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Defect of Iodide Metabolism and Its Implication for Thyroid Cancer Therapy

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The prevalence of thyroid cancer is relatively low (0,74% in men and 2.3% in women) compare with other cancers. The prognosis is favorable been obtained through effectiveness of total/near-total thyroid surgery followed by radioiodine therapy (^{131}I) and thyroid stimulating hormone (TSH) suppression therapy with thyroxin. Ten-year survival rates for papillary and follicular thyroid carcinoma are 95 and 90% respectively. In the other hand, the recurrence rate of thyroid cancer is high and only one third of patients with distance metastases respond to ^{131}I with complete remission. Some of thyroid cancer and their metastasis exhibit reduced ^{131}I therapy with respect to normal thyroid tissue.

Natrium/sodium iodine symporter (NIS) is an integral plasma membrane glycoprotein, in which NIS mediates the active transport of iodine (I^-) at the basolateral plasma membrane of thyroid follicular cell against the iodine electrochemical gradient, its stimulated by TSH. Iodine is shifted from cytoplasma across the apical plasma membrane toward the colloid, a process is mediated by pendrin and apical transporter. At the cell-colloid interface, organification of I^- is catalyzed by thyroxin peroxidase (TPO). Iodine is oxidized and incorporated into some tyrosyl residues within the thyroglobulin (Tg) molecule, the complex is stored extracelulary in the colloid. Although papillary and follicular thyroid carcinomas retain the majority of biological properties of normal thyroid cell, a variety of biochemical defects has been demonstrated. Furthermore biological activity of peroxidase, although normal in benign cold adenomas, was decrease or absent in thyroid carcinomas, as a result a low iodine organification. As consequence, in thyroid cancer tissues a low intra-thyroidal iodine concentration or short residence time, a low degree of iodinated of thyroglobulin and low rate of thyroid hormone sintesis

Tissue uptake of iodine ia about 1% of the administrated activity in normal thyroid tissues, whereas it ranges from 0.1% to 0.001% in neoplastic tissues and average residence time to 3-5 days sometimes shorter, whereas it range from 6-8 days in normal thyroid tissues. This short half-life may be due to abnormalities in the organification process.

The outcome of ^{131}I therapy depends on the biological half-life of the isotope in the taget cells and the dose of radioactivy attained in the tumor. Uptake and organification are the two major steps of iodine metabolism and they defect obtain low radiation dose to thyroid cancer cells, these are mainly due to decrease expression of functional genes encoding NIS and abnormalities in the organification process, at least in part related to a defect in the peroxidase system

Keywords : iodine metabolism, uptake, organification,natrium iodide symporter, thyroxine peroxidase

Defects of Iodine Metabolism and Its Implication for Thyroid Cancer Therapy

Epidemiologi

- Prevalence of thyroid cancer
  - 0.74% men
  - 2.3% women
- Prognosis
  - Near/total thyrodectomy
  - Radioiodine therapy
  - LT4 suppression therapy
- Ten-years survival rates
  - Papillary : 95%
  - Follicular : 90%
- Recurrence rate
- Respond to I-131 : some exhibit reduced I-131 respect to normal thyroid tissue

Concluding Remarks

- Outcome of I-131 therapy depends
  - Uptake of radio isotop
    - Decrease of NIS gene → protein
  - biological half-life of radio isotop attained in tumor
    - Abnormalities in organification process : such as peroxidase system