Age at diagnosis of AIDS at this hospital to October 1987

Age (years)	No of patients
0-19	2
20-24	19
25-29	26
30-34	48
35-39	57
40-44	33
45-49	31
50-54	7
55-59	6
60-64	2
≥65	4

transbronchial biopsy did not show any pathogen. He was treated with co-trimoxazole and hydrocortisone. After 14 days of co-trimoxazole he had improved clinically and radiographically and was discharged receiving maintenance treatment.

Comment

Both these patients were positive for HIV antibody and had a clinical and radiological presentation suggestive of *P carinii* pneumonia that responded to treatment; thus the criteria for a diagnosis of AIDS were satisfied.[1] In case 2 the diagnosis was complicated by the previous amiodarone treatment, though pneumonitis induced by amiodarone is unusual at a daily dosage less than 400 mg.[2,3] Chest infections are common in the elderly. The increasing incidence of HIV infection and a reluctance of older homosexuals to admit to at risk behaviour may mean that elderly patients will die without AIDS being diagnosed. In the United States 10% of patients with AIDS are over 50, 2·5% over 60, and 0·4% over 70. The table shows the age distribution of our patients with AIDS up to October 1987. Six of 235 (2·5%) patients were over 60.

P carinii pneumonia should be considered in all patients with atypical chest infections, even when there are no apparent risk factors.

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Parkinsonism, tremor, and depression induced by cinnarizine and flunarizine

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Cinnarizine and flunarizine are piperazine derivatives with antihistamine properties and calcium channel blocking activity. Several recent reports have described extrapyramidal reactions and depression associated with their use.[1-3]

Methods and results

In Spain a system of spontaneous reporting of adverse drug reactions has been operating since 1983. Around 5000 reports have been received, of which 86 refer to cinnarizine as the suspected drug, 25 to flunarizine, and five to both drugs taken simultaneously. Of these 116 reports 87 described extrapyramidal symptoms or depression, or both: cinnarizine had been taken in 70 cases, flunarizine in 13, and both drugs in four.

Seventy patients developed tremor and parkinsonism while being treated with cinnarizine (see table). They were not taking other drugs likely to induce parkinsonism, except for three patients, one of whom was also taking sulpiride, one thiethylperazine and dimenhydrinate, and one thioridazine (he subsequently recovered when cinnarizine was withdrawn without stopping thioridazine). Eight additional patients (two men, six women) presented with parkinsonism and three men presented with tremor while being treated with flunarizine (5 mg/day in one patient and 10 mg/day in 10). Four other patients developed parkinsonism (two men) or tremor (one man, one woman) while treated simultaneously with both drugs.

Four patients (two men, two women, aged 24 to 67) presented with depression while taking flunarizine (three patients, one of them also with tremor) or cinnarizine (one patient, who also presented with parkinsonism). The daily dose of flunarizine was 10 mg and of cinnarizine 150 mg. The intervals between starting drug treatment and the appearance of the first symptoms ranged from two days (in this patient tremor was also noted) to 10 months. The four patients improved when treatment stopped; three of them improved during the first month, but no exact information was available about the fourth. None of these patients were taking any other drug which could have contributed to their depression.

Characteristics of 70 patients with parkinsonism or tremor induced by cinnarizine. Unless otherwise stated, results are numbers (and percentages) of patients

	Parkinsonism	Tremor
No of patients:	39	31
Women*	24	20
Men*	13	11
Median age (range) (years)	78 (53-90)	68 (38-85)
Dose (mg):		
<150	3 (8)	12 (39)
150	28 (72)	14 (45)
>150	6 (15)	5 (16)
Unknown	2 (5)	
Induction period:		
<1 month	7 (18)	6 (19)
1-6 months	6 (15)	6 (19)
6-12 months	6 (15)	10 (32)
1-3 years	10 (26)	5 (16)
>3 years	5 (13)	0
Unknown	5 (13)	4 (13)
Recovered after withdrawal of drug:		
Within 1st 3 months	13 (33)	17 (55)
In 3-6 months	9 (23)	0
In 6-18 months	2 (5)	1 (3)
Unknown	4 (10)	5 (16)
Not within 1st 3 months	4 (10)	6 (19)
Not in 3-6 months	1 (3)	0
Not in 6-12 months	1 (3)	0
Not in >1 year	1 (3)	0
Unknown	4 (10)	2 (7)

*The sex of two patients with parkinsonism was unknown.

Comment

In Spain cinnarizine is marketed in 10 pharmaceutical preparations, eight of which are fixed dose combinations with other drugs. The most common indications are cerebral and peripheral arterial insufficiency. The top selling preparations contain 75 mg per tablet, and the recommended dose is 75 mg twice a day. Approved indications for flunarizine are the same as for cinnarizine. In the United Kingdom cinnarizine is marketed as 15 mg tablets for vestibular disorders and motion sickness, with a maximum recommended dose of 30 mg three times a day.[4] In Spain 5-7% of the population over the age of 60 may be receiving long term cinnarizine.[5] The consumption of flunarizine is also high: in 1986, 1·2 million units were dispensed. Not surprisingly therefore a large number of cases of extrapyramidal symptoms and depression attributed to these drugs have been assembled by our national scheme.

As the table shows, parkinsonism can be induced even by daily doses of cinnarizine of less than 150 mg. Patients with tremor tended to be younger (Mann-Whitney U test, p=0·0043), however, and seemed to have taken lower cumulative doses than those with parkinsonism (Mann-Whitney U test, p=0·0417). Patients with flunarizine induced parkinsonism (median age 63) were younger than those affected by cinnarizine (median age 78) (Mann-Whitney U test, p=0·0059), and these differences were apparently not related to different indications for the use of each drug.

Cinnarizine and flunarizine are piperazine derivatives structurally related to some phenothiazines, and this may explain their extrapyramidal effects. Their calcium channel blocking activity may also contribute to this effect. We have started a case-control study with the aim of quantifying the risk of extrapyramidal disorders associated with these drugs.

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Dangerous oronasal obstruction in weak senile patients

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During routine surveillance in this 320 bed nursing centre patients are sometimes found in a dangerous condition of dyspnoea and cyanosis. We describe five cases in which this condition was caused by oronasal obstruction.

Case reports

Case 1—An 85 year old woman with severe Alzheimer's disease was emaciated, drank little, and remained bedridden; she was receiving no drugs. She was found in a dangerous dyspnoeic and cyanotic state; the nostrils were sucked in during inspiration but a certain degree of inspiration was audible. Attempts to open the tightly closed mouth met with little success and were repelled by the patient. There was a deviated nasal septum swelling of the mucosa. A disposable catheter (Charrière 12, 13 cm long) was inserted into the smaller nostril. Dyspnoea and cyanosis resolved within several minutes, at which time the patient opened her mouth spontaneously. She had neither teeth nor dentures. The nasal catheter was removed several hours later. There was no recurrence.

Case 2—A 76 year old woman with severe Alzheimer's disease was dehydrated and wasted; she was receiving 50 mg pentazocine four times daily as an analgesic. Years ago she had broken her nose. She was found in bed in a highly dyspnoeic and cyanotic state. Her toothless mouth was closed tightly and the nostrils were sucked in. The nasal mucosa was swollen. A nasal airway was introduced and the symptoms resolved within five minutes.

Case 3—An 89 year old woman was transferred to the nursing centre in a weak condition after having been admitted with gastric haemorrhaging. One evening she was found to be feverish and severely dyspnoeic and cyanotic. The nostrils were sucked in during inspiration and her toothless mouth was closed tightly. Again a disposable catheter alleviated the obstruction. The nasal septum was deviated and the mucosa was swollen. She suffered three more episodes the same night. Three days later she died of bronchopneumonia.

Case 4—A 78 year old woman with heart failure, extreme polyarthrosis, and a general loss of strength was receiving frusemide, prazosin, haloperidol, and promethazine (as a hypnotic). She remained bedridden, ate poorly, and developed a decubitus ulcer. Several days before her death she became cyanotic with tightly closed toothless mouth and pinched in nostrils. Nasal catarrh and a deviated nasal septum were found. A nasal catheter was introduced but was removed by the patient. The nose was taped so that the nostrils could not be pulled inwards by suction; the patient did not protest.

Case 5—An 88 year old woman who had suffered a complete stroke was receiving digoxine and dytaurese. In the past she had broken her nose. She had neither teeth nor dentures. One week before her death she developed a respiratory tract infection. She ate and drank little and became bedridden. The next day she suffered an episode similar to those experienced by the patients in case 1-4. There was no recurrence. She died of aspiration pneumonia.

Comment

Since 1984 five women in this centre have been found suffering from dangerous oronasal obstruction: a tightly closed mouth without teeth and dentures, sucked in nostrils, a deviated nasal septum, and swollen nasal mucosa. They were bedridden, cachectic, and dehydrated but not unconscious. They did not raise the alarm. Three of them were in a terminal phase. Though a restrictive medical policy is followed in such cases, the obstruction can easily be eliminated with a disposable catheter.

Upper airway obstruction may occur when, in addition to imperfect patency of the nose, inspiratory suction is greater than the ability of the oropharyngeal muscles to keep the mouth and throat open. In babies with small upper airways this phenomenon can be observed during sleep and can lead to their sudden death[2]; factors other than suction within the nose, mouth, and throat can also contribute to sudden infant death.[3] Weak senile patients can suffer this oronasal obstruction even while awake if there is also a catarrhal inflammation of the nose and a pre-existing deviated nasal septum. Though the oral cavity is softer without teeth or dentures, it is not clear why patients with nasal obstruction do not breathe through the mouth. The first patient (like the others usually a nasal breather) did this on another occasion when her nose was carefully blocked by pinching.

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