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Case Reports

The Use of Hyaluronidase for Treatment of Extravasations in a Premature Infant

SLY ***Siu,*** KL ***Kwong,*** SST ***Poon,*** KT ***So***

Abstract We reported the use of modified Gault's technique of subcutaneous hyaluronidase and saline flushing in the treatment of a deep partial-thickness chemical burn due to parenteral nutrition extravasation in an infant born at 34 weeks' gestation. Dramatic response was obtained. The toxicity of hyaluronidase is minimal and the modified Gault's technique is easy to perform with basic neonatal ward equipment.

Key words Extravasation; Hyaluronidase; Premature infant

Introduction

Extravasation is the inadvertent leakage of infused fluid into surrounding tissue, which may cause damage.[1] About 4% of infants leave neonatal intensive care units with cosmetically or functionally significant scars, thought to be caused by extravasation injuries.[2] A recent survey carried out in the United Kingdom revealed a lack of consensus on the management of extravasation injuries in preterm infants.[1] Infiltration with hyaluronidase and saline had been recommended[3] but local experience is limited. We report a premature baby with extravasation injury in whom subcutaneous hyaluronidase and saline flushes were used with dramatic response.

Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital, Tsing Chung Koon Road, Tuen Mun, N.T., Hong Kong, China

SLY **Siu** （蕭鑒儀） *FHKAM(Paed)*
KL **Kwong** （鄺玲） *FHKAM(Paed)*
SST **Poon** （潘善婷） *MBBS*
KT **So** （蘇鈞棠） *FHKAM(Paed)*

Correspondence to: Dr SLY **Siu**

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Case Report

An infant of 34 weeks' gestation weighing 1520 grams was delivered by caesarean section. Apart from transient tachypnoea of newborn and transient asymptomatic hypoglycaemia, his perinatal course was uneventful. Enteral feeding was introduced at 14 hours of life. Supplementary parenteral nutrition was started on day 2 of life via a peripheral vein on the dorsum of his right foot. After one hour of parenteral nutrition infusion, an area of black discoloration was noted over the intravenous site, which covered about eighty percent of the surface area of the right foot dorsum (Figure 1). Orthopaedic surgeon was consulted. The severity of extravasation injury was at least a second degree or more serious chemical burn. The blisters were aspirated and subcutaneous hyaluronidase and saline flushes were then commenced within 90 minutes.

Technique of Flushing the Extravasated Area

Only one preparation of hyaluronidase with 1500 units per vial was available in our hospital. Under strict aseptic conditions, one vial of hyaluronidase was diluted out in 1 ml normal saline. Then, 0.1 ml of the solution was again diluted with 0.9 ml normal saline, making up the final concentration at 150 units per ml. This volume was injected into the subcutaneous tissue of the extravasation site at the

leading edge in 5 aliquots using a 25-gauge needle. Multiple small punctures were made around and within the affected area with a 18-gauge needle. A 20-gauge intravenous catheter (angiocath®) was then inserted subcutaneously at the leading edge of the affected area. Using a syringe attached to the catheter, normal saline was injected. Repeated saline flushes of the extravasation area were performed. Excess fluid was removed by gentle massage towards the punctured sites.

Outcome

An immediate improvement in skin colour was noted after the procedure. The damaged area was then dressed with oily fine mesh gauze (Jelonet®) and kept covered. Twice daily wound dressing was carried out. Healing was rapid, with almost no sign of the injury noted after 5 days (Figure 2).

Figure 1 Extravasation injury over right foot dorsum.

Figure 2 Right foot dorsum five days after extravasation injury.

Discussion

The mechanisms of extravasation necrosis are incompletely understood, but the degree of damage appears to be related to osmolality, pH, and the dissociability of ions.[4] Hyaluronidase has proved effective in decreasing the harm caused by extravasated hyperalimentation solutions in rabbits.[5] Furthermore, free drainage of the extravasated fluid through skin puncture sites[6] and the promotion of dilution and absorption of the substance by injection of saline with hyaluronidase[5] have been tried.

In our case, the parenteral nutrition that resulted in extravasation injury was composed of dextrose, calcium, potassium, and other ions, and the osmolarity was clearly higher than that of the human serum. Hyperosmolarity is thought to disrupt the transport mechanism of the cell membrane, resulting in cell death by fluid inhibition.[7] Calcium and potassium salts are slightly acidic, hypertonic and capable of precipitating proteins to produce cell death directly.[8] It is well known that solutions of amino acids are acidic and act as buffers.[9] After extravasation, the interstitial pH of the peri-venous tissue could become acidic and remain outside the physiologic range.[9] That could enhance the cell damage caused by hyperosmolarity and the presence of ions.[9]

We believed that the extravasation injury in our patient was serious and warranted further action. The chemical burn attained in our baby was at least deep partial-thickness as the affected area blistered (easily unroofed), a feature that is almost always present in deep partial-thickness burns.[10] Moreover, the extravasation site was black and charred.[10] For this degree of burn, it usually takes over 21 days to heal and scarring may be severe.[10] The use of hyaluronidase in our baby saved him from these sufferings.

Hyaluronidase is an enzyme that depolymerizes hyaluronic acid, a mucopolysaccharide part of the tissue cement of the tissue spaces.[9] This has proved useful in preventing soft tissue necrosis after extravasation of parenteral nutrition solutions.[5] Subcutaneous administration of the enzyme increases tissue permeability and facilitates the absorption of injected substances by allowing the rapid diffusion of the drug over a larger area.[9] Thus, the extravasated material is rapidly diluted and absorbed from the tissue and the injury is minimised. The onset of action is immediate and the effect lasts about 24-48 hours.[11]

The toxicity of hyaluronidase is minimal.[9] Adverse effects are rare, mainly allergic reactions manifested as urticaria.[11] Hyaluronidase should not be injected directly

into cancerous or infected areas because of the potential for increasing invasiveness of neoplasm or disseminating infection.[11] Furthermore, it should not be used for extravasation management of dopamine or alpha agonists.[11]

Gault's technique required brief general anaesthesia and involved infiltration with hyaluronidase (1 vial = 1500 units) to break down or hydrolyse the hyaluronic acid of the connective tissues.[12] Four small exit stab incisions were made around the periphery of the area of extravasation, and 500 ml normal saline was flushed through the subcutaneous space to cleanse it.[12] To prevent damage to the underlying nerves, tendons or joints, a blunt-ended cannula with side holes was employed to instill the saline.[12] The central component of a "Verres" needle (used to insufflate the abdomen during laparoscopy) had proved ideal for the process.[12] However, "Verres" needle is not available in our department. Thus, we modified the Gault technique by replacing the stab incisions with needle punctures and "Verres" needle with a 22-gauge intravenous catheter (angiocath®). In this way, the need for general anaesthesia is obviated and the saline flushout can be carried out conveniently with just basic neonatal ward equipment.

In conclusion, our modified Gault's procedure using hyaluronidase is easy to perform and has shown a dramatic effect in treating extravasation of parenteral nutrition solution in our baby.

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