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Editorial/Van die Redaksie

Continuous subcutaneous insulin infusion

It is now 60 years since insulin was first used to treat a patient with diabetes mellitus, and yet the morbidity and mortality resulting from this disease are still considerable. Diabetes is the commonest cause of blindness and one of the most frequent causes of chronic renal failure in developed countries today. Recently, increased attention has been paid to the quality of diabetes control and how this relates to the prevalence of diabetic microvascular disease. Several studies have attempted to define this problem, the largest and most complete one being that of Pirart,[1] whose follow-up of 4 400 patients over a period of 26 years showed a clear relationship between the degree of blood sugar control and the prevalence of retinopathy, nephropathy and neuropathy. This relationship was particularly noticeable with proliferative retinopathy, the most common cause of blindness, which was virtually limited to the patients who were poorly controlled.

In pregnancy the degree of blood glucose control in the mother has a direct bearing on the incidence of complications in the baby, including macrosomia and the predisposition to neonatal hypoglycaemia and subsequent brain damage. Interestingly, even congenital abnormalities, which occur at a higher rate in the babies of diabetic mothers than in the normal population, can be related to the quality of maternal blood glucose control in early pregnancy.[2]

The treatment of diabetes has therefore become aggressive and the criteria for blood sugar control have become more stringent, the aim being normalization or near-normalization of blood sugar levels. Since the blood sugar level can now be monitored by the patient at home, fine adjustments can rapidly be made to the insulin regimen according to the prevailing glucose status. To attain euglycaemia, the use of continuous subcutaneous insulin infusion (CSII) has increasingly been investigated over the last few years.[3,4] CSII is given by means of a small portable infusion pump set to deliver a low-dose infusion continuously on a 24-hour basis. At meal times the patient activates a mechanism on the pump which delivers a predetermined bolus dose. Although still in the experimental phase, the pump would at face value appear to have several advantages. Firstly, very small adjustments can be made to the basal infusion so that blood sugar levels can be maintained within a narrow euglycaemic range. Secondly, the bolus delivered at meal times can be altered both in terms of timing and quantity. The patient is no longer 'locked-in' to eating a specific amount at a specific time. A meal can even be missed if it is inconvenient.

Using the portable pump together with intensive home-monitoring of blood sugar levels, many patients have succeeded in attaining a euglycaemic state. It has become evident from several studies and case reports that some of the microvascular complications of diabetes are reversed when the blood sugar value returns to normal. Thus the Steno Study Group from Denmark reported an improvement in background retinopathy and urinary albumin excretion in a group of patients treated by CSII for 6 months. A control group of diabetics treated in the conventional way deteriorated during this period.[5] In another group of diabetics, tight control resulted in improved peripheral and autonomic nerve function,[6] and in diabetic children growth retardation has been reversed.[7] However, none of these trials has continued long enough for us to be sure that CSII will ultimately prevent the development of diabetic complications.

A disadvantage of the portable pump is the possibility of its failure, either as a result of intrinsic mechanical problems or due to disconnection of the tubing. Indeed, in studies done to assess the effects of inadvertent pump failure occurring at night, marked increases in serum ketone values within an hour of its disconnection have been demonstrated. More alarmingly, a rise in serum potassium to a level of 6 mmol/l within 6-8 hours of disconnection occurred.[8] Furthermore, if the insulin in the syringe and the pump is not changed frequently, excessive crystalline aggregation and insulin inactivation occur.

However, these problems do not appear to be serious or insurmountable. During 1981 the Center for Disease Control in Atlanta investigated 11 deaths in patients using insulin pumps. None of the deaths could be attributed to pump failure, although some were due to hypoglycaemia which resulted from over-intensive therapy rather than from mechanical problems.

Lastly, if euglycaemia is the aim of therapy one must ask whether excellent control can be obtained by more conventional means. Several studies have shown unequivocally that multiple insulin injections with self-monitoring can control diabetes as well as CSII.[9]

What then is the current place for CSII? The American Diabetes Association has recently suggested that CSII may be useful in the long term in diabetics who have failed to achieve acceptable control despite intensive conventional therapy, including a suitable diet, multiple injections of insulin (either of a single type or in a combined form containing long- and short-acting insulins), and good patient motivation and compliance.[10] Furthermore, portable infusion devices should only be prescribed and managed by diabetologists trained in their use. Trained staff who can develop an overall treatment regimen for the patient and provide intensive patient education must be available. It must be emphasized that the success of this treatment ultimately depends on patient co-operation and in no way allows discarding of diet or daily scheduling of events necessary for total diabetic management. In particular, the patient has to monitor his own blood glucose level scrupulously, while the physician should be able to provide a 24-hour telephone communication service.

Finally, it should be recognized that there are limitations with all systems, and that even CSII may not solve the problem of control. Although CSII is an exciting new development in diabetic care it has yet to prove itself universally, and should be used only under well-controlled conditions in the appropriate setting.

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Current trends in medical defence

Some of the most valuable documents that come across a doctor's desk in the course of the year are the annual reports of the Medical Defence Union and the Medical Protection Society. Any doctor who neglects to read the annual report of his defence organization should have his head read, as the saying goes.

The report of the MDU for 1982 has a particularly informative section entitled 'Current trends in Medical Defence'. Not for nothing is the telegraphic address of the MDU 'Damocles', a name expressly chosen to symbolize the legal threat always hanging over every practising doctor. The Union has a membership of over 103 000 doctors and dentists practising all over the world, except in the USA and Eastern Europe.

The report calls attention to a phenomenon of which we should all be aware, namely the increasing number of calls on its services, as well as the fact that the cost of dealing with each claim has more than doubled in 4 years.

In the UK one cause for the increase in claims is the readiness with which legal aid can be obtained by about 70% of the population. Another cause, which operates in South Africa, is the publicity surrounding large awards of damages for personal injuries; patients and relatives naturally identify, sometimes incorrectly, with a newspaper or television report. Thirdly, expectations of medicine have now perhaps become unreasonably high, so that disappointment turns to bitterness and thoughts of litigation.

Apart from these circumstances, over which medicine has little control, there are others which are in the control of all of us. One is the need to ensure the highest standards of kind and courteous communication when something goes wrong. So often, the French phrase that 'it is the first step that counts' applies when a practitioner fails to deal correctly with the first vague complaint. It is also as well to remember that claims may arise a long time after the event. A classic instance of delay recently occurred in a celebrated obstetric case in the UK, in which an attempted forceps delivery in 1970 led to a trial of the obstetrician in 1978, successful appeal in 1979 and a final finding by the Law Lords that the obstetrician had not been negligent 10 years after the event.

These delays emphasize the paramount importance, so often overlooked, of keeping good records. It is illogical but a fact of life that in cases of claims for negligence the quality of the defendant's work is often judged by the quality of his record-keeping rather than his actual performance. Many a practitioner has had cause to regret an inadequate or hastily scribbled note or referral letter. In one recent case in Britain the patient alleged that he had not been warned about a certain side-effect of his treatment and the judge accepted the patient's evidence. A note by the doctor when the drug was first prescribed would have established his innocence of the charge.

Various other little shortcomings of medical practice may sow the seeds of a later claim. One is unfortunately associated with the growth of group practice, so that patients are seen by a variety of doctors, none of whom is completely acquainted with the patient's case. In addition the use of rotas and deputizing services in Britain has enhanced these problems. A tyrannical or inefficient receptionist protecting her doctor has featured more and more in claims in Britain recently, and it is possible that the same sort of situation may arise here.

The report of the MDU also points out that, contrary to the alleged conspiracy of silence when something has gone

wrong, there is no shortage whatsoever of medical experts prepared to testify on behalf of potential plaintiffs. The Union has always advised members with appropriate expertise to assist as fully as possible a claimant's attorney because considerations of natural justice must always take precedence over professional loyalties. Unfortunately, there are a few well-known characters prepared to help claimants beyond the limits of their own expertise, not to mention hospital doctors prepared to criticize a general practitioner without personal knowledge of the problems of general practice.

What can be done to stem the tide of increasing litigation? The Union indicates that there are certain basic ground rules but no easy answer. The first point is to be aware of the problem and that the chances of having to defend a claim for negligence have increased annually. The second point is the necessity for keeping up to date (our forthcoming *Journal of Continuing Medical Education* should help in that respect), and in particular the need to note any changes in the law relating to medical practice and to take heed of the various warning notices issued about adverse drug effects. Appropriate checking and supervision of one's medical and non-medical subordinates can assist in avoiding trouble just as much as meticulous record-keeping.

Ill-advised and hasty comment on one's colleagues may prove the starting point of a claim. Lastly, it is still true that an excellent doctor-patient relationship at all times will go a very long way to avoiding unpleasant, time-consuming and stressful legal complications.

Digoksien-teenliggame en digitalisvergiftiging

Digitalisderivate word al eeue lank gebruik sonder dat daar 'n spesifieke teenmiddel teen oordosering of vergiftiging bestaan, maar so een is nou blykbaar ontwikkel. Wanneer lewensgevaarlike toksisiteit (te wyte aan 'n oordosis wat per abuis of in 'n selfmoordpoging geneem is) in die verlede voorgedoen het, was slegs ondersteunende maatreëls moontlik, bv. die toediening van lidokaïen vir ernstige ventrikulêre aritmieë, atropien of 'n gangmaker vir bradikardie of die behandeling van gepaardgaande hiperkalemie. Gelukkig word digoksien redelik gou uitgeskei, met 'n halfleeftyd van $1^1/_2$ dae.

Nou is digoksien-teenliggame egter beskikbaar, en Smith *et al.*[1] het onlangs verslag gedoen oor 'n multisentrum kliniese proefneming waarin hulle gesuiwerde digoksien-spesifieke Fab-fragmente van skape gebruik het vir die behandeling van gevorderde digitalisvergiftiging. Al die pasiënte met hierdie vergiftiging was teen konvensionele terapeutiese behandeling weerstandig. Hulle het skape met 'n digoksien/serumalbumien-konjugaat ingeënt en die antiserum van diere met hoë titers van antiliggame en met 'n hoë spesifisiteit versamel. Hiervan het hulle 'n ru IgG-fraksie verkry wat hulle in Fab- en Fc-fragmente gekloof het deur behandeling met papaïen.

Elk van die twintig sentrums in die studie is voorsien van 1 000 mg Fab. Altesaam 26 pasiënte wat wesenlike of potensiële lewensgevaarlike digitalisvergiftiging gehad het en wat weerstandig was teen konvensionele behandeling, is met hierdie substans behandel. Ten minste 23 van die 26 pasiënte was in 'n toestand van gevorderde digoksienvergiftiging. Van hierdie 23 het 20 die middel ontvang vir die behandeling van 'n hartsiekte, en het 13 groot dosisse per abuis of in 'n selfmoordpoging geneem. Negentien van die 23 het serum-digoksienkonsentrasies groter as 5 ng/ml ten tye van die Fab-toediening gehad. Drie pasiënte is eintlik vir digitoksienvergiftiging behandel, maar die tekens en simptome was dieselfde. Die meeste pasiënte het aan naarheid en braking (gewoonlik akuut) gely en 11 het hiperkalemie gehad. Al 26 pasiënte het standaardbehandeling vir hiperkalemie en aritmieë en geleidingstoornisse ontvang.

Al die pasiënte het aanvanklik 'n gunstige respons op die Fab-fragment-dosisse getoon wat bereken is om op 'n molêre basis gelykstaande te wees aan die hoeveelheid kardioglukosied in die pasiënt se liggaam. Vier pasiënte wat na langdurige hipotensie en lae kardiale omsetvermoë behandel is, het aan serebrale of miokardiale hipoperfusie gesterf. 'n Ander pasiënt wat in 'n selfmoordpoging 'n massiewe oordosis digoksien ingeneem het, het na terugkerende ventrikulêre aritmieë gesterf. In die oorblywende pasiënte is aritmieë en hiperkalemie baie gou omgekeer en hulle het ten volle herstel. Die behandeling het geen nadelige effekte tot gevolg gehad nie.

Die outeurs glo dat behandeling met hierdie gesuiwerde digoksien-spesifieke Fab 'n baie effektiewe en hoogs-spesifieke metode is om gevorderde, lewensgevaarlike digitalisvergiftiging teen te werk. Dit is wel so dat 'n lukrake gekontroleerde proefneming 'n voordeel bo die huidige benadering sou hê, maar die duidelike sukses van hulle vroeë ondervinding sal ernstige etiese probleme oplewer indien so 'n proefneming aangepak sou word. Een van die probleme wat nog te bowe gekom moet word, is die ontwikkeling van genoegsame voorsiening van hierdie teenliggame, terwyl 'n ander die toepaslike aanduidinge vir gebruik is. Indien verdere ondervinding die afwesigheid van ernstige nadelige effekte toon, mag hierdie behandeling meer ingrypend en op 'n groter skaal toegepas word.

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