



## Neuroleptics: swallowing disorders

● Convincing and detailed case reports and various types of retrospective studies have shown that neuroleptics can cause swallowing disorders, or dysphagia. These disorders are not only troublesome but can have serious consequences, including dehydration, wasting, a feeling of suffocation, asphyxiation, and potentially fatal aspiration pneumonia.

● The patients most at risk appear to be those on long-term neuroleptic therapy and who have extrapyramidal disorders (including tardive dyskinesia), as well as patients who have been taking a neuroleptic for a few days or whose dose had recently been increased. The disorders generally resolve after neuroleptic dose reduction or withdrawal.

● Dynamic radiological investigations have shown dyskinetic movements from the tongue to the top of the oesophagus, abnormal oesophageal contractions, and slowed movements.

● These disorders have been attributed to sedation, tardive dyskinesia, acute dyskinesia, dry mouth due to the atropinic effect, and sialorrhoea due to alpha-2 blockade.

● Dysphagia may thus occur in a wide range of patients on neuroleptic therapy. Symptoms tend to improve after a dose reduction in young patients with acute dyskinesia. Management is more problematic in older patients with tardive dyskinesia on long-term neuroleptic therapy, as neuroleptic withdrawal carries a risk of symptom aggravation. When an Alzheimer's patient has trouble eating or tends to cough during meals, the possible role of a neuroleptic should be kept in mind and the implicated drug withdrawn.

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**D**ysphagia includes a variety of symptoms: difficulty swallowing food or liquids, with a sensation of "sticking" or obstruction as food passes through the mouth, pharynx or oesophagus (1,2). These symptoms cannot only affect quality of life but can also be life-threatening (a)(3).

Cases of dysphagia attributed to conventional, newer or hidden, neuroleptics have been published in detail, drawing attention to this adverse effect, which is often overlooked but can be fatal (1-16).

### Dehydration, weight loss and wasting

Some case reports mention complications such as dehydration, weight loss and wasting.

**Unexplained disorders.** Seven patients, aged 35 to 76 years, who had been taking neuroleptics for a few weeks to more than 10 years were hospitalised for dehydration, eating difficulties, aspiration of solid food or liquids, or weight loss (up to 18 kg), with no obvious cause (6,7,14,17,18). Two patients had no apparent history of swallowing disorders (17), while this information was unavailable in the other 5 cases.

Three patients required insertion of a nasogastric tube (6,14,18). One patient had abnormal movements of the tongue, lips, pharynx and extremities (6). Another patient had abnormal movements of the lips and tongue (rabbit syndrome), and dyskinesia of the extremities (b).

**Regression of symptoms after dose reduction.** These swallowing disorders and their complications generally resolved between 2 days and 6 weeks after switching to a different neuroleptic, or a dose reduction or withdrawal of the implicated neuroleptic. In 3 cases, radiological examinations showed abnormal movements from the oropharyngeal junction to the oesophagus (6,14).

**Various neuroleptics implicated.** Most of the patients were taking several neuroleptics on hospital admission,

including *chlorpromazine*, *cisapride*, *clozapine*, *haloperidol*, *levomepromazine*, *oxypertine*, *sulpiride* and *trifluoperazine* (6,7,14,17-19).

### Potentially fatal suffocation, asphyxiation and aspiration

Dysphagia can provoke a feeling of suffocation, or true suffocation, while eating. Cases of fatal asphyxiation have been reported. Some patients had extrapyramidal disorders (including tardive dyskinesia) and had been taking neuroleptics for long periods, while other patients had just started neuroleptic therapy or had recently had a dose increase (5,9,10,20).

**Informative cases.** A 66-year-old schizophrenic man with tongue dyskinesia who had been taking neuroleptics since the age of 25 experienced episodes of asphyxiation, then started to regurgitate solids and fluids. His doctor tried substituting another neuroleptic and adjusting the dose several times but the patient died suddenly of food asphyxiation (9).

A 76-year-old Alzheimer's patient developed swallowing disorders after a *risperidone* dose increase, and improved when *risperidone* was replaced by another neuroleptic (20).

A 24-year-old man who had been taking *olanzapine* for 5 days for a manic episode complained of sialorrhoea, difficulty swallowing saliva, and then difficulty swallowing food and liquids. He had no extrapyramidal symptoms. A nasogastric feeding tube had to be inserted. The ►►

a- Swallowing disorders (dysphagia) may have an oral, pharyngeal or oesophageal origin (ref 2). They are often mechanical, due to excessive food intake or a narrow oesophagus. They are sometimes linked to neuromuscular disorders, especially to weak peristaltic contractions, defective inhibition of swallowing, or oesophageal lesions. Various drugs can cause neuromuscular or oesophageal disorders that lead to swallowing difficulties. Other drugs that are known to cause dysphagia include benzodiazepines, muscle relaxants such as botulinum toxin and dantrolene; antibiotics such as tetracycline and ciprofloxacin; bisphosphonates such as alendronic acid; and cancer drugs (refs 27,30).

b- The rabbit syndrome consists of involuntary perioral movements. This tardive dyskinesia is an adverse effect of long-term neuroleptic therapy (ref 6).

disorders disappeared a week after olanzapine withdrawal (5).

**Epidemiological data.** An Australian team examined regional death registers and identified 70 deaths due to choking, either due to solid gastric contents blocking the trachea or bronchi, a type of aspiration (31 deaths), or a food bolus lodged in the larynx or laryngopharynx (39 deaths). They then examined the patients' psychiatric history and psychotropic consumption. Using various Australian databases, they estimated the prevalence of psychiatric disorders and psychotropic consumption in the general population (21). The authors estimated that schizophrenia was about 20 times more frequent in the study population than in the general population (95% confidence interval (CI) 11.9-44.6) and that use of thioridazine, a neuroleptic, was 90 times more frequent (95% CI 37.2-228.5) (22).

**Aspiration pneumonia**

Aspiration pneumonia is one of the complications of dysphagia.

Cases of aspiration pneumonia in patients taking neuroleptics have been published in detail (12,13). For example, a 64-year-old patient was hospitalised for an episode of dyspnoea and asphyxiation followed by cardiovascular collapse. He had been taking clozapine for 10 years. He had been complaining of swallowing difficulties for 4 years, and had experienced episodes of regurgitation and hiccups. Radiological findings were compatible with aspiration pneumonia, and showed hypomotility of the oesophagus (13).

**A case-control study.** A case-control study based on a primary care database was conducted in the Netherlands between 1996 and 2006. It focused on 1944 patients aged 65 years or older who had received a first neuroleptic prescription. The 258 patients who experienced a first episode of community-acquired pneumonia were compared with 1686 controls matched for sex, age and year of inclusion. One-quarter of the patients with pneumonia died within 30 days following diagnosis. Ongoing neuroleptic use was associated with a roughly two-fold higher risk of pneumonia (a statistically significant, dose-dependent difference compared with previous use (odds ratio 2.61 for atypical neuroleptics (95% CI: 1.48-4.61) and 1.76 (95% CI: 1.22-2.53) for conventional neuroleptics). Atypical neuroleptics were associated

with an increased risk of fatal pneumonia, with an odds ratio of 5.97 (95% CI: 1.49-23.98) (23).

In 2005, the US Food and Drug Administration (FDA) issued a warning on the use of neuroleptics in elderly patients, owing to an increase in mortality, mainly due to pneumonia (24).

**Mechanisms: extrapyramidal disorders, sedation, dry mouth, sialorrhoea**

Neuroleptics, both conventional and atypical, have adverse effect profiles that include extrapyramidal and sedative effects associated with dry mouth or sialorrhoea, thus contributing to swallowing difficulties (25).

**Dynamic radiological investigations of dysphagia.** Dynamic radiological investigations have shown various disorders: dyskinetic movements from the tongue to the top of the oesophagus; abnormal oesophageal contractions; slowed movements of the tongue and lips; an increase in swallowing time; aspiration of small quantities of unswallowed liquids; altered pharyngeal movements; and incomplete laryngeal closure (1,6,9,11,15,18,20).

The radiological abnormalities generally disappeared after the neuroleptic dose was reduced or the implicated drug was replaced or withdrawn (1,7,13,15,18).

**Extrapyramidal disorders.** The majority of patients with swallowing difficulties also had extrapyramidal disorders, including involuntary movements of the tongue, lips, cheeks and pharynx, acute dyskinesia, and orobuccal tardive dyskinesia. In some cases, the swallowing difficulties were the main extrapyramidal symptom (c)(1,6,8,9).

**Sedative effects.** Sedation is a risk factor for onset of swallowing disorders (26,27).

**Dry mouth and sialorrhoea.** The atropinic effect of some neuroleptics can cause dry mouth, thus making swallowing difficult (26,28,29).

Paradoxically, other neuroleptics can cause sialorrhoea through their alpha-2 blocking action (26).

**In practice: keep the possible role of a neuroleptic in mind, and withdraw it if possible**

At the very least, swallowing disorders are a source of discomfort; at worst, they can be fatal. Neuroleptic-related dysphagia can occur in a variety of settings.

Symptoms generally improve after a neuroleptic dose reduction in young patients with acute dyskinesia.

In older patients who have tardive dyskinesia and are on long-term neuroleptic therapy, dysphagia is difficult to manage, as neuroleptic withdrawal may aggravate symptoms.

When a patient with Alzheimer's disease has trouble eating or coughs during meals, the possible role of a neuroleptic should be kept in mind, and the implicated drug withdrawn.

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*c- Tardive dyskinesia generally develops after several years of neuroleptic use. Symptoms may worsen if the neuroleptic is withdrawn or the dose is reduced. They tend to improve a few months or years after neuroleptic withdrawal, especially in young patients (ref 31).*

**Literature search and methodology**

Our literature search was based on prospective, continuous scrutiny of contents listings of the main international journals, Current Contents-Clinical Medicine, and member bulletins of the International Society of Drug Bulletins (ISDB) at the Prescrire library; as well as systematic consultation of clinical pharmacology textbooks (Martindale The Complete Drug Reference, Stockley's Drug Interactions). We also accessed the following databases: Embase/Excerpta Medica Drugs and Pharmacology (1991-3<sup>rd</sup> quarter 2010), Medline (1950-July week 1, 2010), Reactions (1992-July 2010), and Cochrane (2010, Issue 2).

This article was prepared using the standard Prescrire methodology, which includes verification of the choice of documents and their analysis, external review, and multiple quality controls.

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