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Biochemistry of Pheochromocytoma

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ABSTRACT

Several clinical disorders mimic the signs and symptoms of pheochromocytoma; the definitive diagnosis of this condition thus rests primarily on showing excessive and inappropriate production of catecholamine. Because pheochromocytoma is fatal if undiagnosed, biochemical tests used to detect it should have a high sensitivity. Pheochromocytoma is a catecholamine producing tumor that can cause severe hypertension and other systemic disturbances. In this article biochemistry of pheochromocytoma is reviewed by first summarizing its introduction, genetics, biosynthesis and storage of catecholamine, then finally describing its metabolism. In the management of hospitalized sick patients with pheochromocytoma, if the clinician gets information about biochemical abnormalities in function of adrenal gland; it will not only help him for rapid diagnosis and immediate treatment but also for preventing the life threatening complications.

Key words : Nanosuspensions, Hydrophobic Drugs.

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The 2004 WHO classification of endocrine tumors defines pheochromocytoma as a tumor arising from catecholamine-producing chromaffin cells in the adrenal medulla—an intra-adrenal paraganglioma. Closely related tumors of extra-adrenal sympathetic and parasympathetic paraganglia are classified as extra-adrenal paragangliomas [17]. Although arbitrary, this nomenclature serves to emphasize the distinctive properties of tumors in different locations. In contrast to adrenal and extra-adrenal sympathetic paragangliomas, those from parasympathetic tissue (mainly in the head and neck) rarely produce significant amounts of catecholamines.

Pheochromocytomas are rare tumors (benign and malignant) of chromaffin cells that usually arise in the adrenal medulla, occasionally (about 10%) in paraganglia. The incidence is between 2-8/1,000,000 people. Among hypertensive patients, their prevalence is 0.13% and among individuals with incidental adrenal masses, their occurrence is 6.5%. They may occur as isolated lesions, or as part of familial endocrine syndromes. Their production of catecholamines results in hypertension that may be episodic. In addition to hypertension, clinical symptoms include sweating, headache and palpitations [12].

Genetics:

Hereditary catecholamine-producing pheochromocytomas and paragangliomas can be caused by germ-line mutations in any one of five genes identified to date: the rearranged during transfection (*RET*) proto-oncogene, in which mutations lead to multiple endocrine neoplasia type 2 (MEN2); the von Hippel–Lindau (*VHL*) gene, in which mutations lead to VHL syndrome; the neurofibromatosis type I (*NF1*) gene, which is associated with von Recklinghausen's disease; and genes encoding succinate dehydrogenase subunits D (SDHD) and B (SDHB), which are associated with familial nonsyndromic pheochromocytomas or paragangliomas. Mutation in a sixth gene encoding succinate dehydrogenase subunit C, *SDHC*, have so far been reported only in parasympathetic paragangliomas. Mutation testing, now routinely available for four of the above genes (*RET*, *VHL*, *SDHB*, and *SDHD*), demonstrates that germ-line mutations are responsible for well in excess of the 10% of tumors previously thought to be hereditary[1,9,11,14,15,16]. Most importantly, 7.5–27.0% of tumors without an obvious syndrome or family history result from otherwise unsuspected germ-line mutations in one of these four genes The overall hereditary predisposition for pheochromocytoma is, therefore, estimated to be approximately 20-30%. The high prevalence of unsuspected mutations indicates a need for more widespread genetic testing of patients with these tumors than is currently practiced. The panel of experts at the ISP agreed that, although there is now a reasonable