European Journal of Anaesthesiology 1997, **14**, 1–2

EDITORIAL

Post-operative central anticholinergic syndrome

Central anticholinergic syndrome is defined as an absolute or relative reduction in cholinergic activity in the central nervous system [1]. In anaesthetic practice the syndrome was originally described in connection with drugs with central anticholinergic actions, such as hyoscine butylbromide (scopolamine) [2]. Later, many other drugs with no direct anticholinergic effects were implicated. This may be by modulation of other neurotransmitters which reduce cholinergic activity, but the mechanisms by which the syndrome occurs have not been fully explained [1].

The reported clinical features of the central anticholinergic syndrome in the post-operative period are non-specific. If they are all components of the syndrome the central nervous system would be widely involved (Table 1). There are said to be two forms of the syndrome: hyperactive or depressed. Peripheral anticholinergic symptoms may also occur but could by masked by peripheral cholinesterase inhibitors.

Table 1. Reported clinical features of post-operative central anticholinergic syndrome

Agitation	Emotional instability
Amnesia	Muscular inco-ordination or weakness
Ataxia	Nausea and vomiting
Asynergia	Hyperpyrexia
Dysarthria	Hyperalgesia
Clouded Sensorium	Convulsions
Confusion	Opisthotonus*
Excitement	Torticollis*
Somnolence	Tetraplegia†
Coma	Stimulation or depression of ventilation
Apprehension	Stereotyped movements
Hallucinations	Fatigue
Illusions/delusions	Diminished power of concentration
Delirium	Medium or long term mental impairment
Paranoia	Decreased reaction times
	EEG-behaviour dissociation

Table modified from Rupreht and Dworacek 1989 [1]. Other references: *[3], †[4].

Diagnosis rests on clinical features, exclusion of other conditions, and a positive response to a centrally acting cholinesterase inhibitor, usually physostigmine [1].

The incidence of the post-operative syndrome has been estimated as 9.4% after general anaesthesia and 3.3% after regional anaesthesia with sedation [1], although an incidence as high as 40% has been claimed [5]. In their paper in this issue of the journal [6], Link *et al*. report an incidence of 1.9% in a broad mix of 962 adults after general anaesthesia, with a subgroup of women recovering from major gynaecological surgery having an incidence of 10%. These figures are in stark contrast with experience in the UK where central anticholinergic syndrome is diagnosed rarely. United Kingdom anaesthetists are either unaware of the syndrome, or do not believe it exists.

Choice of anaesthetic technique and drugs may be an important determinant of reported incidence. Anaesthetists who use long acting drugs (benzodiazepines or barbiturates) will see a large number of patients who recover slowly from anaesthesia. Link *et al*. state that less than 3% of their study population were given droperidol as part of their anaesthetic, but eight of 18 patients with the syndrome received between 2.5 and 25 mg. The total number of patients given diazepam and phenobarbitone premedication is not stated, but nine of 18 affected patients received one of these drugs. What constitutes normal recovery from anaesthesia and a definition of what is abnormally prolonged are not stated. Clearly, the earlier that features of the syndrome are sought the higher will be their incidence in the post-operative period. Interindividual variations in anaesthetic drugs and technique, as well as variations in pharmacokinetics and pharmacodynamics, must also be taken into account.

From the clinical features it is obvious that the list of differential diagnoses is long. As there is no diagnostic test, the diagnosis is made by exclusion of hypoxia, hypercapnia, hyperthermia, hypothermia, urea and electrolyte and acid-base disturbances, endocrine abnormalities, and neurological disturbance

https://doi.org/10.1046/j.1365-2346.1997.00074.x Published online by Cambridge University Press

from surgery, vascular disease or trauma [1]. The extensive list of symptoms and signs means that central anticholinergic syndrome is a potential diagnosis in patients with just about any form of neurological abnormality, and that the incidence could be inversely proportional to the rigour with which other diagnoses are excluded. In some settings, rigorous exclusion of all other conditions may be simply impossible in the immediate post-operative period. The diagnosis, therefore, is heavily dependent on a response to physostigmine, whose central effects extend beyond the cholinergic system [7,8]. Perhaps central anticholinergic syndrome is a misnomer, and central physostigmine responsive syndrome is a more accurate description.

This does not mean that post-operative central anticholinergic syndrome should be dismissed out of hand. The case report by Sun [9] cannot easily be explained by any other diagnosis. This is a report of three general anaesthetics in one patient, who took 14 and 10 h to regain full consciousness after repair of retinal detachment under general anaesthesia that included reversal of neuromuscular blockade with neostigmine and atropine. On the third occasion, an identical anaesthetic to the second was given but without reversal of neuromuscular blockade. This time the patient was fully conscious 10 min after the end of the anaesthesia. Physostigmine was not available in the hospital involved.

Physostigmine shortens wakening times after general anaesthesia [10]. However, its duration of action is about 30–60 min after intravenous (i.v.) injection [11] and, in common with other 'antidotes' such as naloxone and flumazenil, there is a danger of later recurrence of symptoms. Reported side effects of physostigmine in this setting include nausea and vomiting, abdominal cramps [10,12,13] and bradycardia and hypotension [13]. It would therefore seem appropriate to avoid treating one drug's side effects with another drug that exposes patients to other risks. We should accept that some patients recover from anaesthesia more slowly than others, and perhaps the safest course of action is to observe and support them during this time. Careful choice of anaesthetic technique and drugs tailored to individual circumstances should reduce the need for prolonged support. Until a more rigid definition is available, preferably supported by a controlled trial, differences in the reported incidence of post-operative central anticholinergic syndrome seem likely to continue.

B. Cook and A. A. Spence
Edinburgh

References

1 Rupreht J, Dworacek B. The central anticholinergic syndrome in the postoperative period. In: Nunn JF, Utting JE, Brown BR, eds. *General Anaesthesia*, 5th Edn. London: Butterworths, 1989: 1141–1148.
2 Holzgrafe RE, Vondrell JJ, Mintz SM. Reversal of postoperative reactions to scopolamine with physostigmine. *Anesth Analg* 1973: **52**: 921–925.
3 Dehring DJ, Bhagwandas G, Peruzzi WT. Postoperative opisthotonus and torticollis after fentanyl, enflurane and nitrous oxide. *Can J Anaesth* 1991; **38**: 919–925.
4 Rathgeber J, Kukowski B, Zenker D. Storungen der Vigilanz bei Intensivpatienten. Zentralanticholinerges Syndrom als Differentialdiagnose der Hirnstamlasion. *Anaesthesist* 1992; **41**: 699–701.
5 Torline RL. Central anticholinergic syndrome – the forgotten diagnosis? *Anesthesiology Review* 1993; **20**: 47–50.
6 Link J, Papadopoulos G, Dopjans D, Guggenmoos-Holzman I, Eyrich K. Distinct central anticholinergic syndrome following general aneasthesia. *Eur J Anaesthesiol* 1997; **14**: 15–23.
7 Ebied AM, Attia RR, Sundaram P, Fischer JE. Release of vasoactive intestinal peptide in the central nervous system in man. *Am J Surgery* 1979; **137**: 123–127.
8 Rupreht J, Schneck HJ, Dworacek B. Physostigmin-Neuere pharmacologische Befunde und ihre Bedeutung fur den Einsatz in der Praxis. *Anaesthesiologie und Reanimation* 1989; **14**: 235–241.
9 Sun KO. Central anticholinergic syndrome following reversal of neuromuscular blockade. *Anaesth Intens Care* 1993; **21**: 363–365.
10 Hill GE, Stanley TH, Sentker CR. Physostigmine reversal of postoperative somnolence. *Can Anaesth Soc J* 1977; **24**: 707–711.
11 Hartvig P, Wiklund L, Lindström B. Pharmacokinetics of physostigmine after intravenous, intramuscular and subcutaneous administration in surgical patients. *Acta Anaesthesiol Scand* 1986; **30**: 177–182.
12 Pettersson J, Gordh TE, Hartvig P, Wiklund L. A double blind trial of the analgesic properties of physostigmine in postoperative patients. *Acta Anaesthesiol Scand* 1986; **30**: 283–288.
13 Hartvig P, Lindström B, Pettersson E, Wiklund L. Reversal of postoperative somnolence using a two rate infusion of physostigmine. *Acta Anaesthesiol Scand* 1989; **33**: 681–685.

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