

Other Biomarkers in Midgut Neuroendocrine Tumors (NETs)

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Introduction

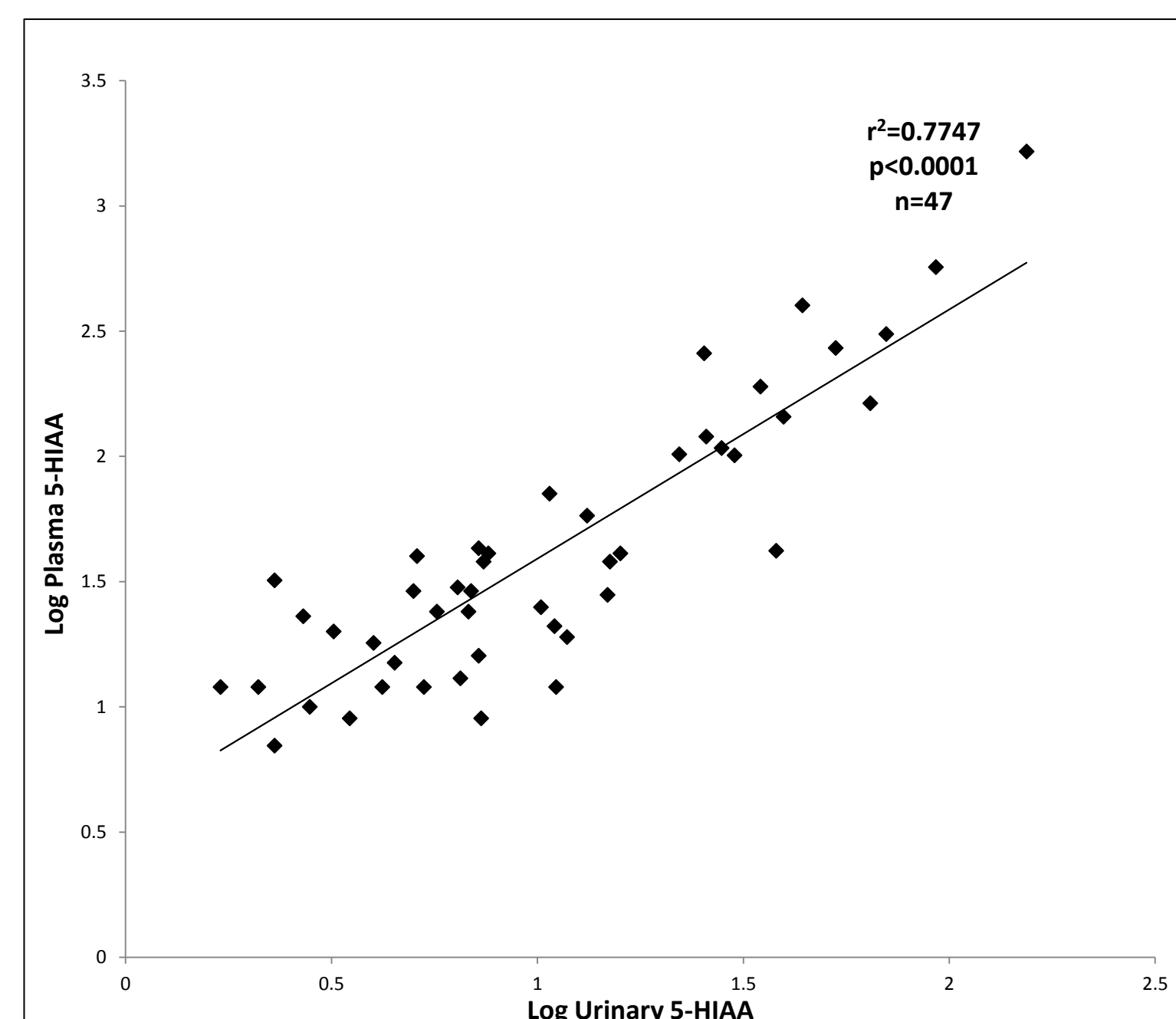
5-hydroxyindoleacetic acid (5-HIAA) is used for the evaluation of neuroendocrine tumors (NETs), however the current 5-HIAA assay requires a twenty-four hour urine collection which is inconvenient.

Methods

We developed a gas chromatography-mass spectroscopy (GC-MS) based plasma 5-HIAA assay. We compared 24-hour urine 5-HIAA values with single fasting plasma 5-HIAA values in 115 mixed variety NET patients, a subset of 72 patients with only small bowel NETs, and another subset of 47 patients with small bowel NETs with liver metastasis. We also compared the information gained from urinary and plasma 5-HIAA values with other biomarkers of midgut NET activity in order to determine the plasma assay's clinical implications.

Results

In a group of 115 patients with all types of NETS, in a subgroup of 72 mid gut NET patients and in another subgroup of 47 mid gut NETS with liver metastasis, the correlation between the urine and fasting plasma 5-HIAA values were highly statistically significant ($p < 0.0001$, $p < 0.0001$, $p < 0.0001$). Comparison of the proportions of normal or abnormal urinary and plasma 5-HIAA values to the proportions of chromogranin, serotonin, neurokinin or pancreastatin values that were in the normal or abnormal range yielded essentially identical information.



		Neurokinin A					Neurokinin A					Pancreastatin					Pancreastatin		
Urinary 5-HIAA		Normal	Elevated		Plasma 5-HIAA		Normal	Elevated		Urinary 5-HIAA		Normal	Elevated		Plasma 5-HIAA		Normal	Elevated	
	Normal	25 (34%)	0 (0%)	34.7%		Normal	27 (38%)	1 (1%)	38.9%		Normal	17 (24%)	8 (11%)	34.7%		Normal	24 (33%)	4 (6%)	38.9%
Elevated	37 (51%)	10 (14%)	65.3%	Elevated	35 (49%)	9 (13%)	61.1%	Elevated	13 (18%)	34 (47%)	65.3%	Elevated	6 (8%)	38 (53%)	61.1%	Elevated	6 (8%)	38 (53%)	61.1%
		86.1%	13.9%			86.1%	13.9%			41.7%	58.3%			41.7%	58.3%			41.7%	58.3%

		Chromogranin A					Chromogranin A					Serotonin					Serotonin		
Urinary 5-HIAA		Normal	Elevated		Plasma 5-HIAA		Normal	Elevated		Urinary 5-HIAA		Normal	Elevated		Plasma 5-HIAA		Normal	Elevated	
	Normal	23 (32%)	2 (3%)	35.2%		Normal	25 (35%)	3 (4%)	39.4%		Normal	15 (25%)	8 (13%)	37.7%		Normal	17 (28%)	6 (10%)	37.7%
Elevated	16 (23%)	30 (42%)	64.8%	Elevated	14 (20%)	29 (41%)	60.6%	Elevated	11 (18%)	27 (44%)	62.3%	Elevated	9 (15%)	29 (48%)	62.3%	Elevated	9 (15%)	29 (48%)	62.3%
		54.9%	45.1%			54.9%	45.1%			42.6%	57.4%			42.6%	57.4%			42.6%	57.4%

Above: Comparison of the percent of patients with normal and elevated biomarkers values compared to urinary (<6mg/24hrs, normal) or plasma 5-HIAA values. Small bowel primaries only.
 Left: Urinary 5-HIAA values versus plasma 5-HIAA values for small bowel primaries with liver metastasis. Log-scale scatterplot of urinary 5-HIAA values versus plasma 5-HIAA values for patients with small bowel primary NETs with liver metastasis (n=47).

Conclusions

Plasma fasting 5-HIAA values are proportional to urinary 5-HIAA values and provide similar clinical correlation with other biomarkers.