Skin necrosis following Haemaccel

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Summary: Haemaccel is a plasma substitute in frequent clinical use with a low incidence of side effects. I report a patient who developed necrotic blisters following two Haemaccel-insulin infusions, a previously undescribed complication. The rationale behind carrier solutions for insulin therapy is discussed and some of the problems associated with Haemaccel use are considered. I conclude by urging caution in the use of Haemaccel as a carrier solution for insulin therapy.

Introduction

Haemaccel (Hoechst) is a 3.5% colloidal solution of polygeline, a polymer of urea and polypeptides derived from denatured gelatine. It is widely used as a plasma substitute and has been advocated as a carrier for low dose, constant infusion, insulin therapy because of its ability to reduce adsorption of insulin on to plastic infusion sets (Kraegan et al., 1975).

Although this combination may produce thrombophlebitis and Haemaccel alone may produce a variety of skin reactions, the problem of skin necrosis as described below has not previously been reported.

Case history

A unemployed 57 year old man, with no history of atopy, urticaria or previous exposure to Haemaccel, was admitted to hospital with retrosternal chest pain of 10 days duration. He had experienced mild angina for 3 years, controlled by oral nitrates. There was no family history of atopy, ischaemic heart disease or diabetes mellitus. On examination he looked ill, pulse 110 beats/min, blood pressure 120/80 mmHg, with a fourth heart sound and bilateral basal crepitations. His electrocardiogram had inverted T waves in leads I, AVL and V3-6, chest X-ray confirmed pulmonary oedema and random plasma glucose was 17.7 mmol/l. Other investigations including serum potassium, plasma calcium, pH and venous bicarbonate were normal; IgE was not determined.

In view of his ischaemic heart disease accurate control of the blood sugar was attempted by a syringe pump containing 50 U of Actrapid MC insulin and 50 ml of Haemaccel infused at 1–4 ml/h (1–4 U/h) through a cannulated peripheral vein. After 36 hours a flaccid blister containing serous fluid on an erythematous base had developed over the site of the indwelling cannula (Venflon, Vigon Products), the dimensions being 1.5 cm high and 1.5 × 5 cm in area (Figure I).

The infusion was discontinued and recommenced on the other arm with a new solution of Actrapid MC and Haemaccel. In less than 24 hours this site also became blistered but less severely than before. In both instances there was no evidence of thrombophlebitis and saline could be flushed freely through the cannula. No other drugs, including heparin, had been administered by this route. A third infusion containing saline and Actrapid MC was started, producing adequate control of his blood sugar with no skin reactions developing at 48 hours when subcutaneous insulin was commenced.

Over a period of several days the blistered surfaces became more flaccid, finally sloughing off to reveal a bacteriologically sterile, necrotic base. Surgical advice was sought concerning skin grafting, but in view of his medical problems both areas were allowed to heal by granulation.

After 8 days he was discharged home with regular dressing of the healing areas supervised by the district nurse. When reviewed 6 weeks later he had achieved a reasonable exercise tolerance with no further angina, blood sugar was well controlled with twice daily insulin, and the necrotic areas had healed with minimal scar tissue. Rechallenge or skin prick testing to Haemaccel was not performed.

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that insulin coats the surface of the infusion equipment as a monolayer and that adsorption ceases once all the surface is coated (Hirsch et al., 1981). The use of low surface area infusion and initially flushing the system with an insulin solution, may thus obviate the need for carrier solutions. Page et al. (1974) have also concluded that such insulin losses are of little clinical significance and are easily overcome by an increased rate of infusion.

Since the introduction of Haemaccel in 1976, eleven cutaneous reactions have been documented (Hoechst, personal communication) including urticaria, itchy erythematous rashes and erythema multiforme. The majority of these reactions occurred when Haemaccel was either infused rapidly or used in normovolaemic patients, an indication not recommended by the manufacturers. The mechanism for these reactions is thought to be histamine release and since 1981 when the manufacturing process was modified to remove histamine releasing substances, only three adverse reactions have occurred, namely erythema multiforme, periorbital oedema and an anaphylactoid reaction.

Thrombophlebitis has been described in 8 out of 9 patients receiving intravenous Haemaccel-Actrapid infusions, and in 8 out of 17 patients when a saline-insulin infusion containing 6 ml of Haemaccel was used (Gwilt et al., 1982). However, the severe blistering reaction seen in this patient has not previously been reported. It is difficult to explain the mechanism for the reaction, but true allergy is unlikely in view of his non-atopic history and absence of previous exposure. The Haemaccel used to make up the syringe pump for each arm came from two unopened packs, of different batch numbers, both within their expiratory date and clear to naked eye examination, so it is improbable that both units could have been faulty or contaminated.

Adhesive strapping may produce an allergic contact dermatitis but was not the culprit on this occasion, both blisters being proximal to the strapping and similar materials were used to secure the third cannula. It is possible that extravasation of Haemaccel into the surrounding tissues would produce a blister, although Hoechst have not received any reports of such problems and moreover this is unlikely in this patient as saline could easily be flushed through the cannula, which bled briskly when disconnected.

The reaction reported above, which has not previously been associated with Haemaccel-insulin infusions, underlines the problems which may occur with this combination. Although Haemaccel reduces losses of insulin from adsorption, the need for a carrier solution at all is in some doubt. In view of the risks of thrombophlebitis and other cutaneous reactions, I conclude by recommending caution in the use of Haemaccel-insulin infusions.

**Discussion**

It has been shown that the accurate control of blood sugar during myocardial ischaemia, by the use of intravenous insulin, is probably beneficial (Gwilt et al., 1982). However, concern has been expressed that insulin may be adsorbed onto the plastic of infusion lines, producing variability in the amount of insulin administered, and therefore making accurate control of blood sugar difficult (Weisenfeld et al., 1968).

A variety of vehicles has been proposed to prevent insulin adsorption, including polygeline (Kraeggan et al., 1975), 0.5–1% albumin, dextrans, or even the patient’s own blood (Ege, 1983). It has been suggested that insulin coats the surface of the infusion equipment as a monolayer and that adsorption ceases once all the surface is coated (Hirsch et al., 1981). The use of low surface area infusion and initially flushing the system with an insulin solution, may thus obviate the need for carrier solutions. Page et al. (1974) have also concluded that such insulin losses are of little clinical significance and are easily overcome by an increased rate of infusion.

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References

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