Patients' self administration of hydrocortisone

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Br Med J 1990;301:1312

Properly managed, Addison's disease carries a normal life expectancy.^{1,2} The only related risk of death is inadequate glucocorticoid replacement treatment at times of illness or other stresses; this can lead to an adrenal crisis. All patients should know how to adjust their steroid dose when they are ill, and they should know which illnesses require such adjustment. We believe that all patients should have a supply of injectable hydrocortisone at home and be able to give themselves an injection if vomiting persists or if there is delay in obtaining medical attention. As it is the policy of our unit to instruct all patients in these matters we audited our patients to determine their knowledge.

Patients, methods, and results

Twenty six patients with Addison's disease were identified from unit records, 22 women and four men with a mean age of 49 (range 18-79) years and mean duration of disease of 15 (1-35) years. Patients were sent a multiple choice questionnaire of 33 questions: six questions inquired about background information and current steroid replacement treatment and nine referred to self treatment practice with oral steroids during illness and 18 to self treatment with parenteral steroids. Twenty five (96%) patients replied.

Fifteen patients had never changed their oral steroid dosage. Nine of these had had Addison's disease for over 16 years and three for over 30 years. Seven patients were wholly correct about which illnesses required adjustment of dosage, 15 were partially correct, and three were totally wrong.

Ten responders (40%) claimed never to have been instructed in injecting hydrocortisone. Although the case notes recorded instruction in only three of these patients, all should have been instructed in accordance with unit policy. None of the 10 patients had a home supply of injectable hydrocortisone. Fifteen responders recalled instruction, and written confirmation of this appeared in six of their case notes. Only six had a home supply of injectable hydrocortisone. One of these six had no needles or syringes, and the expiry date of one patient's supply had passed. A further two patients thought they would not be able to inject themselves. Thus only two patients among the cohort of 25 responders could self administer parenteral hydro-

cortisone, but one of them did not take the parenteral steroids on holiday.

Seventeen of the 25 patients had received parenteral steroids in the past. For 11 patients this had been an imminent or established adrenal crisis requiring inpatient treatment with intravenous hydrocortisone; the other six had received parenteral steroids at the time of elective surgery. None of these patients had had intramuscular hydrocortisone before admission. Only two of these patients currently had injectable hydrocortisone at home, and both were unable to self administer it. Twenty patients (80%) always carried either a steroid card or Medicalert bracelet indicating that they were on maintenance steroids for Addison's disease.

Comment

Nearly half of these patients with Addison's disease had had an adrenal crisis, yet the group as a whole remained ignorant. Only a quarter had injectable hydrocortisone at home, and only two could self administer it. In a population well served by general practitioners this may not jeopardise the patient, but in rural areas, inner city environments, or transient accommodation patients may be in danger of an adrenal crisis if medical advice is delayed. Rectal hydrocortisone is well absorbed and provides adequate cortisol for up to eight hours and may be an effective alternative to parenteral hydrocortisone.³

All our patients have now been sent a follow up instruction sheet and will be issued with injectable hydrocortisone and needles. Further instruction in using intramuscular hydrocortisone will be arranged. We suggest that, as part of the routine care of patients with Addison's disease, the knowledge of self treatment should be reinforced verbally and with an instruction sheet so that patients can self administer intramuscular steroids if necessary.

We thank Dr M Hartog, reader in medicine, Bristol Royal Infirmary, for permission to study his patients and Mrs Marion Mitchard for secretarial assistance. GDB is funded by Fidia.

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(Accepted 5 October 1990)

Hypoalbuminaemia after prolonged treatment with recombinant granulocyte macrophage colony stimulating factor

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Br Med J 1990;301:1312-3

Treatment with recombinant granulocyte macrophage colony stimulating factor is being evaluated in various clinical circumstances including after chemotherapy, and bone marrow transplantation, and in aplastic anaemia, the myelodysplastic syndrome, and AIDS.

Most trials have used intermittent dose regimens (for example, two weeks of treatment followed by two weeks without treatment), and dosages up to 32 µg/kg/day have been well tolerated with only minor side effects. At very high dosages serious side effects such as fluid retention, pericarditis, and thromboembolism have occurred.^{1,2}

We are evaluating the clinical value of recombinant granulocyte macrophage colony stimulating factor in the myelodysplastic syndrome and aplastic anaemia. The factor is given daily subcutaneously for 12 weeks, the initial dosage of 3 µg/kg/day being increased to 10 µg/kg/day after four weeks if there has been no response. Patients who respond (neutrophil count $>1.5 \times 10^9/l$) subsequently receive maintenance treatment for two weeks in every four. Patients are required to have normal renal and liver function at entry. We have treated nine patients, four of whom developed

hypoalbuminaemia. This finding has not to our knowledge been reported previously.

Case reports

Case 1—A 67 year old man with refractory anaemia with an excess of blasts developed hypoalbuminaemia while taking recombinant granulocyte macrophage colony stimulating factor at 3 µg/kg/day; his albumin concentration fell further when the dosage was increased to 10 µg/kg/day (figure). He developed oedema but had no evidence of heart failure or liver dysfunction. He did not have proteinuria or evidence of faecal loss of albumin. During maintenance treatment his albumin concentration recovered and fell only slightly with each treatment.

Case 2—A 78 year old woman with refractory anaemia received recombinant granulocyte macrophage colony stimulating factor at dosages of 3 and 10 µg/kg/day. Her albumin concentration fell to 20 g/l, and she developed oedema and ascites. There was no evidence of urinary or faecal loss of protein. Her albumin concentration improved only temporarily when infusions of albumin were given (figure). She developed several life threatening infections and severe wasting and died of gastrointestinal haemorrhage.

Case 3—A 70 year old man with refractory anaemia with an excess of blasts received recombinant granulocyte macrophage colony stimulating factor at dosages of 3 and 10 µg/kg/day. Hypoalbuminaemia of 21 g/l occurred (figure) but did not cause symptoms. He failed to respond to 12 weeks' treatment. He subsequently developed acute myeloblastic leukaemia and died of septicaemia.

Serum albumin concentration (normal range 35-50 g/l) in four patients who developed hypoalbuminaemia during treatment with recombinant granulocyte macrophage colony stimulating factor (dosages and duration of treatment indicated by horizontal bars)

Case 4—A 53 year old man with severe aplastic anaemia received recombinant granulocyte macrophage colony stimulating factor at dosages of 3 and 10 µg/kg/day. While he was receiving 10 µg/kg/day his albumin concentration fell to 19 g/l (figure). He failed to respond to treatment, which was stopped after 10 weeks. He died of septicaemia.

Comment

The fall in albumin concentration that occurred in these four patients was related to the duration of treatment and dosage of recombinant granulocyte macrophage colony stimulating factor. Hypoalbuminaemia recovered when treatment was withdrawn in case 1.

Transgenic mice, which carry the murine gene for granulocyte macrophage colony stimulating factor and express continual high serum concentrations of granulocyte macrophage colony stimulating factor, developed a fatal wasting syndrome.³ It was speculated that this was due to enhanced production of tumour necrosis factor. Treatment with granulocyte macrophage colony stimulating factor enhances production of other cytokines including interleukin 1, interferon γ, and tumour necrosis factor,^{4,5} and side effects of treatment have been ascribed to the release of these cytokines. Serial serum concentrations of tumour necrosis factor, interleukin 1, and interferon γ in two of our patients (cases 1 and 2) showed no consistent relation with the development of hypoalbuminaemia.

The finding that hypoalbuminaemia may occur during treatment with recombinant granulocyte macrophage colony stimulating factor suggests that caution should be exercised in using this growth factor over a long period.

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(Accepted 15 August 1990)

ONE HUNDRED YEARS AGO

Twelve months ago the Hospitals Association undertook the work of organising and maintaining an effective street ambulance for the metropolis. London was mapped out into districts on the basis of the police divisions, and it was decided that there should be 152 ambulances, including the 58 already at the police stations. The Chief Commissioner of the Metropolitan Police, the chief officer of the Metropolitan Fire Brigade, the authorities of the London hospitals, the railway companies, and others, have lent their co-operation, and placed suitable stations at the disposal of the Hospitals Association free of expense. A trial, conducted by the police and hospital authorities, extending over a period of three months, resulted in the unanimous selection of an ambulance having an iron frame, three bicycle wheels, with india-rubber tyres, and all the requisite appliances for rendering first aid to the injured, and this form has accordingly been adopted. There are now 40 Hospitals Association ambulances stationed within the four-mile circle, 20 being at fire brigade

stations, 15 at hospitals, 4 at industrial dwellings, and one at Holborn Viaduct. Permission has been obtained from the Chief Commissioner of the Metropolitan Police to station ambulances at various cab ranks; and, as soon as receptacles for these can be constructed, and a few other details are arranged, 18 stations of this class will be opened. Application is being made to the various metropolitan vestries for permission to place on lamp posts in large thoroughfares, near each ambulance station, notice plates stating where the nearest litter may be found. The completion of this service in every detail will shortly be an accomplished fact. The yearly cost, which is estimated at £300, will be defrayed by subscription, and already a sum of £1,500, to cover the initial outlay, has been received. The Right Hon. the Earl of Meath will take the chair at the last meeting of the seventh session of the Hospitals Association, at which a paper on the New Street Ambulance Service of the Metropolis will be read by Mr. Thomas Ryan, Secretary to St. Mary's Hospital. (*British Medical Journal* 1890;ii:912.)