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EDITORIAL

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Tumor Necrosis factor receptor: Fc fusion protein does not improve septic shock and may increase mortality in human

The importance of knowing and understanding the physiopathology of diseases is obvious. When relevant, new information is integrated and hypotheses are generated, particularly with the aim of interfering in the disease process. Thus, hope of preventing or treating the disease arises. But before evidence concerning efficacy is obtained, there is a strong tendency to apply the results in practice.

This scenario is illustrated by a recently published article on the treatment of septic shock with the tumor necrosis factor receptor (TNFR:Fc).[1] As it is known, the administration of TNF[2] may reproduce various aspects of shock pathogenes.[2,3] As the article states, TNF antibodies have a protective effect in animal models of septic shock.[4,5]

Thus, interfering with TNF effects became a great hope in the treatment of septic shock. Yet when the safety and efficacy of TNFR:Fc was tested in humans, using three different doses in a randomized controlled trial (RCT) against placebo, no effect on mortality was observed at the lower doses, and indeed the high dose appeared to be associated with *increased* mortality.

Although the study group sample size was relatively small, there is only a small probability that this kind of treatment may help, rather than harm septic shock patients. Thus, this hope, obtained after many years of high technology research, has been shattered.

While the importance of blocking the TNF effect, after the mastocite has been stimulated, may be reevaluated, further research and new hope are needed and again, as in this case, the use of RCTs will distinguish between theoretical and true efficacy.

While it may be difficult and laborious to accept, the best way to know whether a new treatment is good or not is to test the hypothesis by designing and conducting a RCT. Theoretical hypotheses are important pathways for research question formulations which eventually must be tested by RCTs.

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