Review Article

Hypothyroidism and dysfunction of peripheral nervous system

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Abstract:

Current research indicates peripheral nerve dysfunction is a well-documented feature of clinical hypothyroidism. In hypothyroid patients, median motor and sensory nerves are most commonly affected. Sensorimotor nerve conduction impairment occurs in hypothyroidism and the degree of impairment might be related to the degree of thyroid deficiency. It is suggested that neuropathy is not an uncommon manifestation in the newly diagnosed hypothyroidism.

Introduction:

Hypothyroidism is a clinical condition resulting from reduced circulating levels of free thyroxine (FT_4) and triiodothyronine (FT_3).[1] However, the thyroid hormones increase the metabolic activities of almost all tissues of the body. The basal metabolic rate can increase 60 to 100 percent above normal when large amount of hormones are secreted.[2] The thyroid gland is not essential for life, but it's absence or hypo function during fetal and neonatal life results in severe mental retardation and dwarfism.[3] The prevalence of primary hypothyroidism is 10/1000 but increases to 50/1000 if patients with sub-clinical hypothyroidism (normal FT_4, raised TSH) are included and the female: male ratio is approximately 6:1.[4] Clinical features of hypothyroidism depend on the duration and severity of the diseases. A consequence of prolonged hypothyroidism is the infiltration of many body tissues by the mucopolysaccharides, hyaluronic acid and chondroitin sulphate, resulting in a low-pitched voice, poor hearing, slurred speech due to a large tongue, and compression of median nerve at the wrist.[4] However, Hypothyroidism might be reversible at early stages; on the other hand irreversible cases might have longer duration of diseases or might present etiologies other than hypothyroidism. Long term accumulation of mucinous tissue is the possible cause of irreversibility.[5]

In hypothyroidism, delayed distal latencies with lower nerve conduction velocities were observed in median and ulnar nerves for both motor and sensory conduction, in peroneal nerves for motor conduction and in sural nerve for sensory conduction in nerve conduction study by using electromyogram machine.[6] Majority of the hypothyroid female patients with a diagnosis of polyneuropathy had electrophysiological evidence of prominent sensory neuropathy involving the median nerve.[7]

Some investigators reported that, there is sub-clinical peripheral nerve involvement in new hypothyroid patients. They found slow sensory nerve conduction in sural and median nerves of hypothyroid female compared to euthyroid control.[8]

Clinical menifestation of hypothyroid neuropathy:

Most of the hypothyroid patients complain some sensory symptoms like tingling sensation, numbness, paraesthesia, burning pain and some motor symptoms like weakness, muscle fatigability, stiffness and crump.[9] Again, decreased tendon reflexes, decreased muscle strength, positive Phalen's test and Tinel's sign at the wrist (test for clinical diagnosis of carpal tunnel syndrome) were also found in some hypothyroid female.[10]

Consequences of conventional theraphy:

Some investigator revealed that, sensory and motor sign/symptoms such as tingling sensation, numbness, loss of vibration, pain, decreased muscle strength and delayed tendon reflexes were still persisted in hypothyroid patients even after 1 year of thyroxine replacement therapy.[12]

However, For clinical diagnosis of peripheral neuropathy, elicitation of reflexes, assessment of strength of major muscle groups on both side to evaluating motor system and fine/crude touch, two point discrimination test, pin prick, vibration sense to evaluating sensory system were observed in some study and they found the significant alteration in maximum newly diagnosed hypothyroid patients.[10]

After thyroxine therapy, the central and peripheral nerve conduction velocities returned to normal limits, whereas the abnormalities in amplitude were still persisted[11]. In a follow-up study, Kasem et al. (2014) demonstrated that abnormalities related to entrapment neuropathy and

polyneuropathy in hypothyroid patients can be reversed within 3 months of thyroid hormone replacement therapy. But the researchers also found that, 13.8% of the patients still had carpal tunnel syndrome after 3 months of thyroxine replacement therapy and were subjected to surgical decompression.

Again, motor conduction studies were done bilaterally on median, ulnar and posterior tibial nerve with respect to distal latency (DL). Moreover, amplitude of compound muscle action potential (CAMP) and motor nerve conduction velocity (MNCV) were also observed.[9]

Effects of thyroid hormone deficiency on single nerve:
In hypothyroidism, major effected nerve is median nerve. The mechanism involved in the development of neuropathy in hypothyroidism still remains unclear. Some investigator suggested that the weight gain in hypothyroids may be the contributory factors for the nerve conduction abnormalities.[13] The increased body weight and BMI in hypothyroids might be due to accumulation of mucopolysaccharides, hyaluronic acid and chondroitin sulphate in the interstitial spaces which, because of their hydrophilic nature retain water along with them resulting in weight gain.[4] In addition, decreased rate of basal metabolism also causes increased body weight in hypothyroidism.[2] On the other hand, an overall slowness in all metabolic pathways is seen in hypothyroidism. Due to the reduction of the carbohydrate metabolism, glycosaminoglycans cannot be broken down, instead accumulate in the entrapment regions leading to entrapment neuropathy.[14] Hypothyroidism produces alteration of fluid balance and peripheral tissue edema, which may lead to carpal tunnel syndrome development.[15]

It has been suggested that carpal tunnel syndrome (CTS) in hypothyroidism develops as a result of the mucinous infiltration in the perineurium and endoneurium of median nerve. The increased pressure as results of this infiltration is transferred to the median nerve and causes focal demyelination.[16] However, long term accumulation of mucinous tissue is a possible cause of irreversibility of CTS to replacement theraphy.[5] Again, the cause of irreversibility to replacement therapy in hypothyroid patients may be related to duration and severity of illness and also to treatment regimens[5] Moreover, some researchers also explained that, deposition of glycosaminoglycans in nerves and soft tissues surrounding them with resultant axonal degeneration and segmental demyelination forms the pathological basis of alteration in peripheral nerve function in thyroid hormone deficiency.[17]

Effects of thyroid hormone deficiency on multiple nerve:
Hypothyroidism may affect the multiple peripheral nerves of our body. depresses the gene activation for synthesis of myelin basic protein, required for myelination thereby causes impairment of nerve conduction velocities as well as loss of tendon reflexes.[18] In hypothyroidism, the deficiency of ATP, reduced ATPase and Na^+ K^+ pump activity cause subsequent alteration of pump dependent axonal transport and may leads to peripheral neuropathy.[19] The peripheral nerve dysfunction was also linked to the morphological evidence of primary axonal degeneration in the form of shrinkage of axons, disintegration of neurotubules and neurofilaments and active axonal breakdown.[20] However, a decrease in density of sodium channel causes a decrease in peripheral nerve conduction velocity and increase in latencies of evoked potential in hypothyroidism[21]. Whereas, decreased core temperature in hypothyroidism is another cause of reduced nerve conduction velocities due to reduced sodium and calcium currents.[21] The common complaints of hypothyroid neuropathy are usually pain, cramps, paresthesia in the finger due to median sensory nerve involvement.[7] Whereas, muscle weakness and decreased tendon reflexes due to involvement in median and ulnar motor nerve of upper limbs and common peroneal nerve of lower limbs.[9] In hypothyroidism, most frequent cause of peripheral nerve damage is median nerve entrapment at wrist but sensory-motor polyneuropathy such as ulnar, common peroneal and sural neuropathy can also be seen.[19] However, the mononeuropathy i.e. involvement of single nerve may be secondary to compression due to deposition of myxedematous tissue and the polyneuropathy i.e. involvement of more than one nerve may be due to either a demyelinating process or the axonal degeneration. The combination of both this two factors results in the development of the peripheral neuropathy.[22]

Conclusion:
Despite limitations in existing knowledge and need for further research, it is suggested that peripheral nerve dysfunction is a well-documented feature of clinical hypothyroidism. In hypothyroid patients, median motor and sensory nerves are most commonly affected. Sensorimotor nerve conduction impairment occurs in hypothyroidism and the degree of impairment might be related to the degree of thyroid deficiency. So, according to the recent research, it has been stated that, thyroid hormones deficiency affect not only our central nervous system but also it's a hidden threat for our peripheral nervous system.

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