REAL-TIME RADIOISOTOPIC SYSTEMIC LEAKAGE MONITORING DURING HYPERTHERMIC ISOLATED LUNG PERFUSION WITH TNF-α

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BACKGROUND-AIM

Hyperthermic Isolated Lung Perfusion (HILP) is an effective way to treat locally advanced malignancies, as well as multiple metastases in a single organ. This technique in fact allows delivering high-dose chemotherapy to a single organ/district, while avoiding systemic toxicity. Monitoring the shunt from the circuit to the bloodstream is however mandatory, especially whenever Tumor Necrosis Factor-α (TNF) is used, as this drug can cause severe and potentially lethal complications, should an excess leakage occur.

Radio-isotopic leakage monitoring has been extensively validated on limb perfusion, however its utilization in the lungs setting presents some specific challenges and is to this date still experimental. In this study, we compared measured TNF-α leakage with its corresponding radio-isotopic estimation at different time points.

METHODS

15 consecutive patients were submitted to HILP for multiple lung metastases from soft tissue sarcoma. The procedure lasted 90 minutes, after bolus administration of TNF-α, whose concentration was sampled in the isolated circuit and in the peripheral blood at baseline and after 3, 15, 30, 60 and 90 minutes. For radioisotope leakage monitoring, in vivo erythrocytes labeling was performed in the systemic circulation with 0.2 MBq/Kg of 99mTc; baseline counts were then recorded at steady state, using a γ-scintillation probe secured over the temporal artery. Thereafter a bolus of 2 Mbq/Kg of 99mTc labeled erythrocytes was injected in the isolated circuit while peripheral blood activity was measured every five minutes. Leakage Factor (LF) was calculated using the following formula:

\[
\text{Decay-Corrected Counts} - \text{Baseline counts} \times \text{Systemic Volume} \\
\text{Baseline Counts} \times 0.1 \times \text{Total Volume} \times \text{Systemic Volume}
\]

where Total Volume refers to the estimated total blood volume and Systemic Volume to the difference between Total Volume and the volume within the perfusion circuit.

RESULTS

Average TNF-α concentrations in the circuit were 1352±273 ng/ml; these levels began to decrease after 60 minutes (p<0.001).

Serum average TNF-α levels remained stable throughout the study at 0.6±1.66 ng/ml. Average LF was 2.9±1.8%. In three patients TNF-α peripheral concentration significantly increased from minute 3 (p<0.05); in all cases this leakage was promptly detected by an increase in the LF and compensatory procedures were immediately started. No patients showed immediate or late sign of systemic toxicity. Overall, correlation between actual leakage (expressed as ratio between circuit and systemic TNF-α levels) and measured LF was excellent, with average R-value of 0.85±0.16.

CONCLUSION

Radio-isotopic monitoring of drug leakage during HILP is a feasible and reliable method. Its use permits to immediately adopt corrective maneuvers to avoid drug loss from the isolated circuit, thus minimizing toxic effects.