Ketamine Hydrochloride

(BANM, USAN, rINNM)

CI-581; CL-369; CN-52372-2; Hidrocloruro de ketamina; Ketamiinihydrokloridi; Ketamin Hidroklorür; Kétamine, chlorhydrate de; Ketamin-hidroklorid; Ketamin-hydrochlorid; Ketaminhydroklorid; Ketamini hydrochloridum; Ketamino hidrochloridas; Ketaminy chlorowodorek. (±)-2-(2-Chlorophenyl)-2-methylaminocyclohexanone hydrochloride.

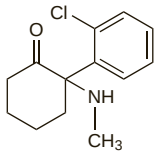
Кетамина Гидрохлорид

$C_{13}H_{16}ClNO,HCl$ = 274.2.

CAS — 6740-88-1 (ketamine); 1867-66-9 (ketamine hydrochloride).

ATC — N01AX03.

ATC Vet — QN01AX03.



(ketamine)

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of ketamine:
Animal trank; Animal tranquilizer; Bump; Cat tranquilizer; Cat valium; Elephant tranquilizer; Green; Honey oil; Horse tranquilizer; Jet; Jet fuel; K; "K"; K wire; Kay Jay; K-blast; Keets; Keezy; Keller; Kellys day; Kenny; Ket; Keta; Ketaset; KFC; Kit kat; Kit-Kat; Kitty; KKK; Klarko K Kat; Klarky Kat; Kustard; Lady K; Naughty horsey; Old Man; Property of Sir John; Purple; Regretamine; Special K; Special "K"; Special la coke; Super acid; Super C; Super K; Tranquilizer; Triple K; Vetamine; Vitamin K; Wonky.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*

Ph. Eur. 6.2 (Ketamine Hydrochloride). A white or almost white crystalline powder. Freely soluble in water and in methyl alcohol; soluble in alcohol. A 10% solution in water has a pH of 3.5 to 4.1. Protect from light.

USP 31 (Ketamine Hydrochloride). A white crystalline powder having a slight characteristic odour. Soluble 1 in 4 of water, 1 in 14 of alcohol, 1 in 60 of dehydrated alcohol and of chloroform, and 1 in 6 of methyl alcohol; practically insoluble in ether. pH of a 10% solution in water is between 3.5 and 4.1. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Incompatibility. Ketamine hydrochloride is incompatible with soluble barbiturates. The US licensed product information recommends that when use of diazepam and ketamine is required they should be given separately and not mixed in the same giving equipment.

Esketamine Hydrochloride *(BANM, rINNM)*

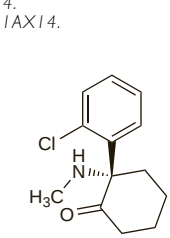
Esketamiinihydrokloridi; Eskétamine, Chlorhydrate d'; Eskétamine, chlorhydrate de; Esketamin-hydrochlorid; Esketaminhydroklorid; Esketamini hydrochloridum; Esketamino hidrochloridas; Hidrocloruro de esketamina; *S*-Ketamine Hydrochloride.

Эскетамина Гидрохлорид

CAS — 33643-46-8 (esketamine).

ATC — N01AX14.

ATC Vet — QN01AX14.



(esketamine)

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Esketamine Hydrochloride). A white or almost white, crystalline powder. Freely soluble in water and in methyl alcohol; soluble in alcohol. A 10% solution in water has a pH of 3.5 to 4.5. Protect from light.

Adverse Effects

Emergence reactions are common during recovery from ketamine anaesthesia and include vivid often unpleasant dreams, confusion, hallucinations, and irrational behaviour. Children and elderly patients appear to be less sensitive. Patients may also experience increased muscle tone, sometimes resembling seizures. Blood pressure and heart rate may be temporarily increased by ketamine; hypotension, arrhythmias, and bradycardia have occurred rarely.

Respiration may be depressed after rapid intravenous injection or with high doses. Apnoea and laryngospasm have occurred. Diplopia and nystagmus may occur. Nausea and vomiting, lachrymation, hypersalivation, and raised intra-ocular and CSF pressure have also been reported. Transient skin rashes and pain at the site of injection may occur.

See also Adverse Effects of General Anaesthetics, p.1779.

Effects on the cardiovascular system. Ketamine has been advocated by some for maintaining or increasing cardiovascular performance in selected patients during induction of anaesthesia as it may increase blood pressure and heart rate.[1] However, there have been reports of reduced cardiac and pulmonary performance in severely ill patients[1] and of arrhythmias.[2]

Some of the cardiovascular effects of ketamine may be attenuated by premedication with diazepam[2] or clonidine.[3]

1. Waxman K, *et al*. Cardiovascular effects of anesthetic induction with ketamine. *Anesth Analg* 1980; **59:** 355–8.
2. Cabbabe EB, Behbahani PM. Cardiovascular reactions associated with the use of ketamine and epinephrine in plastic surgery. *Ann Plast Surg* 1985; **15:** 50–2.
3. Tanaka M, Nishikawa T. Oral clonidine premedication attenuates the hypertensive response to ketamine. *Br J Anaesth* 1994; **73:** 758–62.

Effects on the liver. Changes in liver enzyme values have occurred after ketamine in an initial dose of 1 mg/kg followed by continuous infusion as a 0.1% solution.[1]

1. Dundee JW, *et al*. Changes in serum enzyme levels following ketamine infusions. *Anaesthesia* 1980; **35:** 12–16.

Effects on mental state. Mental disturbances following ketamine anaesthesia may vary in incidence from less than 5% to greater than 30%.[1] See also Abuse, below.

1. White PF, *et al.* Ketamine—its pharmacology and therapeutic uses. *Anesthesiology* 1982; **56:** 119–36.

Effects on the skin. Harlequin-like colour skin changes were reported[1] in a 9-month-old boy during anaesthesia with ketamine 15 mg.

1. Wagner DL, Sewell AD. Harlequin color change in an infant during anesthesia. *Anesthesiology* 1985; **62:** 695.

Malignant hyperthermia. Malignant hyperthermia has been reported in a patient given ketamine.[1]

1. Rasore-Quartino A, *et al.* Forma atipica di ipertermia maligna: osservazione di un caso da ketamina. *Pathologica* 1985; **77:** 609–17.

Precautions

Ketamine is contra-indicated in patients in whom elevation of blood pressure would be a serious hazard including those with hypertension or a history of cerebrovascular accident. Cardiac function should be monitored in patients found to have hypertension or cardiac decompensation. Ketamine should be used with caution in patients with elevated CSF pressure. It can raise intra-ocular pressure and should not be used in the presence of eye injury or increased intra-ocular pressure.

Ketamine does not reliably suppress pharyngeal and laryngeal reflexes and mechanical stimulation of the pharynx should be avoided unless a muscle relaxant is used.

The use of ketamine should be avoided in patients prone to hallucinations or psychotic disorders. Verbal, tactile, and visual stimuli should be kept to a minimum during recovery in an attempt to reduce the risk of emergence reactions.

See also Precautions for General Anaesthetics, p.1779.

Abuse. Health care workers in the USA were alerted to the dangers associated with the abuse of ketamine as long ago as 1979.[1] Similar concern had also been voiced in the UK[2] over the abuse of ketamine at social gatherings where it has been taken intranasally or orally. A WHO expert committee[3] considered in 2006 that the available information on ketamine was not sufficient to warrant international control. Studies in *animals* have shown that ketamine can produce dependence, however, reports of dependence in humans are limited (see below). Although tolerance may occur there is no evidence of a withdrawal syndrome (but see below). Ketamine abuse has been reported in a number of countries.

Ketamine produces a state of psychological dissociation resulting in hallucinations and out of body or near death experiences. It can induce a state of helplessness in which the user loses awareness of the environment and this together with severe loss of coordination and pronounced analgesia can put the user at great risk. Furthermore, some users experience a state in which they are unconcerned about whether they live or die. Ketamine has the potential for compulsive repeated use and there have been reports of users self-injecting ketamine several times a day for prolonged periods. Dependency may develop[4,5] and withdrawal symptoms requiring detoxification can occur.[4] Frequent use may produce long-lasting memory impairment.[6] Other adverse effects include a report[7] of an acute dystonic reaction in a 20-year old man following self-administration of ketamine intravenously.

In one case series[8] of 20 patients presenting to hospital after ketamine abuse the most common symptoms included anxiety, chest pain, and palpitations. Frequent complications included agitation and rhabdomyolysis. Symptoms were generally short lived with most patients discharged within 5 hours.

Some[2] suggest that patients seeking medical attention are best placed in a quiet darkened room to recover with diazepam being given for unresponsive panic attacks while others advocate that such patients should be admitted to an intensive care unit for close monitoring.[9] The use of intravenous fluids to prevent rhabdomyolysis has also been recommended.[8]

Long-term and frequent abuse of ketamine has been associated with adverse effects on the urinary tract.[10-12] Patients may present with symptoms of dysuria, frequency, urgency, urinary incontinence, suprapubic pain, and haematuria. Examination has shown in some cases a contracted shrunken bladder and ulcerative cystitis. Complications have included hydronephrosis and renal impairment.

Ketamine is tasteless, odourless, and colourless and has been misused to incapacitate the victim and produce amnesia in sexual assaults and drug-facilitated rape ('date rape').[4]

1. Anonymous. Ketamine abuse. *FDA Drug Bull* 1979; **9:** 24.
2. Jansen KLR. Non-medical use of ketamine. *BMJ* 1993; **306:** 601–2.
3. WHO. WHO expert committee on drug dependence: thirty-fourth report. *WHO Tech Rep Ser 942* 2006. Also available at: http://libdoc.who.int/trs/WHO_TRS_942_eng.pdf (accessed 06/08/08)
4. Smith KM, *et al*. Club drugs: methylenedioxymethamphetamine, flunitrazepam, ketamine hydrochloride, and γ-hydroxybutyrate. *Am J Health-Syst Pharm* 2002; **59:** 1067–76.
5. Jansen KLR, Darracot-Cankovic R. The nonmedical use of ketamine, part two: A review of problem use and dependence. *J Psychoactive Drugs* 2001; **33:** 151–8.
6. Curran HV, Monaghan L. In and out of the K-hole: a comparison of the acute and residual effects of ketamine in frequent and infrequent ketamine users. *Addiction* 2001; **96:** 749–60.
7. Felser JM, Orban DJ. Dystonic reaction after ketamine abuse. *Ann Emerg Med* 1982; **11:** 673–5.
8. Weiner AL, *et al*. Ketamine abusers presenting to the emergency department: a case series. *J Emerg Med* 2000; **18:** 447–51.
9. Gill PA. Non-medical use of ketamine. *BMJ* 1993; **306:** 1340.
10. Chu PSK, *et al.* 'Street ketamine'-associated bladder dysfunction: a report of ten cases. *Hong Kong Med J* 2007; **13:** 311–13.
11. Shahani R, *et al*. Ketamine-associated ulcerative cystitis: a new clinical entity. *Urology* 2007; **69:** 810–12.
12. Cottrell AM, *et al*. Urinary tract disease associated with chronic ketamine use. *BMJ* 2008; **336:** 973.

Neurosurgery. Although the idea that ketamine should not be used in patients at risk from rises in intracranial pressure has limited its use in neurosurgical patients, a review[1] considered that if used with controlled ventilation and a GABA receptor agonist, and without nitrous oxide, it did not appear to have adverse effects in this group, and there was some evidence from *animal* studies that it might have neuroprotective properties.

1. Himmelseher S, Durieux ME. Revising a dogma: ketamine for patients with neurological injury? *Anesth Analg* 2005; **101:** 524–34.

Interactions

Inhalational anaesthetics, such as ether and halothane, and other cerebral depressants may prolong the effect of ketamine and delay recovery. Prolonged recovery has also occurred when barbiturates and/or opioids have been given with ketamine. It has been recommended that ketamine should not be used with ergometrine.

See also Interactions of General Anaesthetics, p.1779.

Neuromuscular blockers. For the enhancement of the effect of *tubocurarine* or *atracurium* by ketamine, see p.1904.

Thyroid drugs. For a reference to increased cardiovascular adverse effects with *levothyroxine*, see p.2173.

Xanthines. For a reference to seizures and tachycardia attributed to an interaction between ketamine and *theophylline*, see p.1145.

Pharmacokinetics

After intravenous boluses, ketamine shows a bi- or triexponential pattern of elimination. The alpha phase lasts about 45 minutes with a half-life of 10 to 15 minutes. This first phase, which represents ketamine's anaesthetic action, is terminated by redistribution from the CNS to peripheral tissues and hepatic biotransformation to an active metabolite norketamine. Other

metabolic pathways include hydroxylation of the cyclohexone ring and conjugation with glucuronic acid. The beta phase half-life is about 2.5 hours. Ketamine is excreted mainly in the urine as metabolites. It crosses the placenta.

◊ References.

1. Clements JA, Nimmo WS. Pharmacokinetics and analgesic effect of ketamine in man. *Br J Anaesth* 1981; **53:** 27–30.
2. Grant IS, *et al.* Pharmacokinetics and analgesic effects of IM and oral ketamine. *Br J Anaesth* 1981; **53:** 805–9.
3. Grant IS, *et al.* Ketamine disposition in children and adults. *Br J Anaesth* 1983; **55:** 1107–11. **14:** 144P.
4. Geisslinger G, *et al.* Pharmacokinetics and pharmacodynamics of ketamine enantiomers in surgical patients using a stereoselective analytical method. *Br J Anaesth* 1993; **70:** 666–71.
5. Malinovsky J-M, *et al.* Ketamine and norketamine plasma concentrations after iv, nasal and rectal administration in children. *Br J Anaesth* 1996; **77:** 203–7.

Uses and Administration

Ketamine is an anaesthetic given by intravenous injection, intravenous infusion, or intramuscular injection. It produces dissociative anaesthesia characterised by a trance-like state, amnesia, and marked analgesia which may persist into the recovery period. There is often an increase in muscle tone and the patient's eyes may remain open for all or part of the period of anaesthesia. Ketamine is used in general anaesthesia for diagnostic or short surgical operations that do not require skeletal muscle relaxation, for the induction of anaesthesia to be maintained with other drugs, and as a supplementary anaesthetic (see p.1780). It also has good analgesic properties in subanaesthetic doses. It is considered to be of particular value in children requiring frequent repeated anaesthesia. Recovery is relatively slow.

Ketamine is given as the hydrochloride but doses are expressed in terms of the equivalent amount of base; ketamine hydrochloride 1.15 mg is equivalent to about 1 mg of ketamine.

- For induction in adults and children the dose given by *intravenous injection* may range from the equivalent of 1 to 4.5 mg/kg of ketamine; a dose of 2 mg/kg given intravenously over 60 seconds usually produces surgical anaesthesia within 30 seconds of the end of the injection and lasting for 5 to 10 minutes.
- The initial *intramuscular* dose may range from 6.5 to 13 mg/kg; an intramuscular dose of 10 mg/kg usually produces surgical anaesthesia within 3 to 4 minutes lasting for 12 to 25 minutes. For diagnostic or other procedures not involving intense pain an initial intramuscular dose of 4 mg/kg has been used. Additional doses may be given for maintenance.
- For induction by *intravenous infusion* a total dose of 0.5 to 2 mg/kg is usually given at an appropriate infusion rate. Maintenance is achieved with 10 to 45 micrograms/kg per minute, the infusion rate being adjusted according to response.

Use should be preceded by atropine or another suitable antimuscarinic. Diazepam or another benzodiazepine may be given before surgery or as an adjunct to ketamine to reduce the incidence of emergence reactions.

The *S*-isomer, esketamine, is also given for similar uses in anaesthesia.

◊ Reviews.

1. Hirota K, Lambert DG. Ketamine: its mechanism(s) of action and unusual clinical uses. *Br J Anaesth* 1996; **77:** 441–4.

Administration. Although ketamine hydrochloride is usually given intravenously or intramuscularly, oral[1,2] and rectal[3] dosage has been used successfully in children. Intranasal use of ketamine with midazolam in a neonate requiring anaesthesia has also been reported.[4] Unfortunately the onset of sedation with these three routes is too slow for emergency procedures and therefore a jet-injector of ketamine was developed[5] to provide non-traumatic, painless, and rapid anaesthesia in children. Intranasal and transdermal use may be useful in the management of pain (below); oral, rectal, and subcutaneous routes have also been tried.[6]

1. Tobias JD, *et al.* Oral ketamine premedication to alleviate the distress of invasive procedures in pediatric oncology patients. *Pediatrics* 1992; **90:** 537–41.
2. Gutstein HB, *et al.* Oral ketamine preanesthetic medication in children. *Anesthesiology* 1992; **76:** 28–33.
3. Lökken P, *et al.* Conscious sedation by rectal administration of midazolam or midazolam plus ketamine as alternatives to general anesthesia for dental treatment of uncooperative children. *Scand J Dent Res* 1994; **102:** 274–80.
4. Louon A, *et al.* Sedation with nasal ketamine and midazolam for cryotherapy in retinopathy of prematurity. *Br J Ophthalmol* 1993; **77:** 529–30.
5. Zsigmond EK, *et al.* A new route, jet-injection for anesthetic induction in children–ketamine dose-range finding studies. *Int J Clin Pharmacol Ther* 1996; **34:** 84–8.
6. Kronenberg RH. Ketamine as an analgesic: parenteral, oral, rectal, subcutaneous, transdermal and intranasal administration. *J Pain Palliat Care Pharmacother* 2002; **16:** 27–35.

Nonketotic hyperglycinaemia. Ketamine was tried with strychnine in a newborn infant with severe nonketotic hyperglycinaemia (p.2393) and resulted in neurological improvement, although motor development remained unsatisfactory.[1] It was thought that ketamine might act by blocking N-methyl-D-aspartate (NMDA) receptors, which are activated in the CNS by glycine.

1. Tegtmeyer-Metadorf H, *et al.* Ketamine and strychnine treatment of an infant with nonketotic hyperglycinaemia. *Eur J Pediatr* 1995; **154:** 649–53.

Pain. For a discussion of pain and its management, see p.2. Ketamine is used for its analgesic action in neuropathic or other pain unresponsive to conventional analgesics. (For mention of its use for outpatient procedures in children, see p.3.) Systematic reviews have found the evidence for such use to be limited,[1,2] and have also differed on its value for postoperative pain,[3-5] but it has been suggested[1] that ketamine is a reasonable third-line option for pain where standard analgesics have failed. Subcutaneous, intramuscular, intravenous, epidural, intrathecal, intranasal, transdermal, rectal, and oral routes have all been tried.[1,6]

1. Hocking G, Cousins MJ. Ketamine in chronic pain management: an evidence-based review. *Anesth Analg* 2003; **97:** 1730–9.
2. Bell RF, *et al.* Ketamine as an adjuvant to opioids for cancer pain. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2003 (accessed 16/06/05).
3. Elia N, Tramèr MR. Ketamine and postoperative pain—a quantitative systematic review of randomised trials. *Pain* 2005; **113:** 61–70.
4. Bell RF, *et al.* Perioperative ketamine for acute postoperative pain. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2006 (accessed 16/05/06).
5. Subramaniam K, *et al.* Ketamine as adjuvant analgesic to opioids: a quantitative and qualitative systematic review. *Anesth Analg* 2004; **99:** 482–95.
6. Kronenberg RH. Ketamine as an analgesic: parenteral, oral, rectal, subcutaneous, transdermal and intranasal administration. *J Pain Palliat Care Pharmacother* 2002; **16:** 27–35.

Status epilepticus. For the suggestion that ketamine may be tried in refractory status epilepticus, see p.469.

Preparations

BP 2008: Ketamine Injection;
USP 31: Ketamine Hydrochloride Injection.

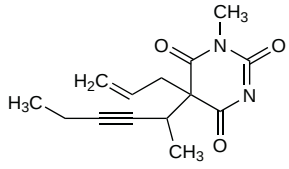
Proprietary Preparations (details are given in Part 3)
Arg.: Cost; Inducmina; Ketalar; Ketanest; ***Austral.:*** Ketalar; ***Austria:*** Ketanest; ***Belg.:*** Ketalar; ***Braz.:*** Ketalar; ***Canad.:*** Ketalar; ***Chile:*** Ketalar†; ***Cz.:*** Calypsol; Narkamon; ***Denm.:*** Ketalar†; ***Fin.:*** Ketalar; Ketanest; ***Ger.:*** Keta†; Ketanest; ***Gr.:*** Ketalar†; ***Hong Kong:*** Ketalar; ***Hung.:*** Calypsol; ***India:*** Ketalar; Ketmin; ***Indon.:*** Anesject; Ivanes; Ketalar; KTM; ***Irl.:*** Ketalar; ***Israel:*** Ketalar; ***Malaysia:*** Calypsol†; Ketava; ***Mex.:*** Ketalin; ***Neth.:*** Ketanest; ***Norw.:*** Ketalar; ***NZ:*** Ketalar; ***Philipp.:*** Ketaject; Ketamax; Ketazol; Quetanex; ***Pol.:*** Calypsol; Ketanest; ***Port.:*** Ketalar; ***Rus.:*** Calypsol (Калипсол); ***S.Afr.:*** Brevinaze; ***Spain:*** Ketolar; ***Swed.:*** Ketalar; ***Switz.:*** Ketalar; ***Thai.:*** Calypsol; Keta-Hameln†; Ketalar; ***Turk.:*** Ketalar; ***UK:*** Ketalar; ***USA:*** Ketalar; ***Venez.:*** Keiran.

Methohexital *(BAN, rINN)*

Méthohexital; Methohexitalum; Methohexitone; Metoheksitaali; Metohexital. (±)-5-Allyl-1-methyl-5-(1-methylpent-2-ynyl)barbituric acid; 1-Methyl-5-(1-methyl-2-pentynyl)-5-(2-propenyl)-2,4,6(1*H*,3*H*,5*H*)-pyrimidinetrione.

Метогекситал

$C_{14}H_{18}N_2O_3$ = 262.3.
CAS — 151-83-7; 18652-93-2.
ATC — N01AF01; N05CA15.
ATC Vet — QN01AF01; QN05CA15.



Pharmacopoeias. In *US.*
USP 31 (Methohexital). A white to faintly yellowish-white crystalline odourless powder. M.p. 92° to 96° but the range between beginning and end of melting does not exceed 3°. Very slightly soluble in water; slightly soluble in alcohol, in chloroform, and in dilute alkalis.

Methohexital Sodium *(BANM, rINNM)*

Compound 25398; Enallynymalnatrium; Méthohexital Sodique; Methohexitone Sodium; Metohexital sódico; Natrii Methohexitalum.

Натрий Метогекситал

$C_{14}H_{17}N_2NaO_3$ = 284.3.
CAS — 309-36-4; 22151-68-4; 60634-69-7.
ATC — N01AF01; N05CA15.
ATC Vet — QN01AF01; QN05CA15.

Pharmacopoeias. *US* includes Methohexital Sodium for Injection.
USP 31 (Methohexital Sodium for Injection). A freeze-dried sterile mixture of methohexital sodium and anhydrous sodium carbonate as a buffer, prepared from an aqueous solution of methohexital, sodium hydroxide, and sodium carbonate. It is a white to off-white, essentially odourless, hygroscopic powder. pH of a 5% solution in water is between 10.6 to 11.6.

Incompatibility. Solutions of methohexital sodium are incompatible with acidic substances including a number of antibacterials, antipsychotics, neuromuscular blockers, antimuscarinics, and analgesics. Compounds commonly listed as incompatible include atropine sulfate, pethidine hydrochloride, metocurine iodide, fentanyl citrate, morphine sulfate, pentazocine lactate, silicones, suxamethonium chloride, tubocurarine chloride, and compound sodium lactate injection. Only preservative-free diluents should be used to reconstitute methohexital sodium; precipitation may occur if a diluent containing a bacteriostatic agent is used.

Stability. Solutions of methohexital sodium in Water for Injections are stable for at least 6 weeks at room temperature; however reconstituted solutions should be stored no longer than 24 hours as they contain no bacteriostatic agent. Solutions in glucose or sodium chloride injections are stable only for about 24 hours.

Adverse Effects and Precautions

As for Thiopental Sodium, p.1795.

Excitatory phenomena are more common and induction less smooth with methohexital than with thiopental. Methohexital should be used with caution, if at all, in patients with a history of epilepsy.

See also Adverse Effects and Precautions for General Anaesthetics, p.1779.

Incidence of adverse effects. In a study of 4379 uses of methohexital in 2722 dental patients the total dose ranged from 20 mg to 560 mg (with a mean of 151 mg), and the duration of treatment was 8 to 32 minutes.[1] Complications included: restlessness not controlled by diazepam (292 cases), respiratory complications (214), uncontrollable crying during recovery (73), pain along vein (45) with thrombophlebitis (5), jactitations (22), and allergic reactions (10).

1. McDonald D. Methohexitone in dentistry. *Aust Dent J* 1980; **25:** 335–42.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were receiving methohexital, and the American Academy of Pediatrics[1] considers that it is therefore usually compatible with breast feeding.

In a study[2] of 9 breast-feeding women undergoing general anaesthesia, it was estimated that the exposure of a breast-fed infant to methohexital would be less than 1% of the maternal dose after induction with methohexital. Breast feeding was not interrupted during the study and none of the infants appeared drowsy or sedated.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 26/05/04)
2. Borgatta L, *et al.* Clinical significance of methohexital, meperidine, and diazepam in breast milk. *J Clin Pharmacol* 1997; **37:** 186–92.

Effects on the nervous system. Two case reports of seizures induced by methohexital in children with seizure disorders.[1] Seizures are considered a rare adverse effect of methohexital. In 48 000 patients given methohexital, only 3 developed clonic-type seizures.[2]

A case of a tonic-clonic seizure possibly due to an interaction between paroxetine and methohexital is discussed below.

1. Rockoff MA, Goudsouzian NG. Seizures induced by methohexital. *Anesthesiology* 1981; **54:** 333–5.
2. Metriyakool K. Seizures induced by methohexital. *Anesthesiology* 1981; **55:** 718.

Pain on injection. Methohexital is associated with severe pain particularly if veins on the back of the hands are used. The incidence of pain on injection may be reduced by using a forearm vein or by pre-injection with lidocaine.

Porphyria. Methohexital is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Rebound anaesthesia. Rebound of anaesthesia with abolition of reflexes and depression of respiration occurred in a 6-year-old