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Drug-induced memory disorders

● **Dementia is not the only cause of memory loss.**

Memory disorders are often attributed to ageing and sometimes confused with early dementia. A drug-related cause should always be investigated.

The regional pharmacovigilance centre in Poitiers, France, has analysed relevant data from the French pharmacovigilance database (1). 266 cases of memory disorders (excluding dementia) recorded in the database between January 2003 and April 2008 were compared with the 98 995 other recorded adverse effects. Reports involved about twice as many women as men, and the mean age was 55 years (range: 4 to 93 years). Outcome was favourable in 63% of cases.

Many drugs have been found to have a statistically significant estimated relative risk. This was predictable with some drug classes, including the hypnotic drugs *zolpidem*, *zopiclone* and *sodium oxybate* (respective relative risk 25, 11 and 19), as well as benzodiazepines, antidepressants, analgesics, anticonvulsants and neuroleptics.

Other drugs with a relative risk of about 10 included *strontium ranelate* (used in osteoporosis), *mefloquine* (used in malaria), and *loperamide* (a structural opioid analogue used in diarrhoea).

Another French regional pharmacovigilance centre, in Nancy, examined the same data, focusing on drugs other than benzodiazepines and benzodiazepine-like agents, implicated in transient amnesia lasting between 1 and 24 hours, without altered consciousness or neurological signs (2).

Between 1985 and 2007, 51 spontaneous reports were recorded, in a similar number of men and women. Mean age was 57.5 years.

In 20 cases, amnesia occurred within 24 hours after the first dose. 13 patients (25%) had predisposing factors, such as recent invasive medical procedures, anaesthesia, sexual intercourse, and intense emotion or pain.

A single drug was suspected in 38 cases. Most cases involved cardiovascular drugs (11.4%), psychotropics (10.1%), nonsteroidal antiinflammatory drugs (8.9%), anti-infectives (8.9%) and antitussives (7.6%) (2).

Drugs with atropinic effects can also cause memory disorders (3).

Another French regional pharmacovigilance centre, in Limoges, reported the case of a 58-year-old man who had 2 successive episodes of transient amnesia lasting less than an hour. They occurred within the hour following injection of *alprostadil*, a drug the patient had been using to treat erectile dysfunction for one year (4).

In practice. When patients present with memory disorders, it is in their best interests to consider a possible drug-related cause.

Selected references from Prescrire's literature search.

1- Chavant F et al. "Drugs and memory: a case/non case-study in the French pharmacovigilance database" 30th Pharmacovigilance Meeting, Marseille: 15-17 April 2009. *Fundamental Clin Pharmacol* 2009; 23 (suppl 1): **32** (abstract 161).

2- Cosserat F et al. "Drug-induced transient amnesia and transient global amnesia (excluding benzodiazepines): analysis of the French Pharmacovigilance database" 30th Pharmacovigilance Meeting, Marseille: 15-17 April 2009. *Fundamental Clin Pharmacol* 2009; **23** (suppl 1): 48-49 (abstract 245).

3- Prescrire Editorial Staff "Alzheimer's disease: beware of interactions with cholinesterase inhibitors" *Prescrire Int* 2006; **15** (83): 103-106.

4- Crepin S et al. "A case of transient global amnesia following intracavernous administration of alprostadil" 30th Pharmacovigilance Meeting, Marseille: 15-17 April 2009. *Fundamental Clin Pharmacol* 2009; 23 (suppl 1): **31** (abstract 155). Full article: 13 pages.

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Carbimazole: cases of birth defects

● **When possible, it is better to use *propylthiouracil* rather than *carbimazole* to treat hyperthyroidism during pregnancy.**

During pregnancy, *propylthiouracil* is the first-line synthetic antithyroid drug, as no increase in the frequency of congenital malformations, compared to the general population, has been reported during its many years of use (1,2). Moreover, long-term follow-up studies have shown no difference in growth or psychomotor development of children exposed *in utero*.

Between 1990 and 2007, the Nice Regional Pharmacovigilance Centre in France identified 6 reports of congenital malformations after first-trimester exposure to *carbimazole*: there were 3 abdominal wall defects, 2 cases of scalp aplasia, and 1 case of atresia of posterior orifices of the nasal fossae (choanal atresia) (3).

These malformations are consistent with those already reported with *carbimazole* or its active metabolite *methimazole*: scalp aplasia, choanal atresia, oesophageal atresia with oseotracheal fistula, facial dysmorphia, and abdominal wall defects (omphalocele and gastroschisis) (2,3).

In practice. *Carbimazole* is only a second-line treatment during pregnancy. If its use is justified, then the lowest effective dose must be determined, with regular ultrasound monitoring of the face, upper digestive tract and abdominal wall of the fetus.

Selected references from Prescrire's literature search.

1- Prescrire Rédaction "Propylthiouracile: en ville" *Rev Prescrire* 2008; **28** (295): 339-340.

2- "Propylthiouracile" et "Carbimazole". In: "Reprotox" Micromedex Healthcare Series. www.thomsonhc.com accessed 5 June 2009: 16 pages + 2 pages.

3- Koenig D et al. "Birth defects following carbimazole in utero exposure: 6 more cases" 30th Pharmacovigilance Meeting, Marseille: 15-17 April 2009. *Fundamental Clin Pharmacol* 2009; **23** (suppl 1): 30 (abstract 151).