IN VIVO KINETICS OF $^{131}$I-MONOClonAL ANTIBOdIES [ANTI-CEA AND 19-9, F(ab')$_2$] IN HUMANS

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INTRODUCTION

The use of radiiodinated immunococktail against CEA and CA 19-9 has been reported by Chatal et al. (1984, 1985) to improve the detection of malignancies from the gastrointestinal tract. The aim of this work was to study the scintigraphic kinetics of the tracer and the effects of circulating antigens on the pharmacokinetics of the monoclonal antibodies (MoAbs).

MATERIALS AND METHODS

Eighteen patients known or suspected to have primary or metastatic cancer of the gastrointestinal tract were investigated employing a MoAb cocktail [Ab-CEA 1 mg + 19-9 1 mg, F(ab')$_2$, I-131 (iodogen) labeling, IMACIS$_1$]. Whole body images as well as multiple overlapping views were obtained immediately after MoAb administration (111 MBq over 3-5 min) (TO) and at 3 and 5 days (T3, T5), according to the original protocol by Chatal and Rougier (1985). Multiple blood samples were taken up to T1 for serial antigen assay (11 pts) and up to T5 to study blood clearance (6 pts), assuming the value at 5 min equal to 100%. Antigen assay was performed employing commercially available IRMA kits (Elsa-CEA, Elsa-CA 19-9, CIS Diagn.). Effective whole body retention was calculated as percent of TO (geometrical mean of anterior and posterior view whole body scans). After data storage, regions of interest (ROI) were outlined corresponding to precordium (H), right liver lobe (L), right lung (Lu), and tumor (T); ROI counts at T3 and T5 were expressed as percent of the counts recorded at TO. Assuming that H counts reflect mainly the blood activity and L, Lu, and T counts at TO the circulating activity, we calculated T/H, L/H and Lu/H ratios normalized to 1 at TO to avoid the interference due to the patient's body size. The rate of radioactivity decrease between neighboring acquisition times ($-\%$/h) was calculated as:

$$\frac{(x - y) \times 100}{(xt)}$$

where x and y are the ROI counts in the earlier and later acquisition respectively and t is the elapsed time in hours.
RESULTS

After administration of MoAbs, both normal and pathological CEA levels invariably show a drop with a late return towards the basal value (Figure 1). There is a significant correlation between basal values and Δ (basal minus 20 min value) (r = 0.98, p < 0.001). On the other hand, CA 19-9 levels are less influenced and a minor reduction is observed at later times.

Blood radioactivity is associated with the plasma and shows fluctuations up to 45-60 min before decreasing in a biexponential manner (Figure 2). To assess if initial fluctuations were related to the slow administration of the tracer, we studied early blood disappearance after bolus injection of the tracer in two additional patients, and obtained the same time activity curve.

Effective whole body (WB) retention, tumor, liver, lung and precordium time activity course is shown in Figure 3. The organ activity decreases in all the tissues during the time of the study. Although the effective retention in T is higher than in L and Lu both at T3 and T5, the rate of decrease in T is significantly slower in comparison with the other organs only from T0 to T3, while from T3 to T5, T loss is not significantly different from other organs of interest, except the precordium (Table 1).

Lung to heart ratio tends to increase in all but three patients; however, no correlation was found with other parameters. The highest T/H ratios were observed in patients with only slightly elevated serum antigen levels even if there is not a significant correlation between these two parameters. On the other hand, the L/H ratio is directly correlated with the serum antigen levels both considering CEA and CA 19-9 separately, and the sum of their logarithms; the more significant correlation was found at T5 between L/H ratio and log CEA + log CA 19-9 (Figure 4).

Figure 1. Levels of Circulating Antigens (CEA and CA 19-9) in Patients After Administration of Radioiodinated MoAbs.