4 American Academy of Clinical Toxicology and European Association of Poisons Centres. Position statement: single-dose activated charcoal. *J Clin Toxicol-Clin Toxicol* 1997;35:721-41.
5 American Academy of Clinical Toxicology and European Association of Poisons Centres. Multiple-dose activated charcoal. *J Clin Toxicol-Clin Toxicol* (in press).
6 American Academy of Clinical Toxicology and European Association of Poisons Centres. Gastric lavage. *J Clin Toxicol-Clin Toxicol* 1997;35:711-9.
7 Henry JA, Hoffman JR. Continuing controversy on gut decontamination. *Lancet* 1998;352:420-1.
8 Neuvonen PJ, Vartiainen M, Tokola O. Comparison of activated charcoal and syrup of ipecacuanha in preventing drug absorption. *Eur J Clin Pharmacol* 1983;24:557-62.
9 Menzies DG, Busuttil A, Prescott LF. Fatal pulmonary aspiration of oral activated charcoal. *BMJ* 1988;297:459-60.
10 Saetta JP, Quinton DN. Residual gastric content after gastric lavage and ipecacuanha-induced emesis in self-poisoned patients: an endoscopic study. *J R Soc Med* 1991;84:35-8.
11 Pond SM, Lewis-Driver DJ, Williams GM, Green AC, Stevenson NW. Gastric emptying in acute overdose: a prospective randomised controlled trial. *Med J Aust* 1995;163:345-9.
12 American Academy of Clinical Toxicology and European Association of Poisons Centres. Position statement: ipecac syrup. *J Clin Toxicol-Clin Toxicol* 1997;35:699-709.
13 American Academy of Clinical Toxicology and European Association of Poisons Centres. Whole bowel irrigation. *J Clin Toxicol-Clin Toxicol* 1997;35:753-62.
14 Visser L, Stricker B, Hoogendoorn M, Vinks A. Do not give paraffin to packers. *Lancet* 1998;352:1352.
15 Lancashire MJR, Legg PK, Lowe M, Davidson SM, Ellis BW. Surgical aspects of international drug smuggling. *BMJ* 1988:296:1035-7.
16 Choudhary AM, Taubin H, Gupta T, Roberts I. Endoscopic removal of a cocaine packet from the stomach. *J Clin Gastroenterol* 1998;27:155-6.
17 Brown SD, Piantadossi CA. In vivo binding of carbon monoxide to cytochrome c oxidase in rat brain. *J Appl Physiol* 1990;68:604-10.
18 Pace N, Strajman E, Walker EL. Acceleration of carbon monoxide elimination in man by high pressure oxygen. *Science* 1950;111:652-4.
19 Ducasse JL, Celsius P, Marc-Vergnes JP. Non-comatose patients with acute carbon monoxide poisoning: hyperbaric or normobaric oxygenation? *Undersea Hyperb Med* 1995;22:1-9.
20 Thom SR, Tber RL, Mendiguren II, Clark JM, Hardy KR, Fisher AB. Delayed neuropsychologic sequelae after carbon monoxide poisoning: prevention by treatment with hyperbaric oxygen. *Ann Emerg Med* 1995;25:474-80.
21 Raphael J-C, Elkarrat D, Jars-Guincestre MC, Chastang C, Chasles V, Vercken JB, et al. Trial of normobaric and hyperbaric oxygen for acute carbon monoxide intoxication. *Lancet* 1989;ii:414-9.
22 Mathieu D, Wattel F, Mathieu-Nolf M. Randomized prospective study comparing the effect of HBO versus 12 hours NBO in non-comatose CO poisoned patients: results of the interim analysis. *Undersea Hyperb Med* 1996;23: 7-8.
23 Scheinkestel CD, Biley M, Myles PS, Jones K, Cooper DJ, Millar IL, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. *Med J Aust* 1999;170:203-10.
24 Hawton K, Ware C, Mistry H, Hewitt J, Kingsbury S, Roberts D, et al. Paracetamol self-poisoning. Characteristics, prevention and harm reduction. *Br J Psychiatry* 1996;168:43-8.
25 Paracetamol Information Centre. *Guidelines on the management of paracetamol poisoning*. London: Paracetamol Information Centre, 1999.
26 Routledge PA, Vale JA, Bateman DN, Johnston GD, Jones AL, Judd A, et al. Paracetamol (acetaminophen) poisoning. *BMJ* 1998;317:1609-10.
27 Prescott LF, Illingworth RN, Critchley JA, Stewart MJ, Adam RD, Proudfoot AT. Intravenous N-acetylcysteine: the treatment of choice for paracetamol poisoning. *BMJ* 1979;2:1098-100.
28 Dawson AH, Henry DA, McEwen J. Adverse reactions to intravenous N-acetylcysteine during treatment for paracetamol poisoning. *Med J Aust* 1989;150:1329-31.
29 O'Grady JG, Wendon J, Tan KC, Potter D, Cottam S, Cohen AT, et al. Liver transplantation after paracetamol overdose. *BMJ* 1991:303:221-3.
30 Harrison PM, Wendon JA, Gimson AE, Alexander GJ, Williams R. Improvement by acetylcysteine of haemodynamics and oxygen transport in fulminant hepatic failure. *N Engl J Med* 1991;324:1852-7.
31 Jones AL. Mechanism of action of N-acetylcysteine in acetaminophen poisoning. *Clin Toxicol* 1998;36:277-85.
32 Walsh TS, Hopton P, Philips BJ, Mackenzie SJ, Lee A. The effect of N-acetylcysteine on oxygen transport and uptake in patients with fulminant hepatic failure. *Hepatology* 1998;27:1332-40.
33 Denborough MA, Hopkinson KC. Dantrolene and "ecstasy." *Med J Aust* 1997;166:165-6.
34 Jones AL, Simpson KJ. Mechanisms and management of hepatotoxicity in ecstasy (MDMA) and amphetamine intoxications. *Aliment Pharmacol* 1999;12:129-33.
35 Henry JA, Jeffreys KJ, Dawling S. Toxicity and deaths from 3,4-methylenedioxymethamphetamine ("ecstasy"). *Lancet* 1992;340:384-7.
36 Winstock AR, King LA. Ecstasy and neurodegeneration. Tablets often contain substances in addition to, or instead of, ecstasy. *BMJ* 1996;313:423-4.
37 Bismuth C, Dally S, Borron SW. Chemical submission: GHB, benzodiazepines and other knock out drops. *J Clin Toxicol-Clin Toxicol* 1997;35:595-8.
38 Louagie HK, Verstrate AG, De Soete CJ, Baetens DG, Calle PA. A sudden awakening from a near coma after combined intake of gamma-hydroxybutyric acid (GHB) and ethanol. *Clin Toxicol* 1997;35:591-4.
39 Jacobsen D, McMartin K. Methylpyrazole—present status. *J Toxicol-Clin Toxicol* 1996;34:379-81.
40 Brent J, McMartin K, Phillips S, Burkhart KK, Donovan JW, Wells M, et al. Fomepizole for the treatment of ethylene glycol poisoning. *N Engl J Med* 1999;340:8832-8.

Lesson of the week

Insulin as a substance of misuse in a patient with insulin dependent diabetes mellitus

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The relation between substance misuse and poor compliance with treatment is well established in both general medicine and psychiatry.[1 2] Although young patients with insulin dependent diabetes mellitus may have lower rates of comorbid substance misuse,[3] there is direct evidence that their compliance with treatment is poor.[4] Patients with insulin dependent diabetes mellitus have an increased risk of developing a psychiatric disorder, particularly in the early course of their illness,[3] and treating the psychiatric disorder improves glycaemic control.[5]

Hypoglycaemic events are common in people with insulin dependent diabetes mellitus[6] and may be associated with cognitive, affective, and sometimes life threatening sequelae.[7] Specific mood changes caused by changes in blood glucose concentrations are idiosyncratic, and although negative affective states are the most common, positive changes such as giddiness and euphoria are also seen.[8] Although there is a strong relation between severe hypoglycaemia and tight glycaemic control,[9] cases of deliberate misuse of insulin have been reported. Typically, these patients either attempt suicide or feign illness.[10] We report the rare case of a patient with insulin dependent diabetes mellitus and no history of a psychiatric disorder who misused insulin regularly over a two year period for its euphoric effects. The consequences were ultimately serious.

Doctors should be alert to the possibility of insulin misuse, and should consider psychological evaluation, in an insulin dependent diabetic patient with poor control

Case report

A 30 year old man with insulin dependent diabetes mellitus was admitted to hospital. He had lost consciousness for two hours as a result of severe hypoglycaemia, and had then experienced prolonged confusion. The man, a college lecturer, was unmarried. Since his diagnosis three years previously, his diabetic control had been erratic (HbA_{1c} values ranged from 8%

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to 9.5%; normal range 2.7%-4.9%). He had had several episodes of severe hypoglycaemia, most of which had been managed at home. The patient's insulin treatment regimen consisted of a basal bolus dose of intermediate acting insulin at night and rapid acting insulin three times daily before meals.

The hypoglycaemic episode preceding the patient's admission to hospital was unexplained in terms of lifestyle or concomitant physical disease, and there was no evidence of microvascular disease. His HbA_{1c} value at admission was 10.1%, indicating poor recent glycaemic control, and he had failed to keep two outpatient appointments.

The man remained confused for more than three days after hospital admission. Although computed tomograms of the brain were normal and electroencephalographic findings were inconclusive, formal cognitive assessment one month later showed impaired intellectual functioning and memory functioning (performance IQ = 71 and general memory index = 69 on the revised Wechsler memory scale) in someone whose premorbid intelligence had been average (measured on national adult reading test). The patient had no insight into his cognitive dysfunction, but he complied with the recommendation of the psychologist that he should retire from work on health grounds.

Three months later the man was admitted to a psychiatric hospital because of depressed mood and ideas of self harm and was observed to have mood swings and irritability. He had no psychiatric history, although a collateral history from his family suggested an emotionally immature premorbid personality. Repeat cognitive assessment showed some improvement in his memory function (general memory index = 92), and his mood stabilised with antidepressant medication.

At this time he recounted his difficulties in coming to terms with the diagnosis of diabetes, his erratic glycaemic control, and his serendipitous discovery of the potential mood altering effects of hypoglycaemia. He confessed that he had been dosing himself secretly with soluble insulin (three 36 U vials) every two weeks over the previous two years to induce hypoglycaemia. He described a craving for the affective state it induced: "happy … disorientated … like when you're drunk … being unable to perceive things as they really were … feeling helpless."

The patient had no history of substance misuse and drank 8-10 units of alcohol a week. He sought no attention after these episodes of hypoglycaemia, and he prevented coma by having carbohydrate enriched drinks to hand. He clearly differentiated these episodes from the index episode described above which required hospital admission and which, he said, was a suicide attempt. This involved a larger dose of insulin (more than 200 U) and resulted in the coma and cognitive impairment described. Since the disclosure of insulin misuse the patient's medication has been supervised, and although his mood has improved considerably, his prognosis remains uncertain.

Discussion

Misuse of prescribed drugs is well described[11 12] and is not confined to drugs with the potential to create dependency.[13 14] To our knowledge, only four cases of misusing insulin to promote positive affective change have been reported. This is surprising, given the prevalence of both insulin dependent diabetes mellitus and substance misuse. Three of these cases involved people who were not diabetic but injected insulin to "get a kick,"[15] to feel "quite different,"[16] and for the "exquisite pleasure" associated with the perceived risk of death.[17] There is only one previous report of insulin misuse in a patient with insulin dependent diabetes mellitus.[18] That report described a male adolescent with a borderline personality disorder who compulsively sought the excitement and euphoria associated with a rapid lowering of his blood glucose concentration.

In our patient, regular insulin misuse over two years went unrecognised until his psychological distress culminated in a serious suicide attempt and a depressive illness. The consequences of this misuse were serious—a decline in cognitive function led to retirement from work. We alert doctors to the possibility of insulin as a substance of misuse in patients with insulin dependent diabetes and poor control, and recommend psychological evaluation where this is suspected.

Contributors: SB was the consultant psychiatrist to whom the index subject initially disclosed his dependency on the mood altering effects of insulin; at that stage she was unaware that insulin could have this potential for misuse. On the subject's admission to psychiatric hospital, EMC carried out an extensive literature search and then prepared a draft of the paper. DJO'H became involved in the care of the subject during his index admission to hospital in a coma. He supplied information on the subject's physical status and contributed to the final draft.
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1 Caminero JA, Pavon JM, Rodriguez de Castro F, Diaz F, Julia G, Cayla JA, et al. Evaluation of a directly observed six months fully intermittent treatment regimen for tuberculosis in patients suspected of poor compliance. *Thorax* 1996;51:1130-3.
2 Weiss RD, Greenfield SF, Najavits LM, Soto JA, Wyner D, Tohen M, et al. Medication compliance among patients with bipolar disorder and substance use disorder. *J Clin Psychiatry* 1998;59:172-4.
3 Kovacs M, Goldston D, Obrosky DS, Bonar LK. Psychiatric disorders in youths with IDDM: rates and risk factors. *Diabetes Care* 1997;20:36-44.
4 Morris AD, Boyle DI, McMahon AD, Greene SA, MacDonald TM, Newton RW. Adherence to insulin treatment, glycaemic control, and ketoacidosis in insulin-dependent diabetes mellitus. *Lancet* 1997;350:1505-10.
5 Lustman PJ, Griffith LS, Clouse RE, Freedland KE, Eisen SA, Rubin EH, et al. Effects of nortriptyline on depression and glycemic control in diabetes. *Psychosom Med* 1997;59:241-50.
6 Potter J, Clarke P, Gale EA, Dave SH, Tattersall RB. Insulin-induced hypoglycaemia in an accident and emergency department: the tip of an iceberg? *BMJ* 1982;285:1182-90.
7 Gonder-Freerick LA, Clarke WL, Cox DJ. The emotional, social and behavioural implications of insulin-induced hypoglycemia. *Semin Clin Neuropsychiatry* 1997;2:57-65.
8 Gonder-Freerick LA, Cox DJ, Bobbitt SA. Mood changes associated with fluctuations in insulin-dependent diabetes mellitus. *Health Psychol* 1989;8:45-9.
9 Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of longterm complications in insulin-dependent diabetes. *N Engl J Med* 1993;329:977-86.
10 Kaminer Y, Robbins DR. Insulin misuse: a review of an overlooked psychiatric problem. *Psychosomatics* 1989;30:19-24.
11 Freedman JB, O'Dowd MA, McKegney FP, Kaplan IJ, Bernstein G, Biderman DJ, et al. Managing diazepam abuse in an AIDS-related psychiatric clinic with a high percentage of substance abusers. *Psychosomatics* 1996;37:43-7.
12 Szwabo PA. Substance abuse in older women. *Clin Geriatr Med* 1993;9: 197-208.
13 Craig DH, Rosen P. Abuse of antiparkinsonian drugs. *Ann Emerg Med* 1981;10:98-100.
14 Dorman A, Talbot D, Byrne P, O'Connor J. Misuse of dothiepin. *BMJ* 1995;311:1502.
15 Retsas S. Insulin abuse by a drug addict. *BMJ* 1972;iv:792-3.
16 Scarlett JA, Mako ME, Rubenstein AH, Blix PM, Goldman J, Horwitz DL, et al. Factitious hypoglycemia. Diagnosis by measurement of serum C-peptide immunoreactivity and insulin-binding antibodies. *N Engl J Med* 1977;297:1029-32.
17 Odie ELA. Insulin habituation and psychopathy. *BMJ* 1968;ii:346.
18 Scaramuzza A, Castellani G, Lorini R. Insulin abuse in an adolescent with insulin-dependent diabetes mellitus. *Eur J Pediatr* 1996;155:526.

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