Emergency treatment of hyperglycaemia in adult type-2 diabetic patients in primary care settings

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Abstract

Hyperglycaemic crises are common in adult type 2 diabetic patients in the Middle East and other developing countries. These need treatment under certain conditions, as part of the overall goal of striving for good glycaemic control in these patients, in order to delay or prevent diabetic complications. As oral hypoglycaemic agents (OHAs) are inefficient in these circumstances, we have devised a simple easily applied method for rapid control of these episodes. Intravenous saline re-hydration, is given with intramuscular soluble insulin in a dose chosen, according to patient's weight, age and level of hyperglycaemia. Blood glucose concentration is checked 3 hours after insulin injection. This regime reduces hyperglycaemia by an average of 40-60% in 3 hours, which is a more reliable level of reduction than that experienced with OHAs. Where insulin is readily available, its flexible use in this way can help greatly in achieving good glycaemic control in type 2 diabetic patients.

Key words: *Hyperglycaemic crisis, adult type 2 diabetes, soluble (regular) insulin, re-hydration.*

Introduction

Doctors in the Middle East and other developing countries frequently see adult type 2 diabetic patients, with elevated fasting plasma glucose (FPG) concentration or inappropriately high random plasma glucose (PG) above 22.2mmol/l (400 mg %), in outpatient clinics and emergency rooms (ERs). There are various reasons for this, including non-compliance with, or unavailability of, medications; eating inappropriate foods for example excessive date or honey consumption; effect of other medications[1] or even hypovolaemia from relative dehydration in very hot countries.[2] Since some of these patients have no symptoms of hyperglycaemia, the physician often wonders whether to treat them or not.

When the patient is asymptomatic, and the cause is obvious, as in excessive date consumption, or omission of medication, no specific therapeutic intervention is needed, as the hyperglycaemia is appropriate to the circumstances. Patient education and counseling may suffice to restore the patient to the previous level of diabetic control. However, where the patient is symptomatic, newly diagnosed, or just poorly controlled, some action is warranted.

Many patients in these countries are not sufficiently educated to appreciate that lack of symptoms does not necessarily mean that all is well with diabetic control. Socio-cultural factors greatly affect diabetic control and management, especially in developing countries.[3, 4] Health professionals in these countries often have to make the most of each patient contact because compliance with both management advice and clinic attendance is frequently less than ideal. Simple measures are usually more effective and therefore preferable to high technology or more 'state of the art' alternatives because of their universal applicability. In order to ensure optimal diabetic control, excessive inappropriate hyperglycaemia should not be left to the patient to manage, because of these considerations. It should be dealt with when the patient is seen.

Good glycaemic control is now a major objective of good management in diabetes mellitus since it is related to the rate of development and progression of complications. This has been shown for both type1 diabetes[5] and also for type 2 diabetes[6] which affects the great majority of patients. The oral hypoglycaemic agents (OHAs) which are used to treat type 2 disease when dietary measures alone are inadequate, have reduced potency, even at maximum dosage, in the presence of excessive hyperglycaemia.[7-9] This condition exacerbates the pre-existing impaired insulin secretion and sensitivity in this form of the disease,[10] and is therefore considered 'toxic' since it reduces both insulin secretion, action[11,12] and the effectiveness of OHAs. This 'toxicity' is partly reversed when hyperglycaemia is reduced.[12-14] The clinical implication of this is that in type 2 diabetic patients, the occasional use of insulin may help in maintaining the efficacy of OHAs in achieving reasonable glycaemic control, since the benefits of insulin in this situation outlast its period of use.[13,15] Reduction of hyperglycaemia and control of symptoms with OHAs in these patients takes a variable period of time (4 – 12 days), with achievement of desirable or target FPG levels occurring over a much longer period or not at all.

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The following case demonstrates the need for appropriate treatment. A 40 year old man was found incidentally to have developed diabetes, during investigation and treatment of a minor stomach upset. On questioning, he admitted to having symptoms related to diabetes for some weeks and his FPG was 18 mmol/l (324 mg%). He was started on glibenclamide 5mg daily with appropriate diet advice. His symptoms settled over 5 days, and one week later, his FPG was 12.6 mmol/l (227mg %). One week after this FPG was 11.9mmol/l (214 mg %), and 7.8 mmol/l (140 mg%) 2 months from diagnosis. This delayed effect of OHAs is in keeping with the observation that excessive fasting hyperglyacemia especially above 16.7 mmol/l (300 mg %) reduces both insulin secretion and the potency of OHAs.[10] Hence, these drugs are not universally effective in this circumstance. In addition, since chronic hyperglycemia causes irreversible deleterious effects on the B cell[16]and may therefore adversely affect long-term control, it is important to act promptly to reduce it.

The aim of this study was to describe a simple practical way to tackle the common problem of inappropriate hyperglycaemia in adult type 2 diabetic patients by reducing hyperglycaemia rapidly to a level below 14 mol/l or 250 mg% where the definitive oral therapy chosen will work. It encourages compliance with the recommendations subsequently given to patients and their relatives. To achieve this goal, we use insulin for more rapid, predictable and consistent reduction of excessive hyperglycaemia.

Method
Serum acetone, blood urea nitrogen (BUN), electrolytes, creatinine, blood glucose is estimated, and arterial blood gases (ABG) to exclude or confirm keto-acidosis. A total of 123 patients were examined The results help to select patients without serious major organ or systemic disease who are suitable for this treatment. Patients with diabetic keto-acidosis are excluded from this regimen, as they need far more aggressive (in-patient) therapy.

The intra-muscular (IM) route is preferred over the usual subcutaneous one for insulin (which would also be effective), because of its rapid action and consequently reduced period required for this treatment. Subcutaneous injections are absorbed slowly, and absorption is unreliable in dehydrated patients. Continuous intravenous or subcutaneous insulin requires special infusion pumps and more nursing time and supervision. Not all patients can afford, or are willing, to spend the few hours required for this treatment. Those living nearby, or have their own transport, or can be relied on to come back the next day for

further laboratory tests, can be discharged after 1 or 2 hours.

The Treatment
This treatment is given in the Emergency Room (ER) but can be given in other ambulatory care settings like the injection, treatment or re-hydration room where such facilities are available. Suitable patients with no serious systemic disease or organ dysfunction as outlined above are given:

- Intravenous re-hydration therapy as there is usually some degree of dehydration in these patients, with 1 litre of 0.9% saline containing 20 mmol of potassium at a rate of 150-250 ml/hour (approximately 3ml/kg body weight/hr for 80kg patient).
- Intramuscular soluble (regular) insulin 8-15 units, depending on the patient's weight, age, and level of blood glucose according to the scale on Table 1. Patients 65 years and older receive a dose one step lower than weight and blood glucose level would indicate.

The blood glucose concentration is measured 3 hours after the insulin injection, and most patients are discharged about 1 hour later on the oral regimen starting with a small dose for new patients, e.g., glibenclamide 2.5 mg/ day with the main carbohydrate meal of the day, and then titrating it according to future FPG results. Obese patients are started on treatment with metformin.[17] One advantage of this regime is that the blood glucose may also be estimated with any of the commonly available portable glucose meters where full laboratory support is inadequate. [18]

Results
Using this regimen, the average fall in blood glucose concentration at three hours, is 40-60%, with greater falls in the elderly (over 65 years of age), those with very high initial concentrations, above 28 mmol/l (500 mg%), non-obese and newly diagnosed patients. Tables 2 and 3 give the mean percentage falls (rounded to a whole number) at concentration levels 30 mmol/l (540mg%) or less in a recent series of 123 cases, grouped as newly diagnosed and follow-up patients, in whom the pattern was similar.

Occasionally the blood glucose concentration does not fall as expected (or even rises a little in very obese patients), and a little more insulin, up to half of the initial dose may be repeated following the 3-hour post-insulin measurement, with a further 2-3 hour wait for a blood glucose re-check before the patient is discharged. In a few patients, the blood glucose concentration may decrease, to less than 5.6 mol/l

Table 1: Insulin dose according to patient weight and blood glucose concentration

Patient's weight / blood glucose concentration	IM Insulin dose (units)
<60 kg / <22.2 mmol/l (400 mg %)	8
60-80 kg / <22.2 mmol/l (400 mg %)	10
>60 kg / >27.2 mmol/l (500 mg %)	15
>80 kg / >22.2 mmol/l (400 mg %)	15

Table 2: Decrease in plasma glucose concentration 3 hours post-insulin treatment: plasma glucose 22-30 mmol/l (400-540 mg%)

	New patients	Follow up patients
No of patients (n)	17	57
Mean fall (%)	49	42
Range (%)	24-71	22-83
Standard deviation (%)	11.5	14.6

Table 3 : Decrease in plasma glucose concentration 3 hours post-insulin treatment: plasma glucose >30 mmol/l (540 mg %)

	New Patients	Follow up patients
No of patients (n)	10	39
Mean fall (%)	55	50
Range (%)	41-79	38-79
Standard deviation (%)	10.64	12.6

(100 mg %), at the 3-hour post-insulin interval. These patients are usually those who are newly diagnosed or very sensitive to insulin action, or both, and cannot be identified accurately beforehand. A small snack at discharge obviates hypoglycemic symptoms in them. Hourly glucose meter checks following insulin can also help identify these patients.

Discussion

Such short-term use of insulin in primary care settings gains time for both patients and staff, and enables patients to be treated near their homes. It also helps to reduce the resistance and apprehension most patients have about "injection treatment". This would be of much benefit later on, since most of these patients will eventually require insulin to control hyperglycaemia.[20] Insulin use in this way adds to the flexibility in medication usage available to control this naturally unrelentingly progressive disease. The concept of a combination oral therapy from the beginning,[20,21] is another logical approach, as is night time insulin supplementation of OHAs in suitably selected patients,[20] among other options for adequate glycaemic control. Since the long-term goal is prevention or delaying of diabetic complications, we may take all currently available measures, to achieve it. The previous rigid division of patients into oral and insulin treated groups may no longer apply.

Such an approach may also help to slow down the rate of B cell decline in type 2 diabetes, which has been calculated at about 5-7% per year.[6] This means that, 10 years after the diagnosis, at least 50% of these patients would require insulin because of the progressive decrease in B cell function, which is the main cause of the so-called secondary failure of OHAs. This has been our own experience with over 5000 type 2 diabetic patients during the past 15 years. Intensive treatment of hyperglycaemia not only reduces glucose 'toxicity' and improves insulin secretion and sensitivity; it also enhances subsequent response to therapy with OHAs.[13,14] We have found that brief use of insulin is useful in the initial treatment of newly diagnosed or symptomatic patients with severe hyperglycaemia in whom

oral therapy is being considered or is already in use. We use insulin for short periods in type 2 diabetic patients who:

- Have symptomatic hyperglycaemia (e.g. polyuria, polydipsia, dehydration, weakness) at any glucose level
- Are newly diagnosed when presenting with very high fasting blood glucose levels of 22.2 mmol/l (400 mg %) or more.
- Are already on OHAs when presenting with severe fasting hyperglycaemia of over 22.2 mmol/l (400 mg %), to achieve quicker control of hyperglycaemia before continuing with treatment.

This is in general agreement with the recommendations of a recent comprehensive review on the therapy for type 2 diabetes,[19] and the current trend towards a more flexible approach to treatment,[20] or the logical combined use of OHAs from the initiation of therapy.[21, 22]

Acknowledgements

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