TRANSFER OF PLASMA IGF-I INTO LYMPH

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In-vitro experiments suggest free unbound IGF-1 can be transfered intact across the capillary endothelium (1). However, in the intact animal 95% or more of the circulating IGF-1 is bound to specific high molecular weight binding proteins which are thought to restrict the passage of IGF-1 out of the vascular space. In the present study we have examined the transfer of [^{125}I] labelled IGF-1 from blood into lymph of male kid goats as a model for its movement into the extracellular fluid space.

[^{125}I]IGF-1 was injected into the jugular vein of eight anaethesised male Saanen goats (3.5-6wk old; 7-12.5kg). Anaethesia was induced and maintained with Na pentobarbitone. Lymph was collected continuously from the subclavian duct over 10min intervals for 240min. Blood was taken every 10min from a carotid arterial catheter. The amount of lymph collected varied from 60 to 1540mg/10min between animals but was constant within animals.

Plasma levels of [^{125}I]IGF-1 declined rapidly following its intravenous injection. At 4min the amount of radioactivity in plasma was 26±4.3 CPM/mg. By 20min 70.1±2.7% (mean±SEM) of this amount remained in circulation. Thereafter, levels declined more slowly with 53.1±3.1% of the initial total radioactivity remaining at 120min and 41.5±3.0% at 240min. The integrity of the [^{125}I]IGF-1 in plasma remained unchanged throughout the experiment. Total radioactivity in lymph reached a peak value of 4.7±1.3 CPM/mg at 120min. However, at 20min only 65.3 ± 2.2% of the [^{125}I]labelled material in lymph was precipitable by 15% TCA and this fell to 49.9±2.8% by 120min. Thus the amount of intact [^{125}I]IGF-1 in lymph reached its maximum by 20min and was maintained at this level until at least 120 minutes. Thereafter it declined slowly, reflecting the decline in plasma levels. The ratio of intact [^{125}I]IGF-1 in plasma to lymph was approximately 6:1 at 120min and was not significantly altered for the remainder of the experiment.

Sephacryl S-200 column chromatography of plasma and lymph collected between 50 and 90min showed that 6.6±0.8% and 23±4.1% of the intact [^{125}I]IGF-1 remained in the free form. The rest was predominantly associated with the 150 KDa binding protein. The degraded material eluted with or before the salt peak indicating the presence of peptide fragments and free [^{125}I]. The ratio of free [^{125}I]IGF-1 in plasma to lymph was 2:1 and the ratio for bound [^{125}I]IGF-1 was 8:1.

These experiments provide in-vivo evidence that IGF-1 is rapidly transfered intact from the vascular space into lymph. As a significant proportion of [^{125}I]IGF-1 in lymph is in the free, unbound form it would seem that it is this component that is more readily transfered. The results further suggest that tissues may be continuously bathed in IGF-1 from the circulation.

1. Bar, R.S., Boes, M. and Yorek, M. (1986) Endocrinology 118, 1072.

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