the mucosa of the respiratory tract is considered to be a functional whole, changes in the phospholipid metabolism could be of pathogenetic significance. The majority of analgesics inhibit the prostaglandin synthesis by blocking the cyclooxygenase pathway (Szczeklik et al., 1977) of arachidonic acid metabolism and consequently, cause a breakdown in the lipoxygenase route (Parker, 1979; Slapke et al., 1982, 1983). Lipoxygenase products e.g. hydroperoxy fatty acids and leukotrienes as potent mediators of inflammation, proliferation and bronchoconstriction (Parker, 1979; Slapke et al., 1984) seem to play a decisive role in the pathogenesis of analgesics intolerance.

ZUSAMMENFASSUNG

In einer retrospektiven anamnestischen Untersuchung wurden 469 pseudoallergischen Reaktionen nach Einnahme von Analgetika (Analgetika-Asthma-Reaktionen) analysiert, die bei 197 Patienten mit Analgetika-Intoleranz auftraten. Neben meist schweren Asthmaanfällen kam es in 26,5% zu Niesattacken und in 37,5% zu nasaler Sekretion. 86% dieser Reaktionen traten innerhalb von maximal 45 Minuten nach oraler Applikation des Analgetikums auf. Etwa ein Drittel der Analgetika-Asthma-Reaktionen verläuft also mit Beteiligung der Nasenschleimhaut. Damit spiegelt sich die Assoziation von Analgetika-Asthma und chronisch-hyperplastischen Veränderungen der Schleimhaut der oberen Luftwege auch im Ablauf dieser pseudoallergischen Intoleranzreaktion wider.

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Prof. Dr. G. Loewe
Krankenhaus Berlin
Prenzlauer Berg
HNO-Klinik
Fröbelstrasse 15
1055 Berlin
G.D.R.