PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Liposomal delivery of protein 72

ArticleInfo		
ArticleID	:	4158
ArticleDOI	:	10.1186/ccf-1999-2141
ArticleCitationID	:	2141
ArticleSequenceNumber	:	17
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 1999–10–27 OnlineDate : 1999–10–27
ArticleCopyright	:	Current Science Ltd1999
ArticleGrants	:	
ArticleContext	:	1305422

Heidi Robertshaw

Keywords

Endotoxin, liposomal delivery, myocardial dysfunction

Comments

This study continued the vast study of LPS induced sepsis, but also examined novel proteins involved in the pathogenesis of sepsis. It examined the use of liposomal delivery, an unusual method of drug delivery. As with many animal studies, it will be interesting to see if follow-up work confirms its importance in human sepsis and whether the delivery of liposomal HSP-72 may be of clinical use.

Introduction

Many studies have used bacterial lipopolysaccharide (LPS) in animal models to mimic sepsis and endotoxaemia. It has previously been shown that if an animal is repeatedly exposed to small doses of LPS, tolerance develops and the systemic response to a subsequent large dose of LPS is reduced. This preconditioning requires new protein synthesis and it has been noted that heat shock protein 72 (HSP-72) is induced at the same time as the adaptation to LPS. However, it has not been proven that HSP-72 is responsible for this myocardial protection. In addition, HSP-72 induction proteins are noxious when delivered systemically and more than 24 h are required for induction of protection.

Aims

To determine whether HSP-72 may be delivered into the heart directly, whether HSP-72 itself is protective against LPS-induced cardiac depression and to compare the relative protection and time courses required for thermally induced HSP-72 versus liposomally introduced HSP-72.

Methods

HSP-72 was introduced into rat heart before LPS administration. The HSP-72 was either introduced by liposomal transfer or induced by heat shock at 42oC for 15 min, 24 h before LPS administration. The expression of HSP-72 was confirmed using Western blot techniques. Left ventricular pressure was measured as an index of cardiac function.

Results

HSP-72 was expressed in rat heart following induction by heat shock and introduction by liposomal transfer. Cardiac dysfunction (normally induced by LPS) was abolished by thermal induction of HSP-72 (24 hours before LPS administration)and also by liposomal transfer of HSP-72 (90 minutes before LPS administration).

Discussion

This study indicates that HSP-72, delivered by either liposome or induced by heat shock, prevents LPS- induced myocardial contractile dysfunction. Liposomal delivery appears to be an effective method of delivering HSP-72 and has the advantage of providing cardiac protection only 90 min following administration. The authors discuss the continuing mortality and morbidity resulting from sepsis and suggest that understanding the mechanisms of LPS tolerance may lead to the development of new therapeutic strategies.

References

1. Meldrum DR, Meng X, Shames BD, Pomerantz B, Donnahoo KK, Banerjee A, Harken AH: Liposomal delivery of heat-shock protein 72 into heart prevents endotoxin-induced myocardial contractile dysfunction. Surgery. 1999, 126: 136-141.