How its great therapeutic potential can finally be realized

Fibrinolysis refers to the body's natural defense system against blood clots, which are made principally of a protein called fibrin. "Lysis" is the Greek word for dissolving, therefore, dissolving fibrin clots. Fibrinolysis is needed because clots are required to prevent bleeding from vascular injuries, but their sized must be restrained lest they obstruct blood flow, causing diseases like heart attacks and strokes.

Optimal treatment of these conditions requires that circulation to the heart or brain be restored as rapidly as possible to minimize the period of oxygen deprivation leading to irreversible tissue damage. The only means by which restoration of circulation can be achieved rapidly is with therapeutic fibrinolysis. The only alternative is a catheterization procedure like angioplasty, which requires hospitalization and inevitably delays removal of the clot significantly. For example, if effective treatment takes place within 1-2 hours of a heart attack, the mortality is 1%, if it is more than 3 hours, the mortality rises to 6-7%. In addition, the amount of heart damage in the survivors, leading to heart failure, is similarly time-dependent. In stroke, restoring circulation rapidly is just as important.

Unfortunately, fibrinolysis as practiced for the past thirty years has been so disappointing so that it has been replaced by angioplasty whenever possible, despite the delay involved. This stark failure of fibrinolysis is related to a fundamental misunderstanding of how it works, in which only one of two fibrinolytics was believed to do the job.

In the natural system, there are two fibrinolytics, tPA and uPA, but only tPA has been used since 1987. Since only tPA binds tightly to fibrin, it was mistakenly assumed it was alone responsible for fibrinolysis, and this assumption has endured despite overwhelming evidence to the contrary.

For example, tPA and uPA are complementary in their fibrinolytic effects, like the Chinese Ying and Yang, they are two halves that together make a whole. Their combined effects are more potent than either of their individual effects, as easily demonstrated and often published. Even in their individual effects, uPA, rather than tPA, has the significantly greater fibrinolytic effect, in a ratio of 2:1.

Their function is also sequential, with tPA initiating fibrinolysis and uPA continuing and completing it. Therefore, uPA is responsible for 2/3 of the process. A sequential combination, modeled on the natural fibrinolytic design was once tested in a clinical trial of 101 patients with heart attack. The patients all received a small injection of tPA (about 5% of the standard tPA dose) followed by an intravenous infusion of uPA for 90 minutes. This treatment almost doubled the blocked artery opening rate compared to the best tPA clinical result and was associated with a 6-fold reduction in mortality compared to tPA.

These remarkable clinical results in heart attack are unprecedented and were published in a

leading cardiology journal. Despite this, fibrinolysis with tPA alone remained and remains the standard for fibrinolytic therapy. This irrational reaction can only be explained by the old idiom that “old habits die hard” and the new is resisted.

In conclusion, the body’s fibrinolytic system uses both natural fibrinolytics, tPA and uPA, rather than the one that has been used in therapy. Their functions are complementary and were designed to function optimally in a combination, which is a sequential one. When a sequential combination was used in therapy, an unprecedented fibrinolytic effect was achieved, which was also safer due to the much lower doses required by the combination. This design provides the means to finally realize the untapped potential of therapeutic fibrinolysis.

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