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ENSIEME IN TERAPIE

'n Aantal ensieme is waardevolle hulpmiddels met die mediese en chirurgiese behandeling van sekere kondisies. As hul in gesuiwerde vorm versigtig en met oorleg gebruik word, is dit onwaarskynlik dat hul 'n nadelige uitwerking kan hê. Onder hierdie ensieme sorteer die proteolitiese ensieme soos tripsien en die verbinding van streptokinase en streptodornase (SK–SD). 'n Tweede groep, verteenwoordig deur hialuronidase, wat maklik in 'n relatief suiwer vorm verkry kan word, depolimeriseer hialuroniese suur, die grondstof van weefsels.

Kristallyne tripsien is 'n sterk proteolitiese middel wat in 'n neutrale medium (optimum pH 8·0) effektief is. Dit verteer nekrotiese weefsel en proteïene, behalwe fibrien, en word in die vorm van vloeistof of poeier vir wonde gebruik in hoeveelhede wat van die grootte van die wond afhang; gewoonlik word met ongeveer 50 mg. begin maar daarna kan die hoeveelhede geleidelik tot 400 mg. verhoog word. In die plasma is 'n aktiewe anti-tripsien aanwesig wat met aansteeklike en ander siektes toeneem. Die nadele verbonde aan die gebruik van tripsien is dat dit irriterent mag wees, verswakte weefsels mag wegvreet en reaksies mag uitlok as gevolg van die absorbering van proteose; laasgenoemde reaksies kan waarskynlik deur anti-histamienmiddels beheer word. 'n Klein hoeveelheid tripsien binneaars ingespuit het 'n skielike en noodlottige gevolg gehad.

'n Verbinding van streptokinase (in ensiem-aktiveermiddel) en streptodornase maak fibrien, asook sekere selbestanddele, vloeibaar en is uiters waardevol met die behandeling van wonde. 'n Oplossing van 100,000 eenhede SK en ongeveer 25,000 eenhede SD in 10-20 ml. is vir 'n wond geskik en as die wond besonder suur of alkalies is kan van 'n bufferoplossing gebruik gemaak word. Plasmafaktor (plasminogeen of serum profibrienolisien) beïnvloed hul werking en die aktiwiteit van die SK–SD wissel na gelang die hoeveelheid plasmafaktor in die deurgesygde stof. Die koorsreaksies wat hierdie preparaat mag veroorsaak as dit op groot rou oppervlaktes of in toe spasies gebruik word, kan waarskynlik aan die aanwesigheid van pirogene toegeskryf word.

Vir die débridement van 'n wond of 'n brandwond kan SK–SD oplossing of tripsien daarop gespuit word of as nat verbande aangewend word. Vir diep wonde of holtes kan 'n kateter gebruik word en as die holtes bedek is kan 'n inspuiting gegee word mits dat alle voorsorg getref word om enige gevaar van 'n inspuiting in die long of bloedstroom te vermy. Tripsien verrig uitstekende

EDITORIAL

ENZYMES IN THERAPY

A number of enzymes are proving valuable adjuncts to the medical and surgical treatment of certain conditions. It appears that in their purified form they are not likely to do harm if used with care and understanding. Amongst the enzymes thus used in therapy are proteolytic enzymes such as trypsin, and the combination of streptokinase and streptodornase (SK–SD). A second group, represented by hyaluronidase, which is readily available in a relatively pure form, depolymerize hyaluronic acid, the intercellular or ground substance of the tissues.

Crystalline trypsin is a strong proteolytic agent, effective in a neutral medium (optimum pH 8·0), which will digest necrotic tissue and proteins other than fibrin, and is used for that purpose in wounds. It is applied as liquid or powder, the amount depending on the size of the wound; ordinarily about 50 mg. would be used in a first application but the amount may be gradually increased to 400 mg. There is in the plasma an active anti-trypsin which becomes increased in infectious and other diseases. Disadvantages in the use of trypsin are that it may prove irritating, it may possibly erode devitalized tissues, and it may produce reactions from the absorption of proteoses; antihistamine drugs may control these latter reactions. A small amount of trypsin injected intravenously has caused sudden death.

Streptokinase (an enzyme-activator) and streptodornase in combination bring about the liquefaction of fibrin as well as certain cellular elements, and are of great value in the treatment of wounds. A solution containing 100,000 units SK and approximately 25,000 units SD in 10-20 ml. may be used on a wound, and in a buffer solution if the wound is very acid or very alkaline. Their activity is affected by plasma factor (plasminogen or serum profibrinolysin) and the activity of the SK–SD varies according to the amount of plasma factor in the exudate. The febrile reactions that may be produced by this preparation used in closed spaces or on large raw surfaces appear to be due to the presence of pyrogens in the material.

For debridement of a wound or burn SK–SD solution or trypsin may be applied by spray or as a wet dressing. In deep wounds and sinuses the solution may be intro-

diens met die ensiemagtige débridement van koue absesse, sere en wonde in die beginstadium asook om verdikte afskeidings in die asemhalingskanaal vloeibaar en los te maak. SK–SD is besonder waardevol vir die oplossing van gestolde borsbloeding, verdikte empieem-vloeistof, bloedblase in die urineblaas of elders en vir absesse, wonde en sere wat plasminogeen bevat.

Streptokinase aktiveer plasminogeen. Dit is al in 'n onsuiwer vorm uit mens- en beesplasma verkry en mag binnekort vir débridement en moontlik vir die oplossing van binnespierse trombose beskikbaar wees. Plasmien-profibrienolisien, wat deur SK–SD geaktiveer is, het proefondervindelik effektief klonte wat deur natrium morruaat veroorsaak is, opgelos.

Hialuronidase maak die tussenselstof vloeibaar deur die hialuroniese suur te depolimeriseer en dit help om die stowwe in die selle te diffundeer. Hierdie ensiem kan van baie bronne verkry word, vernaamlik van beesteelballe. Dit is beskikbaar in die vorm van 'n droë poeier wat stabiel en maklik oplosbaar is. Die werking word gemeet in troebelheidvermindering-eenhede (TRU) of viskositeitvermindering-eenhede (VRU) en 1 TRU staan gelyk aan 3·3 VRU. Die werking word deur verskeie faktore beïnvloed. Hialuronidase word dikwels met onderhuidingspuitings gebruik om die absorbering van vloeistowwe te bespoedig, dit is veral handig met die behandeling van babas wanneer binneaarse terapie moeilik is. 'n Enkel dosis kan nou of gedurende die beginstadium van die inspuiting gegee word of saam met die inspuiting. As gevolg van die snelle absorbering bestaan daar dieselfde gevare en teenaanduidings as in die geval van baie vinnige inspuitings. Op dieselfde manier word hialuronidase gebruik om die absorbering te verhoog van middels soos kontrasmiddels en geneesmiddels soos penicillin en heparin. Dit word ook gebruik met die spalking van beenbreuke; in oogheelkunde, om die verspreiding van plaaslike verdowingsmiddels aan te help en om die opblaas en vervorming van weefsels te verminder, en om die herabsorbering van bloed en vloeistof soos bv. in pretibiaal-miksedeem en parafimose, aan te moedig.

Die terapeutiese gebruik van ander ensieme word ondersoek en die geleentheid vir navorsing oor hierdie besonder belangrike en interessante onderwerp is groot. 'n Volledige verslag oor die huidige posisie met byna 300 verwysings na literatuur oor die onderwerp het onlangs verskyn.[1]

1. Cliffton, E. E. (1954): Amer. J. Med. Sci., **228,** 568.

duced by means of a catheter. It may be applied in closed cavities by injection, when care must be taken to avoid any danger of injection into the lung or the blood stream. Trypsin has proved most useful in the enzymatic debridement of early chronic abscesses, ulcers and wounds, and also for the liquefaction and clearing of thick secretions in the respiratory tract. SK–SD is most useful in the lysis of clotted haemothorax, thickened empyema fluid, haematomas in the urinary bladder or elsewhere, and in abscesses, wounds and ulcers containing plasminogen.

Plasminogen is activated by streptokinase. It has been obtained in impure form from human and bovine plasma, and may soon be available for use in debridement and possibly for lysis of intravascular thromboses. Plasmin—profibrinolysin activated by SK–SD—has proved effective experimentally in the lysis of clots produced by sodium morrhuate.

Hyaluronidase liquefies the intercellular substance by depolymerization of hyaluronic acid, and thus aids the diffusion of materials to the cells. The enzyme is available from many sources, especially the bovine testis. It is available as a dry powder, which is stable and readily soluble. The activity is expressed in turbidity-reducing units (TRU) or viscosity-reducing units (VRU) and 1 TRU is approximately equal to 3·3 VRU. The activity is influenced by numerous factors. A common use of hyaluronidase is to increase the speed of absorption of fluids in hypodermoclyses; it is particularly useful in infants, in whom intravenous therapy is difficult. A single dose may be given before or during the early part of the clysis, or mixed with the clysis. Because of the rapid absorption there are the same dangers and contra-indications as with very rapid infusions. A similar use of hyaluronidase is the enhancement of absorption of agents such as contrast media and drugs like penicillin and heparin. It is also used in the reduction of fractures; in ophthalmology, to increase the diffusion of local anaesthetics and to reduce ballooning and distortion of the tissues; and to promote the reabsorption of collections of blood and fluid, e.g. in pretibial myxoedema and in paraphimosis. Many other uses have been suggested for this enzyme.

The therapeutic use of other enzymes is being developed and there is much scope for research in this important and interesting field. A full account of the present position has been published recently with nearly 300 references to the literature on the subject.[1]

1. Cliffton, E. E. (1954): Amer. J. Med. Sci., **228,** 568.