Clinical review

Evidence based case report

Helping an obese patient make informed choices

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Not long ago, a patient, whom I will call Mrs Bariatrico, asked me to prescribe a diet pill for her. Mrs Bariatrico is a middle class woman aged 48 years. She is 1.6 m tall and weighs 77.2 kg. Her body mass index is 30.2 and her waist to hip ratio is 1.0. Mrs Bariatrico is healthy and does not smoke. She told me she plans to enrol in a commercial diet programme and believes her ability to change her lifestyle is good.[1] Her main concern is cosmetic—she values "looking good" and considers weight loss an important outcome.

As her primary care provider, I had several concerns. I knew the health insurance system that serves Mrs Bariatrico has no formal weight loss programmes, and the cost of appetite suppressing drugs is not reimbursed. I had some doubts about my own ability to manage obesity and asked the following questions:

- What are the actual health risks associated with obesity in a middle aged woman with few cardiovascular risk factors?
- What are the expected benefits and hazards of weight loss?
- What are Mrs Bariatrico's treatment options and their expected benefits and adverse effects?

Risks of obesity

Obesity is a chronic condition associated with hyperlipidaemia, hypertension, non-insulin dependent diabetes, gall bladder disease, some cancers, sleep apnoea, and degenerative joint disease.[2 3] Assessing the magnitude of risk for these conditions is complicated by several elements: many patients have several interacting risks; measuring the impact of some risks requires large, long cohort studies; and there are several confounding factors such as smoking and the duration of obesity. Regardless of these cautions, studies suggest that people who are more than 20% overweight have prevalences of hyperlipidaemia, hypertension, and diabetes that are between 1.5 and 3.5 times higher than those in people whose weight is normal.[2 3] The morbidity risks increase steadily from a body mass index of 25-30 and more rapidly at higher index values. Mortality risks increase above body mass indices of 20-27.[4 5] Relevant to Mrs Bariatrico, values of 29.0-31.9 in non-smoking middle aged women are associated with a relative mortality risk of 1.7 (95% confidence interval. 1.4 to 2.2; reference body mass index <19).[4]

Expected benefits and hazards

Randomised trials confirm several physiological benefits—including reductions in blood pressure and glucose and lipid concentrations—when weight is reduced by 10-15%.[2] Trials are neither large enough nor long enough to identify survival benefits. One observational study that lasted 12 years showed that an intentional weight loss of 0.5-9.0 kg in overweight women with disorders related to obesity was associated with a 20% reduction in all cause mortality (relative risk = 0.80; 0.68 to 0.94).[6] Potential hazards of weight loss include increased risks of gall stones during rapid weight loss and loss of bone density.[2]

Treatment options

A comprehensive systematic review from the Centre for Reviews and Dissemination evaluates treatment options appropriate for Mrs Bariatrico.[7] These include diet, exercise, and appetite suppressing drugs. A recent book describes many complementary therapies, including herbal remedies and chromium, but none have been adequately evaluated in controlled trials.[8]

Diet and exercise

Randomised controlled trials show that diets allowing an intake of 1200 kcal/day coupled with behaviour modification result in an approximate weight loss of 8.5 kg at 20 weeks.[9] Providing patients with food and meal plans, focusing on restricting fat as well as calories, and encouraging daily self monitoring of weight may be particularly effective strategies.[7] Very low calorie diets of less than 800 kcal/day result in a weight loss of approximately 20 kg at 12 to 16 weeks. One half to two thirds of the weight loss is maintained at one year.[9] Adding regular aerobic exercise results in minimal additional weight loss (approximately 2.5 kg after six months) and limits the amount of weight regained.[10] Resistance exercise has little effect on weight but increases the lean body mass.[10]

Appetite suppressants

Double blind randomised trials of longer than six months' duration show that antidepressant serotonergic agents such as fluoxetine are not effective weight loss treatments.[7 11] Other serotonergic agents, dexfenfluramine and fenfluramine (a racemic mixture of D-fenfluramine and L-fenfluramine), are effective when

BARNABY HALL/PHOTONICA

Wanting to "look and feel good" is often the spur to undertaking difficult lifestyle changes

combined with diet.[7 11] Five trials, in which 1029 patients participated, showed that the weight loss with dexfenfluramine was 2.5 to 8.7 kg greater than with placebo at six months; two trials showed losses of 2.6 and 4.2 kg at 12 months.[11] The combination of fenfluramine and phentermine (colloquially known as fen-phen) resulted in a loss of 9.7 kg after six months compared with placebo. Two new drug are sibutramine (serotonin and noradrenergic reuptake inhibitor) and orlistat (a fat absorption inhibitor). In one multicentre randomised trial, sibutramine showed a 2.8 kg loss compared with placebo at 12 months.[7] In a preliminary report from one centre of a multicentre trial comparing orlistat with placebo, weight reduction with orlistat was 3.1 kg more than with placebo at six months.[12] Trial data beyond 12 months of active treatment are not available for either of the two agents, and effects on mortality are not known.

Adverse effects that occur in more than 10% of patients taking dexfenfluramine include tiredness, diarrhoea, and dry mouth. Use of appetite suppressants (mostly dexfenfluramine) for more than three months is associated with pulmonary hypertension.[13] The risk is estimated at 23-46 cases per million per year or one in 22 000-44 000 patients taking appetite suppressing drugs. Highly publicised case series describe unusual heart valve deterioration in 60 otherwise healthy women taking newer agents.[14 15] Most were taking the combination of fenfluramine and phentermine, but six were taking either fenfluramine or dexfenfluramine alone.[14 15] In addition, a case series of 291 asymptomatic people taking these drugs showed that 92 had evidence of valvular disease, primarily aortic regurgitation.[16] This information prompted manufacturers to withdraw dexfenfluramine and fenfluramine from the market in September 1997.

The informed decision

I gave Mrs Bariatrico feedback on the health risks of obesity, listed the treatment options, and advised her about the expected effects. She viewed the health risks of obesity as relatively minor and reiterated her primary value of losing weight so she would "look and feel good." She was surprised that the weight loss expected from diet pills was not greater and worried about possible serious adverse heart effects. She was determined to try a low fat, low calorie diet and daily exercise. I praised her willingness to tackle difficult lifestyle changes. On her way out the door, she turned, smiled at me, and requested a prescription for phentermine—one of the few remaining appetite suppressants available on the market.

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Endpiece

Limited opportunities

In 1847 Cockburn said, "The whole paying surgical practice of Scotland would scarcely keep one gentleman-like scalpel going."

D Power, *British Masters*

Submitted by Ann Dally, Wellcome Institute for the History of Medicine

Lesson of the week

A foodborne outbreak of organophosphate poisoning

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Indiscriminate use of organophosphates without public education on safety increases the potential threat of foodborne outbreaks of poisoning

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Foodborne diseases have a major impact on public health. Early and correct identification of the cause of an outbreak of food poisoning enables specific treatment to be started as soon as possible, and this can be life saving. We report an outbreak of fatal food poisoning caused by the pesticide malathion.

Case reports

On 6 July 1997, 60 men aged 20-30 years attended a communal lunch at which they ate chapatti, cooked vegetables, pulses, and halva. They all developed nausea, vomiting, and abdominal pain over the next three hours. The men were taken to a local primary healthcare centre where they received treatment for their symptoms. Fifty six responded to the treatment and were discharged home the same day. However, the condition of the remaining four patients deteriorated. Their level of consciousness fell, and they developed respiratory distress and generalised muscular weakness. The next day they were moved to an urban emergency hospital.

Case 1

A 20 year old man presented with miosis, sweating, impaired consciousness, and hypotension. The muscle power in his arms and legs was graded as 3/5. Reflexes in the arms and legs were reduced, but he did not have sensory impairment. He had noticeable weakness of neck flexion, to the extent that he could not raise his head off the pillow. Initial treatment included intravenous fluids, antiemetics, and antibiotics. On the second day after admission to the urban emergency hospital, he developed respiratory insufficiency. Because he needed endotracheal intubation and intermittent positive pressure ventilation, he was transported immediately to a tertiary care hospital. Over the next 24 hours he developed type II respiratory failure with paralysis of thoracic, neck, and diaphragmatic muscles. He underwent tracheostomy and was ventilated mechanically for the next few days. He was treated with atropine and pralidoxime (1 g intravenously), but his neurological status did not improve appreciably, nor did his muscle strength improve much over the nine days after admission to hospital. On day 10 he had a cardiac arrest and could not be revived.

Cases 2, 3, and 4

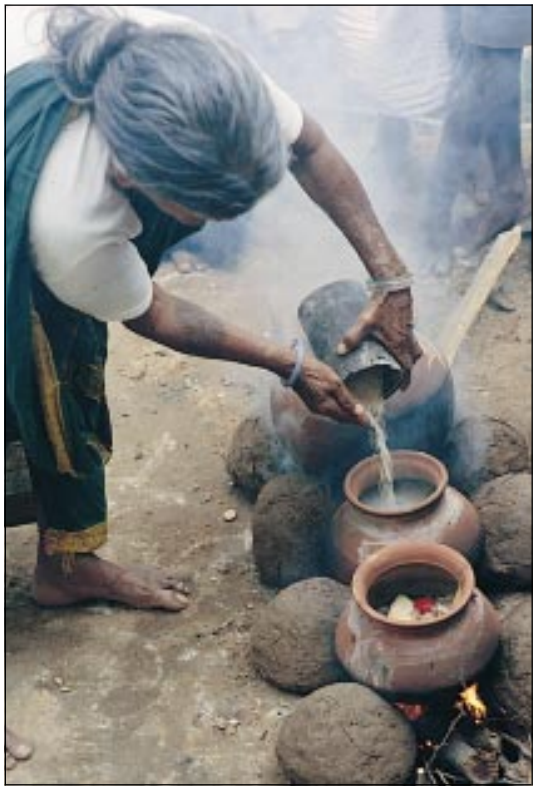
Three patients developed mild generalised muscle weakness and respiratory distress, and their level of consciousness was reduced. They were admitted to the urban emergency hospital for further management, responded to treatment for their symptoms, and were discharged home a week later.

Investigations and assays

The 60 men who succumbed to food poisoning had eaten a lunch cooked in the community kitchen. Detailed questioning of those working in the kitchen showed that on the morning of the outbreak the kitchen had been sprayed with pesticide containing malathion, an organophosphate. The raw materials for cooking were stored in open jute bags. All 60 people who had eaten the meal developed signs and symptoms, but the severity of illness was greatest in case 1. He had eaten at least eight chapatti while the others had eaten three or four.

Before treatment at the tertiary care hospital was started, samples of serum and gastric fluid were obtained from case 1 for *Clostridium botulinum* toxin mouse assay. Samples of the wheat flour, chapatti, spices, and oil used in the meal and samples of faeces and gastric fluid from case 1 were cultured anaerobically for *C botulinum*. The results of toxin bioassay and culture for *C botulinum* were negative. The neurological features of the patients and the history of insecticide spraying prompted the collection of gastric aspirate from case 1 for toxin and chemical analysis. The gastric aspirate was positive for organophosphate.[1] This positive test result was achieved seven days after case 1 had been admitted to the tertiary care hospital.

Food samples from the shared lunch, including leftover chapatti, wheat flour, spices, and oil, were also sent to the toxicology laboratory for analysis. Culture and toxin assay of the sample of chapatti and wheat



FRANCESCO RIZZO/IMPACT

Even simple food may have . . .

DOMINIC SANSONI/EPL

. . . hidden dangers

flour were negative for *C botulinum*, but an organophosphate compound was detected. The remaining foods were negative for toxins and chemicals.

Discussion

In developing countries, the widespread use of organophosphates has been accompanied by an appreciable increase in the incidence of poisoning with these agents. This is a result of their easy availability, indiscriminate handling and storage, and the lack of knowledge about the serious consequences of poisoning. Latest estimates from the World Health Organisation indicate that each year one million serious accidental poisonings and two million suicide attempts involving pesticides occur worldwide.[2]

In the incident we describe, the severity of the illness in case 1 raised the possibility of botulism, and *C botulinium* was sought by microbiological investigation. However, when subsequent investigation showed that the kitchen had been sprayed with insecticide, a complete toxicological examination was carried out. In fact, the presenting features of case 1 were more consistent with organophosphate poisoning than botulism. These included rapid onset of the illness (within three hours of the meal), excessive sweating, depressed level of consciousness, miosis, and hypotension. The rapid clinical improvement seen in most patients (except case 1) over 24 hours was also more consistent with organophosphate poisoning than botulism.

All 60 patients had a well defined cholinergic phase. Cases 1 to 4 subsequently developed symptoms of the intermediate syndrome. The intermediate syndrome set in nearly 24 hours after the exposure to organophosphate, well before the patients had recovered from the initial cholinergic crisis. It is characterised by weakness of the proximal limb muscles, neck flexor muscles, motor cranial nerves, and respiratory muscles; it generally occurs 24-96 hours after poisoning and after the resolution of a well defined cholinergic phase. The respiratory insufficiency in all four cases drew attention to the onset of this syndrome. Even though they did not meet fully the criteria for the intermediate syndrome—mainly because they developed the symptoms early—most of their symptoms and signs agreed with this phase. On the basis of these observations, a diagnosis of early intermediate syndrome was made in these four patients.

A similar observation has been made by Senanayake and Karalliedde in their series of patients with organophosphate poisoning who developed intermediate syndrome.[3] The difference in the severity of the neuropathy and the clinical course observed in our four cases can be attributed to differences in the amount of organophosphate ingested—case 1 ate eight chapatti. Delay in making a correct diagnosis, evaluation, and management of organophosphate poisoning meant that case 1 did not receive appropriate treatment early enough. Furthermore, the development of the intermediate syndrome before its expected onset has been described previously with organophosphates such as dimethoate, fenthion, methamidophos, and monocrotophos—but never with malathion.[4]

The increasing and indiscriminate use of organophosphates as agricultural and household insecticides without any accompanying public education about their storage and safe use increases the potential for more outbreaks of food poisoning. This report is a reminder to epidemiologists, toxicologists, and microbiologists that organophosphate food poisoning is a continuing hazard, especially in developing countries. Health professionals should be familiar with the acute illness syndromes associated with organophosphate poisoning so that they can differentiate between these and the neurological symptoms caused by other forms of poisoning. Skilled and prompt treatment can provide a good outcome for a potentially lethal condition.

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