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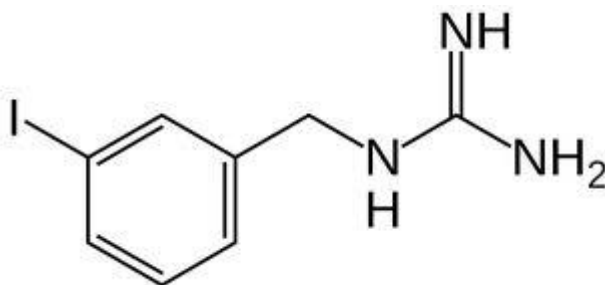
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Recomendamos la lectura del número de Septiembre 2011, de *Seminars in Nuclear Medicine*, que trata monográficamente sobre el radiofármaco:

Meta yodo bencil guanidina (MIBG) en diagnóstico y terapia

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Radioiodinated Metaiodobenzylguanidine (MIBG): Radiochemistry, Biology, and Pharmacology

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As an analogue of adrenergic neurotransmitter norepinephrine (NE), metaiodobenzylguanidine (MIBG) demonstrates high uptake both in normal sympathetically innervated tissues, such as the heart and salivary glands, and in tumors that express the NE transporter (NET), specifically those of neural crest and neuroendocrine origin. In 1994, ^{131}I -MIBG, also known as iobenguane I-131 intravenous, received Food and Drug Administration (FDA) approval as an imaging agent. In 2008, ^{123}I -MIBG was also approved by FDA as a tumor imaging agent. Commercial formulations of radioiodinated MIBG are prepared on the basis of radioiodide exchange reaction with unlabeled MIBG as a precursor and contain large mass amounts of unlabeled MIBG, or “cold carrier,” molecules. Because the cold MIBG molecules competitively inhibit the uptake of radiolabeled MIBG molecules by adrenergic and neuroendocrine cells expressing NET, no-carrier-added (n.c.a.), high specific activity (SA) radioiodinated MIBG preparations have been developed on the basis of electrophilic radioiodination reaction and solid-phase technology by using dibutylstanyl benzylguanidine precursor linked to polymers. On the basis of n.c.a. synthetic procedures, therapeutic doses of [^{131}I]MIBG can be administered with very high SA (1600 mCi/ μmol or 5734 mCi/mg). The very high SA of n.c.a. [^{131}I]MIBG drug would increase the specific cellular uptake of adrenergic neurons and neuroendocrine tumor cells expressing NET.



Preclinical Assessment of Strategies for Enhancement of Metaiodobenzylguanidine Therapy of Neuroendocrine Tumors

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By virtue of its high affinity for the norepinephrine transporter (NET), [¹³¹I]metaiodobenzylguanidine ([¹³¹I]MIBG) has been used for the therapy of tumors of neuroectodermal origin for more than 25 years. Although not yet universally adopted, [¹³¹I]MIBG targeted radiotherapy remains a highly promising means of management of neuroblastoma, pheochromocytoma, and carcinoids. Appreciation of the mode of conveyance of [¹³¹I]MIBG into malignant cells and of factors that influence the activity of the uptake mechanism has indicated a variety of means of increasing the effectiveness of this type of treatment. Studies in model systems revealed that radiolabeling of MIBG to high specific activity reduced the amount of cold competitor, thereby increasing tumor dose and minimizing pressor effects. Increased radiotoxicity to targeted tumors might also be achieved by the use of the α -particle emitter [²¹¹At]astatine rather than ¹³¹I as radiolabel. Recently it has been demonstrated that potent cytotoxic bystander effects were induced by [¹³¹I]MIBG, [¹²³I]MIBG, and [²¹¹At]meta-astatobenzylguanidine. Discovery of the structure of bystander factors could increase the therapeutic ratio achievable by MIBG targeted radiotherapy. [¹³¹I]MIBG combined with topotecan produced supra-additive cytotoxicity in vitro and tumor growth delay in vivo. The enhanced antitumor effect was consistent with a failure to repair DNA damage. Initial findings suggest that further enhancement of efficacy might be achieved by triple combination therapy with drugs that disrupt alternative tumor-specific pathways and synergize not only with [¹³¹I]MIBG but also with topotecan. With these ploys, it is expected that advances will be made toward the optimization of [¹³¹I]MIBG therapy of neuroectodermal tumors.



Pediatrics: Diagnosis of Neuroblastoma

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Neuroblastoma is the most common pediatric extracranial soft-tissue tumor, accounting for approximately 8% of childhood malignancies. Its prognosis is widely variable, ranging from spontaneous regression to fatal disease despite multimodality therapy. Multiple imaging and clinical tests are needed to accurately assess patient risk with risk groups based on disease stage, patient age, and biological tumor factors. Approximately 60% of patients with neuroblastoma have metastatic disease, most commonly involving bone marrow or cortical bone. Metaiodobenzylguanidine (mIBG) scintigraphy plays an important role in the assessment of neuroblastoma, allowing whole-body disease assessment. mIBG is used to define extent of disease at diagnosis, assess disease response during therapy, and detect residual and recurrent disease during follow-up. mIBG is highly sensitive and specific for neuroblastoma, concentrating in >90% of tumors. mIBG was initially labeled with ^{131}I , but ^{123}I -mIBG yields higher quality images at a lower patient radiation dose. ^{123}I -mIBG (AdreView; GE Healthcare, Arlington Heights, IL) was approved for clinical use in children by the Food and Drug Administration in 2008 and is now commercially available throughout the United States. The use of single-photon emission computed tomography and single-photon emission computed tomography/computed tomography in ^{123}I -mIBG imaging has improved certainty of lesion detection and localization. Fluorodeoxyglucose positron-emission tomography has recently been compared with mIBG and found to be most useful in neuroblastomas which fail to or weakly accumulate mIBG.



Iodine-131–labeled Meta-Iodobenzylguanidine Therapy of Children with Neuroblastoma: Program Planning and Initial Experience

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Patients with high-risk neuroblastoma have a poor prognosis, especially in cases of recurrent or relapsed disease. Iodine-131–labeled meta-iodobenzylguanidine (^{131}I -MIBG) can be an effective and relatively well-tolerated agent for the treatment of refractory neuroblastoma. Establishing an MIBG therapy program requires a great deal of planning, availability of hospital resources, and the commitment of individuals with training and expertise in multiple disciplines. Providing ^{131}I -MIBG therapy requires physical facilities and procedures that permit patient care in compliance with the standards for occupational and community exposure to radiation. Establishment of a successful ^{131}I -MIBG therapy program also requires a detailed operational plan and appropriate education for caregivers, parents, and patients.

Current Role of Metaiodobenzylguanidine in the Diagnosis of Pheochromocytoma and Medullary Thyroid Cancer

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Despite early reports of excellent diagnostic characteristics of [^{131}I]/[^{123}I]-metaiodobenzylguanidine (MIBG) in the evaluation of pheochromocytomas/paragangliomas (PHEOs/PGLs) or medullary thyroid cancer as experience with it was accumulated, the sensitivity dropped. Nevertheless, this modality is still useful in the diagnostic work-up of PHEOs/PGLs because it is widely available, and in case of positive scans it might indicate patients who are potential candidates for [^{131}I]MIBG therapy.



Targeted Systemic Radiotherapy of Pheochromocytoma and Medullary Thyroid Cancer

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Targeted systemic radiotherapy constitutes the systemic administration of a radioactive agent that targets a molecule expressed preferentially on cancer cells. The archetypal such therapy is ^{131}I therapy for differentiated thyroid cancers. Radiotherapy typically delivers a calculated radiation-absorbed dose to tumor that takes into account (contiguous) normal tissue. Systemic radiotherapy development currently uses schema more analogous to chemotherapy—a radioactivity estimate that does not cause any irreversible toxicity. Historically, arbitrary amounts of radioactivity shown to be effective, on the basis of retrospective review, were used for thyroid cancer therapy with ^{131}I as well as for neuroendocrine tumor therapy with ^{131}I -labeled meta-iodobenzylguanidine (MIBG). Their established safety record has led to adaptations that include repeat therapies with nontoxic amounts of radioactivity. There remains, however, a lack of clear understanding of the safety limits of systemic targeted radiotherapy. This is probably most true in systemic therapy with MIBG in adult neuroendocrine tumors. Bone marrow is the primary critical organ for most targeted systemic radiotherapy; second organ involvement may be renal, as with MIBG and targeted radiopeptide therapy, or pulmonary, as with radioimmunotherapy. Most therapies have tended toward multiple administrations of subtoxic amounts of radioactivity. Therapy with MIBG in pheochromocytoma as well as targeted radiopeptide therapy in medullary thyroid cancer has followed this model. Radioimmunotherapy appears very promising; a definitive Phase 2 study needs completion. All therapy has shown promise in extending disease survival (as compared with historical controls), with few major structural (or biochemical) responses. This review will attempt to compliment the excellent existing literature by providing an overall systemic therapeutic approach to this promising endeavor.



Cardiac Applications of ^{123}I -mIBG Imaging

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Cardiac autonomic innervation plays a key role in maintaining hemodynamic and electrophysiologic harmony. Cardiac sympathetic function is adversely altered in many disease states, such as congestive heart failure, myocardial ischemia, and diabetes. ^{123}I -mIBG, a sympathetic neurotransmitter radionuclide analog, aids in the detection of sympathetic innervation abnormalities and can be imaged with planar and single-photon emission computed tomographic techniques. Cardiac ^{123}I -mIBG uptake can be assessed by the heart mediastinal ratio (H/M), tracer washout rate, and focal uptake defects. These parameters have been widely studied and shown to correlate strongly and independently with congestive heart failure progression, cardiac arrhythmias, cardiac death, and all-cause mortality. There is accumulating evidence that ^{123}I -mIBG imaging can help to monitor a patient's clinical course and response to therapy. The ability to predict potentially lethal ventricular arrhythmias promises to help more accurately select patients for implantable cardioverter defibrillators, limiting unnecessary devices and identifying additional patients at risk who do not meet current guidelines. ^{123}I -mIBG shows potential to help determine whether greater risk and usually more expensive ventricular assist device therapies or cardiac transplantation might be needed. Although more investigation in larger populations is needed to strengthen previous findings, cardiac ^{123}I -mIBG imaging shows promise as a new technique for recognizing and following potentially life-threatening cardiac conditions.

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