Study of Inorganic Iodine level in prevalent Haemodialysis Patients

Thesis

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Contents

List of Abbreviations

ACE-I ..... Angiotensin converting enzyme Inhibitors
AED ..... Antiepileptic drugs
AIDS ..... Acquired immune deficiency syndrome
AIH ..... Amiodarone-induced hypothyroidism
AIT ..... Amiodarone-induced thyrotoxicosis
BMI..... Body mass index
CAPD ..... Continuous ambulatory peritoneal dialysis
CCBs..... Calcuim channel blockers
CHD..... Coronary heart disease
CHF ..... Congestive heart failure
CKD..... Chronic kidney disease
CVD..... Coronary vascular disease
DIT ..... Diiodotyrosine
ESA..... Erythropoiesis stimulating agents
ECF..... Extracellular fluid
ESRD..... End stage renal disease
FFA..... Free fatty acids
Free T3 ..... Triiodothyronine
Free T4 ..... Free thyroxine
GFR ..... Glomerular filtration rate
HAART ..... Highly active antiretroviral therapy
HCV..... Hepatitis C virus
HD..... Hemodialysis
HIV ..... Human immune deficiency virus
hs-CRP ..... Highly sensitive C-reactive protein
IDD ..... Iodine deficiency disorder
IGF-1 ..... Insulin growth factor-1
IL-1 ..... Interleukin-1
INFα ..... Interferon alpha
LDL ..... Low density lipoprotein
MIT..... Monoiodotyrosine
mRNA..... Messenger ribonucleic acid
NIS..... Sodium iodide symporter
NSAIDs..... Nonsteroidal anti-inflammatory drugs
NTI ..... Non thyroidal illness
PD ..... Peritoneal dialysis
rT3 ..... Reverse T3
TBG ..... Thyroid binding globulin
TG..... Thyroglobulin
TFT..... Thyroid function tests

TNF..... Tumor necrosis factor
TRH..... Thyrotropin releasing hormone
TSH..... Thyroid stimulating hormone
VPA ..... Valproate

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Introduction

The kidney normally plays an important role in the metabolism, degradation, and excretion of several thyroid hormones. It is not surprising therefore that impairment in kidney function leads to disturbed thyroid physiology, all levels of the hypothalamic-pituitary-thyroid axis may be involved, including alteration in hormone production, distribution, and excretion, epidemiologic data suggest that predialysis patients with chronic kidney disease have an increased risk of hypothyroidism; many cases are subclinical ***(Kumar et al., 2015)*.**

Epidemiologic studies show that there is a substantially higher prevalence of thyroid functional disease, and in particular hypothyroidism, in ESRD patients compared with the general population ***(Rhee et al., 2014)***.

These changes seen in patients with ESRD are due to alterations in the peripheral 5′-monodeiodination of T4, reduced levels of plasma proteins that bind T4, the presence of inhibitors of T4 binding to plasma proteins, metabolic acidosis, and effects of medications. Heparin, among other drugs, inhibit T4 binding to plasma proteins and may transiently elevate free T4 levels ***(Mariani & Berns, 2012).***

The kidney plays a role in clearance of iodine, TSH, and thyrotropin-releasing hormone. However, most patients with CKD are euthyroid, with normal TSH and free T4 levels. Patients with uremia may have changes in thyroid

function tests consistent with the euthyroid sick syndrome ***(Mariani & Berns, 2012).***

The decrease of excretion of urinary iodine in CRF increases serum inorganic iodine level and iodine content of the thyroid, which consequently enlarges the gland ***(Kutlay et al., 2005).*** .

Aim of the work

To assess the level of inorganic iodine in prevalent haemodialysis patients and to correlate the findings with thyroid functions tests and thyroid ultrasound.

Thyroid disorders in hemodialysis patients

Thyroid gland is one of the largest endocrine glands in the body. It is found in the anterior neck. The thyroid gland controls rate of use of energy sources, protein synthesis, and controls the body's sensitivity to other hormones. It participates in these processes by producing thyroid hormones, the principal ones are thyroxine (T_4) and triiodothyronine (T_3), which is more active. These hormones regulate the growth and rate of function of many other systems in the body. T_3 and T_4 are synthesized from iodine and tyrosine. The thyroid also produces calcitonin, which plays a role in calcium homeostasis ***(Boulpaep et al., 2009).***

Thyroid hormones production is controlled by a complex mechanism of positive and negative regulation. Hypothalamic TSH-releasing hormone (TRH) stimulates TSH secretion from the anterior pituitary. TSH then initiates thyroid hormones synthesis and release from the thyroid gland. The synthesis of TRH and TSH subunit genes is inhibited at the transcriptional level by thyroid hormones, which also inhibits post-translational modification and release of TSH. Although opposing TRH and thyroid hormones inputs regulate the hypothalamic-pituitary-thyroid axis, Thyroid hormones negative feedback at the pituitary was thought to be the primary regulator of serum TSH levels ***(Chiamolera & Wondisford, 2009).***

The interplay between thyroid and the kidney in each other's functions is known for many years. Thyroid dysfunction affects renal physiology and development. Thyroid hormones affect kidney function by mediating effects on cardiac output and renal blood flow, contributing to changes in GFR. Thyroid hormones also have direct effects on the kidney by influencing GFR, tubular secretory and reabsorptive functions, and electrolyte homeostasis ***(Basu & Mohapatra, 2012).***

On the other side the kidney plays an important role in the metabolism, degradation and excretion of thyroid hormones. CKD affects thyroid function in many ways, including low circulating thyroid hormone levels, altered peripheral hormone metabolism, insufficient binding to carrier proteins, reduced tissue thyroid hormone content and altered iodine storage in the thyroid gland (***Malyszko et al., 2006).***

Even disorders of the thyroid and kidney may co-exist with common etiological factors. In addition, treatment strategies of one disease may affect those of the other organ ***(Basu & Mohapatra, 2012)***

Thyroid disorders in hemodialysis patients:

Despite solid epidemiologic evidence, the nature of this relation is not fully understood due to complexities in thyroid function evaluation in the presence of uremia and other factors such as reduced thyroid hormone signaling at

the level of the nephron and systemic hemodynamic disorders which are consequences of hypothyroidism on the kidney ***(Mariani & Berns, 2012).***

It is not surprising that impairment in kidney function leads to impaired thyroid physiology, all levels of the hypothalamic-pituitary-thyroid axis may be involved, including alteration in hormone production, distribution, and excretion ***(Chonchol et al., 2008).***

The prevalence of subclinical hypothyroidism in general population is 9. 6%, with higher incidence in women and it is found to be linked to an increased frequency of high titer of anti-thyroid antibodies, while the prevalence increases to 17. 9% in patients with GFR <60 mL/min/1. 73m^2 ***(Bell et al., 2007).***

As a consequence, the interest in the recent years was to get benefit from the growing evidence that suggests that overt or subclinical hypothyroidism could represent a therapeutic target to improve quality of life and to decrease mortality and morbidity patients with chronic renal failure ***(Shin et al., 2013).***

Several clinical manifestations of both hypothyroidism and chronic renal failure are alike. Some manifestations of hypothyroidism such as pallor, hypothermia and asthenia may also occur in uremia and the exclusion of diagnosis of hypothyroidism on clinical grounds may be extremely difficult that's why all chronic renal failure patients with