Reversible diminished insulin requirement during acute renal failure

JOHANAN E. NASCHITZ
M.D.

CARMELLA BARAK
M.D.

DANIEL YESHURUN
M.D.

Department of Internal Medicine 'A', Rothschild University Hospital, Haifa, Israel

Summary

Very little is known concerning insulin requirements in diabetic patients who develop acute renal failure, although decrease in daily insulin requirement in patients with chronic renal failure is recognized.

A 46-year-old diabetic patient is described, whose daily insulin requirement decreased from 56 to 8 units per day during an episode of acute post-streptococcal glomerulonephritis causing acute reversible renal failure. The insulin requirement returned to its previous level after the patient recovered.

Key words: insulin, diabetes mellitus, renal failure glomerulonephritis.

Introduction

A decrease in daily insulin dosage in diabetes mellitus with chronic renal failure has been reported (Rutsky et al., 1978; Peitzman et al., 1977). On the other hand, very little is known about insulin requirements in diabetic patients who develop acute renal failure.

We would like to report a diabetic patient who developed acute renal failure due to acute post-streptococcal glomerulonephritis. Her daily insulin requirements decreased from 56 to 8 units, following several hypoglycaemic episodes. The return of her kidney function to normal was associated with an increase of the daily insulin dose to nearly the previous one.

Case report

A 46-year-old diabetic patient was admitted because of oliguria and swelling of her face, 12 days after a sore throat with fever. She had suffered from diabetes mellitus for the last 10 years, requiring 56 units of insulin daily (28 units NPH and 16 units neutral regular insulin in the morning and 12 units NPH insulin in the evening). A blood urea of 5.3 mmol/litre and creatinine clearance of 52 ml/min were recorded at the time of a urinary tract infection 18 months previously.

Physical examination revealed facial swelling and the blood pressure was 140/90 mmHg. The daily urinary output was 400 ml. Laboratory data revealed 7 g per day protein in the urine, and its sediment showed numerous erythrocytes and granular casts. Blood urea was 26.7 mmol/litre, creatinine 274 mmol/litre, uric acid 0.53 mmol/litre, potassium 5.5 mmol/litre and inorganic phosphorus 1.93 mmol/litre. Anti-streptolysin titre rose from 800 to 3200 units; antinuclear antibodies, C3 and C4 levels were normal.

A diagnosis of post-streptococcal glomerulonephritis was made and water intake was restricted. Her diet was ad lib, the daily caloric and carbohydrate intake being practically unchanged from the low carbohydrate diabetic diet she had followed. Within the next few days, acute renal failure developed, with blood urea levels up to 46.8 mmol/litre and creatinine clearance down to 17 ml/min.

During the first days, recurrent episodes of hypoglycaemia were recorded, clinically presenting as weakness, sweating and palpitations. Blood glucose monitored during these episodes, showed levels of 1.9-2.8 mmol/litre and were corrected by intravenous glucose administration. This caused a decrease in the patient's daily insulin requirements. The dose was reduced as far as 8 NPH insulin units per day, while the patient did not suffer from vomiting, and the carbohydrate intake remained stable. Parallel to the improvement in the renal function, an increase in the daily insulin dosage was seen (Fig. 1). The patient was discharged 3 weeks after admission, with renal function and daily insulin requirement similar to the pre-illness ones.

0032-5473/83/0400-0269 $02.00 © 1983 The Fellowship of Postgraduate Medicine
defective glycogenesis al.

and this subjects mechanism This in delivery such that patient. uraemic inhibition of function. Weinrauch, Healy and Agarwal, 1977; Garber, 1973) described (1973) described a 65-year-old diabetic patient who developed hypoglycaemia with a decrease in insulin daily dosage while developing acute renal failure. Weinrauch, Healy and Leland (1978) report a series of diabetic patients who developed renal failure following injection of iodine-containing contrast material used for intravenous pyelography. They noted a decline of the daily insulin requirement and hypoglycaemic episodes in some patients which reversed following the improvement of their renal function.

The pathogenesis of this phenomenon is controversial. Among the possible mechanisms that lead to hypoglycaemia in diabetic patients with renal failure, a decrease in the daily caloric intake caused by lack of appetite or vomiting has been postulated (Runyan, Horowitz and Robbins; Block and Rubenstein, 1970). This mechanism could not be confirmed by Rabau et al. (1973), Frizzel, Larsen and Field (1973), or by us.

A second possible mechanism is related to the inhibition of hepatic delivery of glucose in the uraemic patient. Cohen and Horowitz (1968) showed that such patients did not utilize intravenously administered galactose to the same extent as normal subjects and this was interpreted as indicating defective glycogenesis in the liver. Furthermore, inadequate delivery of gluconeogenic substrates, such as alanine, may be responsible for hypoglycaemia in patients with renal failure (Garber et al., 1974). Lukas, Dinwoodie and Linton (1964) could not substantiate this theory with the aid of the fructose tolerance test, nor did Block and Rubenstein (1970).

It has become increasingly evident that the kidney has an important part to play in the metabolism of insulin. Normally, the kidney metabolizes about 39% of the circulating insulin. In patients with renal failure, renal metabolism of insulin may be decreased by 50–77% according to Rabkin et al. (1970) and Fuss et al. (1974), resulting in higher levels of plasma insulin. A substantial amount of insulin is normally excreted in the urine. As glomerular filtration rate falls, the urinary excretion of insulin is decreased which would lead to an increased amount of insulin remaining in the circulation for any given administered dose (Fuss et al., 1974). These form 2 further possible mechanisms for hypoglycaemia in the uraemic patient.

Due to impaired renal handling, the serum concentration of secretin, gastrin and other intestinal hormones may increase in the uraemic patient. Recent studies by Lerner (1979) indicated that secretin priming resulted in a two-fold improved early insulin output to a subsequent glucose challenge. Whether such a mechanism plays a role in the occurrence of hypoglycaemia in diabetic subjects with renal failure treated with exogenous insulin has not been established.

Berson and Yalow (1957) demonstrated that hypoglycaemia in insulin-treated patients may arise by release of the hormone from circulating insulin-antibody complexes. In vitro studies documented that substantial amounts of free hormone can be released by this mechanism. Unlike insulin that is secreted by the pancreas, a hormone dissociating from circulating insulin-antibody complexes is not under feedback control and may thus give rise to hypoglycaemic episodes (Ichihara et al., 1977). The stability of such complexes may be challenged by certain medications, enzymes or acidosis occurring during acute renal failure such as in our patient. This may lead to accelerated release of free insulin, and consequently hypoglycaemia.

Insulin binding to receptors is subjected to variations either by alteration in receptor number or affinity. Those can be caused by exercise, meals, diet, insulin, growth hormone or other hormones, age, cyclic AMP, changes in pH, presence of ketone bodies, antireceptor antibodies and certain drugs such as sulphonylureas. Hypoglycaemia will thus result from increased insulin binding to receptor cells. A study of insulin receptors may provide insight to pathogenesis of hypoglycaemic episodes that cannot be otherwise explained (Roth et al., 1979). Recently, the demonstration of insulin receptors on circulating erythrocytes may simplify the study and
evaluation of these receptor abnormalities (Gambhir, Archer and Bradley, 1978). We could not find any references to the behaviour of these insulin receptors in acute renal failure.

A decrease in daily insulin requirement in a diabetic patient who suffers from chronic renal failure is thought to be a bad prognostic sign (Rabau et al., 1973). It does not seem, though, that this is true for acute renal failure in diabetic patients as well.

Although this phenomenon of hypoglycaemia in insulin-treated renal patients is so rarely reported, we believe that special attention should be given to the insulin requirement in renal patients in order to prevent hypoglycaemic episodes and their complications. On the other hand, the sudden spontaneous appearance of hypoglycaemia in an insulin-dependent diabetic patient should focus the doctor's attention on the possible development of renal failure.

References


(Accepted 20 July 1982)
Reversible diminished insulin requirement during acute renal failure.

J. E. Naschitz, C. Barak and D. Yeshurun

doi: 10.1136/pgmj.59.690.269

Updated information and services can be found at:
http://pmj.bmj.com/content/59/690/269

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/