Hypoglycaemia and hypothermia due to nimesulide overdose

Editor—Although toxicity due to chronic administration of nimesulide has been reported,1 to the best of our knowledge there is no report about poisoning due to a single ingestion. We report a 20 month old boy who accidentally took a high dose of nimesulide; 40 mg/kg, 8 times the recommended daily dose.

Physical examination was unremarkable. Laboratory findings, including hepatic and renal function, were normal, except for low to borderline glucose concentration (3.27 mmol/1) and mild acidosis (pH 7.35, bicarbonate 16.9 mmol/l). Gastric lavage with activated charcoal and being alert for hypoglycaemia and acidosis was recommended to our intensive care unit. After eight hours, serum glucose concentration was 3.44 mmol/l, venous pH 7.28 and bicarbonate 18.5 mmol/l. His systolic blood pressure and body temperature fell to 60 mm Hg and 35.0°C (axillary), respectively. The patient was rewarmed and the intravenous infusion rate increased to 2000 ml/day. Six hours later, his serum glucose concentration was 4.44 mmol/l, venous pH 7.33, and bicarbonate 16.5 mmol/l. Body temperature and blood pressure rose and 20 hours after admission all vital signs became normal, mild acidosis resolving within 24 hours. He was discharged after 48 hours. Physical examination and laboratory findings were normal six days after discharge.

The most striking events in our patient were the development of hypotension and hypothermia. Hypothermia has been reported due to non-steroidal anti-inflammatory drugs overdose,2 but hypothermia due to the antipyretic action of nimesulide has not been reported. Nimesulide produces a dose dependent antipyretic action in rats by inhibiting COX-23 but its effect under normothermic conditions is not known. Although it has been reported that nimesulide might be given to children with hypoglycaemia,4 it may cause hypoglycaemia in high dosages.

We advise frequent monitoring of vital signs and being alert for hypoglycaemia and acidosis in managing acute nimesulide overdose.

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it can be familial suggesting a learnt behaviour, or developmental and emotional issues may be involved. In America it is classified as an eating disorder, in the UK it is considered a behavioural disorder; it can also be an obsessive-compulsive disorder, or a manifestation of depression.

Our children could shed no light on their compulsion. In six cases the parents found the behaviour so unacceptable that they requested psychological intervention and in four, the behaviour has now stopped. Thus whilst we find this behaviour fascinating, we are no clearer in understanding the aetiology of pica for some in this small population of children with SCD.

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Letters

Maternal nutrition and pregnancy outcome

EDITOR,—Symonds et al raise interesting issues about the potential use of animal models in examining the impact of nutrition during pregnancy on future risk of adult disease.1 However, their discussion of recent epidemiological research in humans includes several important factual inaccuracies. The authors imply that our analyses and those of Godfrey et al grouped women into categories of energy intake, and suggest that different results might have been obtained had “all the raw data points [been used] to determine potential relations between maternal nutrition and birth weight”. Yet as clearly indicated in both papers,1,2 this is precisely the analysis that was conducted. For information, figure 1 shows the relation of maternal energy intake to birth weight in our study. In each paper, the cut points used in tables to illustrate the relationship between energy intake and birth weight were neither “unclear” nor “arbitrary” but were, as stated, tertiles. Symonds et al drew attention to the “striking difference” in energy intake between our study and that of Godfrey et al whilst also suggesting that we should combine our data in a meta-analysis. We argue that the differences are not particularly striking given the different methodologies used for dietary assessment. It would not be appropriate to combine in a meta-analysis data collected in contrasting ways from women at different stages of pregnancy. In any case, our study individually has sufficient statistical power to detect clinically important effects.

In addition, animal experiments above observational epidemiology in humans, Symonds et al confuse two separate issues. First, there is the biologically interesting question of whether maternal diet can influence the outcome of pregnancy. This has already been demonstrated in animals. Second, there is the question of whether maternal diet does influence the outcome of human pregnancy. This question is of clinical and public health importance. It cannot be answered by animal experiments (unless one were to make the dubious argument that the errors associated with extrapolating data from animal models to humans are less than those from using self-reported data on human dietary intake). We do not argue that maternal energy intake can never be associated with birth weight. Under extreme circumstances, such as those in the animal experiments cited by Symonds, or in Third World countries, it may be. However, this is no basis for suggesting it has any importance to populations in industrialised countries.

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Nitrous oxide and vitamin B<sub>12</sub>

EDITOR,—The paper by Kanagasundaram et al on the use of nitrous oxide to alleviate pain, and anxiety during painful procedures fails to mention the effect of this gas on cobalamin metabolism. Nitrous oxide inactivates cob(III)alamin, the active derivative of vitamin B<sub>12</sub>, and essential cofactor for the transfer of the methyl group from methyltetrahydrofolate to homocysteine to form methionine. For subjects with good body stores of cobalamin this effect is unimportant, but no-one using this agent should remain unaware of the potentially devastating complications in the nervous system of using nitrous oxide in subjects who are of borderline or deficient vitamin B<sub>12</sub> status. Onset of subacute combined degeneration affecting the brain and spinal cord is a well documented event when individuals with low body stores of cobalamin are exposed to nitrous oxide.1

There is a long list of situations which put children at risk of cobalamin deficiency—for example, diets low in animal products, synthetic feeding of any description, small bowel malfunction, any prolonged illness with disturbance of feeding behaviour, especially if combined with increased metabolic demands—for example, systemic malignancy or chemotherapy. Children with chronic conditions often need painful procedures, and depleted cobalamin stores may not be apparent unless measurements of serum B<sub>12</sub> are made routinely. What is more, repeated use of nitrous oxide depletes the body stores of cobalamin even in well people. Given the scale of use which would result from routine use of nitrous oxide in children undergoing painful procedures, there should be real concern about the potential for an accident in a child with occult cobalamin deficiency. The message must be: never forget vitamin B<sub>12</sub> when thinking of using nitrous oxide.

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The outcome of specialist registrars in the southwest region

EDITOR,—The UK national directive is to increase consultant paediatric numbers substantially over the next 5–10 years which requires the delivery of suitably trained doctors. Higher specialist training in paediatrics takes five years and there is concern that the current number of trainees will produce more consultants than there are posts, so trainee numbers will still have to be reduced. The southwest regional training committee has expressed concern that trainees are not completing training within five years for a variety of reasons. We therefore reviewed the training times and outcome of the 90 specialist registrars (SpRs) who have trained in our region since the introduction of the Calman training scheme.

The impact of the high proportion of women entering paediatrics needs to be addressed. Our review confirms that 29% of trainees are training flexibly, which will increase their training time for anything up to 10 years. All these are in the flexible training scheme that requires at least eight 40-hour sessions per week, training times will be even further extended. Also our training committee is concerned that five SpRs have resigned before completing training. Four of these are women who resigned because, despite working part-time, they felt that the career process was incompatible with family life.

Of the trainees who trained flexibly and who have obtained consultant posts, four have chosen to work as part time consultants. The other two would have done so had the opportunity been available. Female trainees will be longer to train than their male colleagues and also time out for maternity leave. Moreover, each trainee will not necessarily translate into one whole time equivalent consultant. In our region 47% of trainees are having their Certificate of Completion of Specialist Training (CCST) date reviewed; the average time for them to complete a five year CCST programme based on current calculations is 6.3 years. Reasons include sickness.
Adrenaline syringes: community perspective

Editor,—We read with interest the paper by Unsworth regarding the over prescribing of adrenaline syringes. We are sure we are not the only community paediatric team who have similar concerns, although perhaps from a different perspective. Dr Unsworth writes of the safety issues. We have more experience of the practical problems.

Thanks to the availability of prompt training for school staff by community personnel, it is now rare for a child to actually be excluded from school because they have an adrenaline injection device. However, they may very well be excluded from other activities such as guide camp or trips abroad.

There is also the increasing problem of young people with adrenaline injection devices moving on to college or work places. Who should train staff there?

Other problems with adrenaline injection devices in our local community include two being lost on the bus, and one being accidentally fired into the interphalangeal joint of a child’s thumb with the needle becoming bent like a fish hook.

There is also the issue of keeping them in date. Parents often forget to renew them, particularly those kept in school. Whilst it does not need to be kept in a refrigerator, adrenaline does deteriorate in warm conditions, and injection devices should be checked to make sure the adrenaline inside remains clear and colourless.

Often, an adrenaline injection device has been prescribed with no demonstration to the child or family on how to give it, nor when to give it. Surely adrenaline should also be prescribed in every case? In most children, it is the only medication, which is going to be needed. Dr Unsworth gives no instructions on when to call an ambulance. They could easily make the mistake of trying to take a deteriorating child to hospital in their own car, instead of calling a paramedic ambulance, or even assume that they do not need to go to hospital at all if they have given adrenaline. As Dr Unsworth points out, the adrenaline injection does not always save the child’s life.

We would suggest that when an adrenaline injection device is prescribed it must be demonstrated to both the parent and child (if the child is old enough). A dummy pen is helpful for this. Demonstration should be repeated with each repeat prescription of the device. The child and their family should always have a written management protocol, including instructions on expected symptoms, when to give antihistamine, when to call an ambulance, and when to give adrenaline. Such a protocol can then be passed rapidly to the community paediatric team to support the prompt training of school staff.

It is worth remembering that clinical responsibility for the safe administration of a drug rests with the prescriber.

Mary McGraw
Regional advisor in paediatrics and chairman of the southwest regional paediatric training committee

Controversies in paediatrics?

Editor,—I was very disappointed to see that the first contribution to the Controversy series was not written by a paediatrician. There are plenty of controversial topics in paediatrics, including the one cited. There are also plenty of paediatricians perfectly qualified to be an invited commentator on the topics cited above, again including the topic cited. The absence of a contrasting viewpoint in the latest series of food related deaths.

The BPA and latterly RCPCH have championed for decades the holistic approach to the care of children. Paediatricians are best placed to assess the integrated needs of a child with medical problems. This principle is very relevant to developing areas in which prompt administration of epinephrine will not save every person who has anaphylaxis. Anaphylaxis is a critical situation in which prompt administration of epinephrine may (but occasionally may not) save a life. I think it unarguable that it is better to self treat and probably survive than not self treat and possibly die. Unsworth quotes one early paper about anaphylaxis from the US and more recent British data. These papers all go to more than one point. The adrenaline injection device is prescribed it must be demonstratively trained. Epinephrine may (but occasionally may not) save a life.

It is very hard to prove that epinephrine does not always save the child’s life. I think it unarguable that it is better to self treat and probably survive than not self treat and possibly die. Unsworth quotes one early paper about anaphylaxis from the US and more recent British data. These papers all go to more than one point. The adrenaline injection does not always save the child’s life. I think it unarguable that it is better to self treat and probably survive than not self treat and possibly die. Unsworth quotes one early paper about anaphylaxis from the US and more recent British data. These papers all go to more than one point.

Letters

Adrenaline syringes are vastly over prescribed. Arch Dis Child 2001;84:410–11.

1 Unsworth DJ. Adrenaline syringes are vastly over prescribed. Arch Dis Child 2001;84:410–11.
kits allows normal life to go on, involving school, overnight stays at friends, camping, and other normal activities of childhood. Anecdotally, parents seem to me less stressed when they leave clinic with information (however awful the scenarios described) and reasonable strategies than when they arrive. I have never met a parent who reported being more scared of the epinephrine kits than of the prospect of allergen exposure (with or without epinephrine available).

Families must be taught when to use epinephrine and how to use autoinjection. Until doctors can tell families that anaphylaxis will never happen we should continue to empower families, ensuring they are ready to respond as best they can to the disaster that allergen exposure represents. When anyone develops a real treatment for food related anaphylaxis I can stop prescribing epinephrine kits to people who currently need them.

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Appropriate prescription of epinephrine remains the best available treatment

EDITOR,—Epinephrine kits enable a food allergic child at risk of anaphylaxis to lead a normal life and participate in childhood activities that could easily be denied by a parent terrified of another allergen exposure. Avoidance of allergens rather than rescue epinephrine therapy is the basis of current management of food allergy. However, unexpected exposures are inevitable. Fifty eight per cent of children followed for five years experienced adverse reactions from accidental peanut exposure.1 Peanut is the most common food allergen causing anaphylaxis and pervades all too often, in food processing. Anaphylaxis related to foods most commonly occurs in patients who have had previous severe reactions. However, minor initial reaction does not exclude a subsequent severe reaction to peanut. Any person with a history of anaphylaxis deserves the best available protection. It is reasonable to always have two Epipens available both at home and at school. A second Epipen provides back up if a faulty technique is used or one syringe is damaged. Anaphylaxis may be biphasic, recurring in 3% of children admitted with anaphylaxis.2

As advocates of children, paediatricians are unlikely to hand out epinephrine syringes without due consideration of the impact on the child and his or her family. A comprehensive plan with written information is essential for any child seen with a food allergy whether or not epinephrine is prescribed. Sicherer et al showed 20% of children did not carry epinephrine outside the home and only 55% had unexpired epinephrine on them. However, successful demonstration was associated with repeated prescriptions, membership of a lay organisation for food allergy, and being reviewed by a doctor. Training packages for schools such as that devised by Vickers in Cambridge3 are valuable.

Unsworth states that “Community use should be much more restricted with increased involvement and reliance on trained medical staff”. Food allergy is the most common cause of anaphylaxis in children outside hospital. Early recognition and use of epinephrine is vital for successful outcome. The median time to respiratory or cardiac arrest was thirty minutes in untrained, unprepared anaphylaxis in one series.2 Surely this implies that the community is the setting where epinephrine should be given by appropriately trained parents and carers to a food allergic child with signs of anaphylaxis. Parents should be empowered as limited resources prevent medical staff being present immediately. Indeed, epinephrine IV by trained medical staff also appears to be more hazardous than the use of epinephrine in asthmatic patients.3

In the absence of any other treatments for food related anaphylaxis, the considered use of epinephrine kits as part of an integrated management plan is the best choice.

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Reply

EDITOR,—I was pleased to see that my article provoked lively discussion of this important issue. I am not surprised that likely to be even more concerned about poor compliance. I agree with Wolff and Rumney that adrenaline should never be the sole prescription. In addition to antihistamines, prednisolone has a place. The idea of a written management summary is a good one.

Hourihane contrasted prescription of adrenaline with provision of insulin syringes in diabetes mellitus. We do not restrict provision of insulin syringes in that context because to do so would inevitably encourage hypoglycaemia and ill health in all cases, ranging from coma to retinopathy. The risk benefit ratio is clearly in favour of daily insulin use. By contrast, the “very high” number of adrenaline prescriptions required to (perhaps) prevent death in food allergic individuals, does by contrast raise concerns about the risk benefit ratio.

In our clinics, where we see large numbers of both adults and children, reviewing the last few years we have seen one fatal and two near fatal episodes related to adrenaline usage (submitted for publication). Admittedly, all three were in adults. Hourihane prescribes “epinephrine to “most (but not all) subjects who have reacted to peanut”. He does not say that all others will surely demand adrenaline. He would not prescribe adrenaline in the absence of a significant clinical history of true nut allergy, (and I applaud that) but others regrettably do, and I know from personal experience that once the mistake is made, it is hard to reverse. I like the seat belt analogy, but seat belts have few side effects. Regarding positive and negative predictive values of IgE based allergy blood tests, my point is that often these tests are misleading. Patients with eczema, (a common finding in those presenting with possible nut or food allergy) typically have high background IgE levels and false positives are common.

Dr Abay reminds us that trained medical staff including doctors may administer adrenaline incorrectly. That fact does not justify deligation of responsibility to the general public inste. They are surely more likely to make an informed diagnosis. Patients should be empowered as limited resources prevent medical staff being present immediately. Indeed, epinephrine IV by trained medical staff also appears to be more hazardous than the use of epinephrine in asthmatic patients.3

In the absence of any other treatments for food related anaphylaxis, the considered use of epinephrine kits as part of an integrated management plan is the best choice.

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1 Unsworth DJ. Adrenaline syringes are vastly over prescribed. Arch Dis Child 2001;86:510c. 1 December 2001. Downloaded from http://adc.bmj.com/ on March 26, 2022 by guest. Protected by copyright.