The Effect of Renal Transplantation on Uremic Peripheral Neuropathy

Ihsan M. Ajeena * M.B.Ch.B.,M.Sc.
Alaa H. Abid-Aun** F.I.C.M

Summary:

Six uremic patients were electrophysiologically assessed in regard to some of their peripheral nerves before and two times after they had undergone renal transplantation, in addition to eleven normal subjects as control. The latency, conduction velocity and amplitude of the compound sensory and motor action potential were tested for the ulnar and common peroneal nerves of unilateral limbs. The results of the tests done before the transplantation were similar to other studies showing mixed sensory and motor neuropathies of both axonal degeneration and demyelination types, while these results significantly improved two months after the transplantation, yet some of the parameters were still below normal ranges, and this improvement continued in the second assessment six months after surgery. These results indicate that successful renal transplatntation will improve the peripheral nerve function in those patients.

Introduction:

Uremia is the term generally applied to the clinical syndrome that results from profound loss of renal function [13], and peripheral neuropathy in patient with renal failure has been recognized for over 100 year [19] as a well known complication of these patients [6]. Neuropathy affects the majority of patients reaching end stage renal failure [5,15], in which death of the patient may take place unless some forms of renal replacement therapy is initiated [9] and it is considered as one of the commonest types of the metabolic neuropathies, together with diabetic neuropathy [20]. The majority of researches had stated that mixed axonal degeneration and segmental demyelination that affect both sensory and motor nerve fibers are the major types of this neuropathy [5,14,17,24,26], yet other authors like Asbury et al.,[3] stated that axonal degeneration is more predominant, while Dinn and Crane [8] showed that segmental demyelination is more predominant . also there is a possibility of the occurrence of entrapment neuropathy in uremic patients [10,14,17,20].

There is some evidence that severe uremic neuropathy can be prevented [23] or even slowly partially, never completely, recovered after adequate chronic haemodialysis [11,24], yet Bolton, C. F. considered the effect of chronic haemodialysis in altering the course of uremic neuropathy is still be debated [5].

The aim of this study is to assess the effect of successful renal transplantation surgery on the peripheral nerve function in uremic patients, together with the time of occurrence of any improvement and to which extent it may occur.

SUBJECTS AND METHOD

Eleven uremic patients who were known to have peripheral neuropathy before the indication of the transplantation and that are free from diseases like diabetes mellitus, amyloidosis or vasculitis ((that may induce peripheral neuropathy by themselves)) were tested before the renal transplantation surgery, yet one of them have failure transplantation, another one develops diabetes mellitus after the operation and three dose not shows for the second post-transplantation neurophysiological evaluation, so only six patients ((four males and two females)) were statistically analysed and included. Their ages ranged from 29 – 47 with a mean of ((36.33±8.55)) years.

For comparison, eleven control subjects with ages range from 27 – 46 with a mean of ((35.45±6.41)) years were tested for one time.

After the nature and purpose of this research were explained, an acceptance was taken from each one of the subjects before the beginning of the examination. Also, all conditions required for adequate electrophysiological examination were fulfilled, as comfortable supine position, abduction of the upper limb to 10-15 °, flexion of their upper and lower limbs to10 -15 ° at the elbow and the knee joints respectively, adequate preparation of the skin in the area of the stimulating and recording electrodes, and their temperature fall within normal ranges during all the tests and for all of the subjects.

* *(Department of physiology. College of Medicine / Al- Qadisiya University) neurophysiology.*
** *(Baghdad teaching hospital). nephrology*

DANTEC counter point EMG system machine was used for the electrophysiological analysis and each patient was tested three times: one was done immediately before renal transplantation surgery, the next is done two months after the surgery and the last one was done four months later ((six months after the surgery)). The neurophysiological tests done include measuring the latency, conduction velocity and amplitude of the compound sensory and motor action potentials for a unilateral ulnar and common peroneal nerves. For both of the sensory and the motor fibers, surface electrodes were used for stimulation and recording with the exception of one case that presented ((before the surgery)) with sever edema of the lower limbs that urged the use of needle recording procedure for motor nerve assessment. For the compounds sensory action potential parameter measurements, antidromic procedure was used, i.e. for ulnar nerve, the stimulating electrodes were placed 3 cm proximal to the distal crease of the wrist and the recording were taken from the fifth finger while for common peroneal nerve, the stimulating electrodes were placed 5 cm above and 2 cm medial to the lateral malleolus and the recording were taken from the fifth toe. On the other hand, orthodromic procedure was used for measurements of the compound motor action potential in which sites for stimulation were the same as in the sensory measurements while the recording were done by placing the active recording electrodes over the belly of the extensor digity minimi muscle and over the belly of the extesor digitorum brevis muscle for the ulnar and common peroneal nerves respectively. In both procedures, the reference recording electrodes were placed distally by about 2 cm and the anode of the stimulating electrodes was placed proximally. Mild readjustment of the site of stimulating electrodes might be indicated to get biggest potential on screen.

Using the Statistical Package for the Social Sciences (SPSS), the arithmetic mean and standard error of each of the parameters were calculated. The Independent sample T-test program was used to get the significance level ((P-value)) for all of the parameters tested. A P-value more than 0.05 is considered to be non-significant while a P value of < 0.001 is considered highly significant.

RESULTS

To confirm the presence of peripheral neuropathy in the patients tested, the results of all the neurophysiological parameters were compared between the patients ((before undergoing renal transplantation surgery)) and the control subjects and, together with their level of significance, were shown in Figure (1).

Figure (2), shows the results and the level of significance of the comparison between patients parameters before and two months after undergoing renal transplantation surgery to see if there were any improvement in the nerve function.

As there were improvement in all the neurophysiological parameters tested two months after renal transplantation, we compared these readings with that of the control subjects to know if these improvements reach to normal levels. These results with their significance level were shown in Figure (3).

Figure (4), shows the results and the significance level of the comparison between the readings of the tested parameters in patients two months and six months after undergoing renal transplantation surgery that is so important to know if any further improvement had occurred six months after the surgery.

Finally, we compared the readings obtained from patients six months after successful renal transplantation with that of the control subjects to see if these parameters had returned to the normal levels. The results and the significance level were shown in figure (5).

Figure (1): The comparison of the neurophysiological sensory & motor parameters for Ulnar & Common Per. nerves between patients befor renal transplantaion and control subjects.

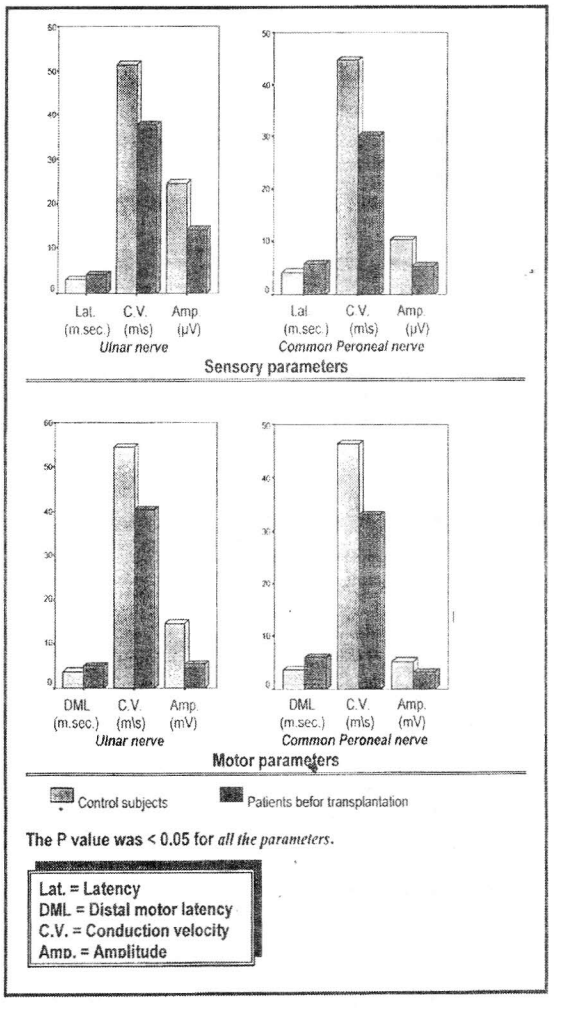
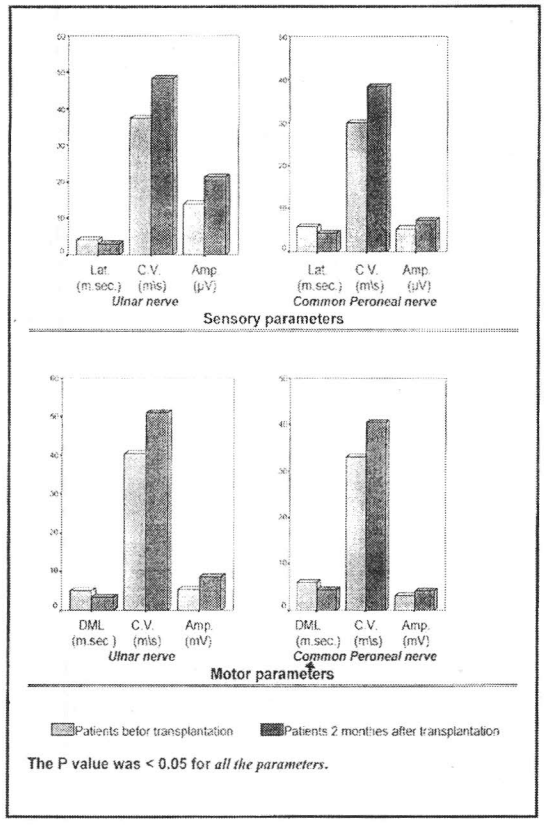
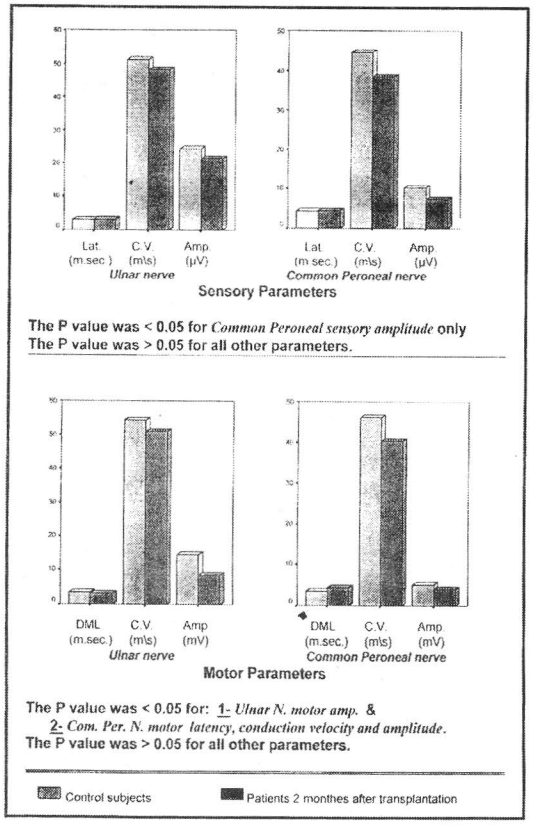


Figure (2): The comparison of the neurophysiological sensory & motor parameters of Ulnar & Common Per. nerves between patients befor and two months after renal transplantaion surgery.



The P value was < 0.05 for *all the parameters.*

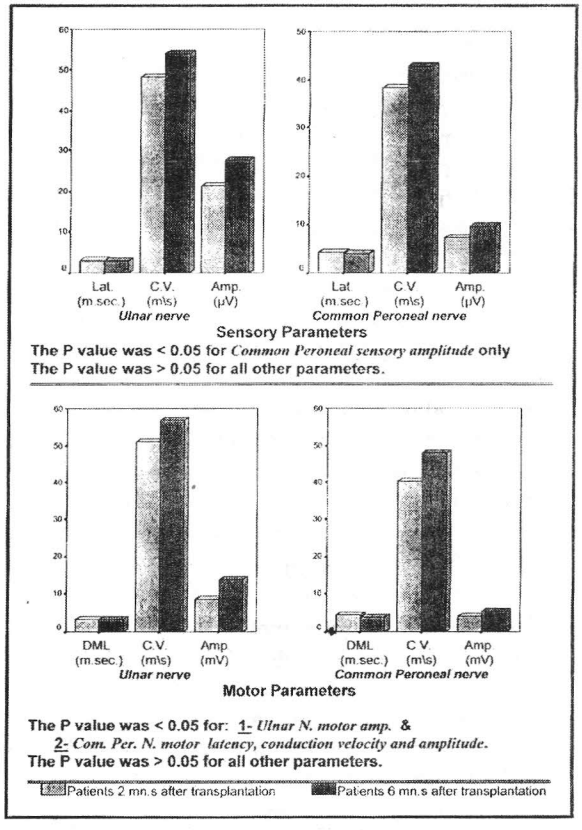
Figure (3): The comparison of the neurophysiological sensory & motor parameters for Ulnar & Common Per. nerves between patients two months after renal transplantaion and control subjects.



The P value was < 0.05 for *Common Peroneal sensory amplitude* only
The P value was > 0.05 for all other parameters.

The P value was < 0.05 for: 1- *Ulnar N. motor amp.* &
2- *Com. Per. N. motor latency, conduction velocity and amplitude.*
The P value was > 0.05 for all other parameters.

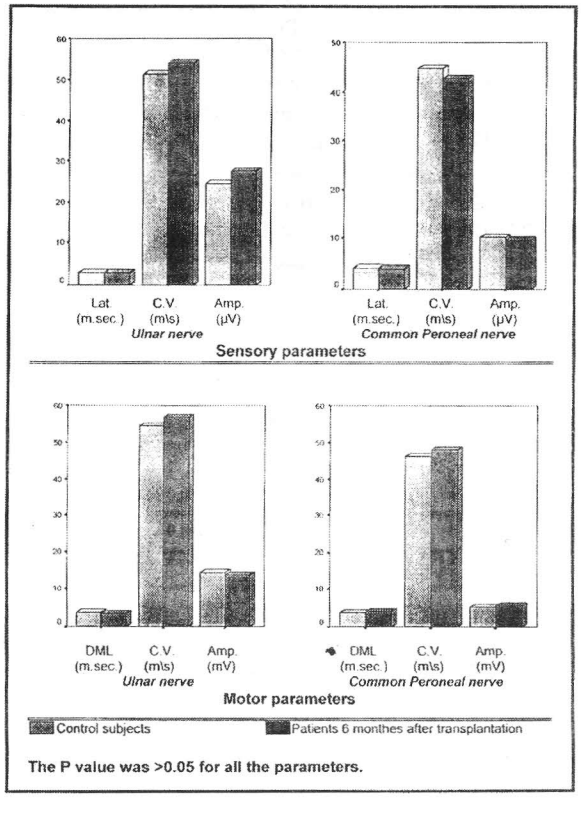
Figure (4): The comparison of the neurophysiological sensory & motor parameters of Ulnar & Common Per. nerves between patients two months and six months after renal transplant surgery.



The P value was < 0.05 for *Common Peroneal sensory amplitude* only
The P value was > 0.05 for all other parameters.

The P value was < 0.05 for: 1- *Ulnar N. motor amp.* &
2- *Com. Per. N. motor latency, conduction velocity and amplitude.*
The P value was > 0.05 for all other parameters.

Figure (5): The comparison of the neurophysiological sensory & motor parameters for Ulnar & Common Per. nerves between patients six months after renal transplantaion and control subjects.



The P value was >0.05 for all the parameters.

DISCUSSION

In this research, we select particular uremic patients because all of them have to be free from other diseases that may induce neuropathy by themselves[9,25], also they must be known to had peripheral neuropathy before the indication of the renal transplantation surgery just to avoid the possible effect of abnormal electrolyte concentration on the peripheral nerve function before undergoing the operation[4,12], as most of them had abnormal concentration by then. Furthermore, the fulfillment of all requirements ((as room temperature and subject position)) of neurophysiological examination were important for accurate readings and subsequently accurate analysis [16,18]. Only the ulnar and common peroneal nerves were tested to avoid the possible presence of entrapment neuropathy ((that usually affects median and posterior tibial nerves))[10,14,17,20] which may be a source of error in the assessment. For these nerves, both sensory and motor fibers were investigated only unilaterally because many of the previous researches and articles had proved that uremic neuropathy is usually generaly distributed [2,14]. Three major neurophysiological parameters were recorded: the latency, conduction velocity and amplitude of compound action potential as the first two of them reflect the state of myelination of the tested fiber, while the last reflects the number of the functioning axons [16,18,22].

The results of comparison between the readings of these parameters in control subjects and patients before undergoing the transplantation surgery showed a significant change in all parameters ((Figure 1)), and this confirm the presence of the mixed peripheral neuropathy in these patients that was consistent with most of other researches [2,14].

Two months after these patients had undergone renal transplantation surgery, another assessment of their peripheral nerves was done and when compared with that done before the surgery. The result shows a significant change in all parameters ((Figure 2)) and this indicates that successful renal transplantation can improve uremic neuropathy, a finding consistent with that of Danziger C.H.[7] who stated that the only potential cure for uremic neuropathy is renal transplantation, also other researchers and authors had proved that more rapid and complete recovery of this type of neuropathy take place only after successful renal transplantation and that improvements involve both the demyelination ((as shown by the shortening of latency and the increment of conduction velocity)) and the axon degeneration ((as shown by the increment of the amplitude))[5,24]. Furthermore, these results compared with that of control subjects ((Figure 3)) and there were a finding that some of the readings still significantly different that mean that two months are not enough for repairing all the neurological damage that had been caused by uremia, a finding consistent with that of Aklouk et al.,[2] who stated that full recovery of the uremic neuropathy requires six to twelve months after transplantation surgery. A third comparison of the readings obtained two months after the surgery was done with that obtained four months later ((six months after the transplantation surgery)), and the results show further significant improvement of some of the neurophysiological parameters, mainly of the amplitude of the compound action potential together with other parameters of common peroneal motor fibers ((Figure 4)), a finding that could be explained by the fact that uremic demyelination is segmental and that paranodal demyelination can be repaired relatively faster by the participation of the preexisting Schwann cells on both sides [5]. Another hypothesis stated by Said and his associates may explain these findings that is, axon degeneration take place secondary to segmental demyelination that had already developed after progressive axonal impairment and so require further time to be repaired [21]. Lastly, it is clearly shown in figure 5 that after six months of the surgery all the neurophysiological parameters had returned to normal as they lack any significant change when compaired with that of the control subjects and so we conclude that successful renal transplantation surgery can improve the peripheral nerve function in uremic patients [1,2,7,20].

REFERENCES

1. *Ahonen, R.E. (1981): Peripheral neuropathy in uremic patients and in renal transplant recipients. Acta. Neuropathol. Berl.,54(1):43-53 (abstract).*

2. *Aklouk, I.; Basic, K.V.; Basic-Jukic, N.; Brunetta, B. and Kes, P.(2004): Uremic poly neuropathy. Acta. Med. Croatica,58(1):59-61.*

3. *Asbury, A.K.; Victor, M. and Adams, R.D. (1963) : Uremic polyneuropathy. Arch. Neurol., 8 : 413 – 28 .*

4. *Avram, M.M.; Feinfeld, D.A. and Huatuco, A.H. (1978): Search for uremic toxin. Decrease Motor Nerve Conduction Velocity and Elevated Parathyroid Hormone in Uremia. N. Engl. J. Med., 298: 1000 – 3.*

5. *Bolton, C.F. (1976) : Electrophysiological changes in uremic neuropathy after successful renal transplantation . Neurology, 26 : 152 – 61.*

6. *Bolton, C.F.; Baltzan, M.A. and Baltzan, R.B. (1971) : Effects of renal transplantation on uremic neuropathy . A Clinical and Electrophysiologic Study . N. Eng. J. Med., 21 : 1170 – 5 .*

7. *Danziger, C.H.(1989): Uremic neuropathy and treatment with renal transplantation. ANNA. J.,16(2):67-70.*

8. *Dinn, J.J. and Crane, D.L. (1970) : Schwann cell dysfunction in uremia . J. Neurol. Neurosurg. Psychiat., 33 : 605 – 8 .*

9. *Edelstein, C.L.; Alkhunaizi, A.; Yaqoob, M.; Shpiro, J.I. and Schrier, R.W. (1998): Etiology, Pathogenesis and Management of Renal Failure. In: Campbell's urology. 7th edit., W.B. Saunders comp., Philadelphia, pp : 315 – 40.*

10. *Emery, J.P.; Geffray, E. and Lemant, P. (1983): Carpal tunnel syndrome in patients with chronic renal insufficiency treated by hemodialysis. Sem. Hop., 14; 59 (15): 1161 – 5.*

11. *Fraser, C.L. and Arieff, A.I. (1988) : Nervous system complications in uremia . Ann. Int. Med., 109 : 143 – 5*

12. *Goldstein, D.A.; Chui, L.A. and Massry, S.G. (1978): Effect of Parathyroid Hormone and Uremia on Peripheral Nerve Calcium & Motor Nerve Conduction Velocity. J. Clin. Invest., 62 : 88 – 93.*

13. Heptinstall, R.H. (1992) : End stage renal disease . In : Pathology of the kidney, 14th edit., Little, Brown and company, London, pp : 713 – 77.
14. Ihsan, M.A., and Hassan, A.A. (2002): Electrophysiological assessment of some peripheral nerves in patients with chronic renal failure. M.Sc. thesis, Univ. of Baghdad, Baghdad.
15. Jennekens, F.G.I.; Mees, E.J. and Most, V.S. (1971) : Clinical aspects if uremic polyneuropathy . Nephron, 8 : 414 – 26 .
16. Kimura, J. (1986): Electrodiagnosis in disease of nerve and muscle: Principle and practice, 5th edit., E.A. Davis comp., Philadelphia.
17. Lagueny, A. (2000): Metabolic and nutritional neuropathies. Rev – Prat., 50 (7): 731 – 5 (abstract).
18. Ludin, H.P. (1980): Electromyography in practice. Translated by Gillioz – Pettigrew, Thieme – Stratton Inc., Stuttgart, New –York.
19. Nielsen, V.K. (1973) : The peripheral nerve function in chronic renal failure VI. Acta. Med. Scand., 194 : 455.
20. Pirzada, N.A. and Morgenlander, J.C. (1997): Peripheral neuropathy in patients with chronic renal failure. A treatable source of discomfort and disability. Postgraduate – Med., 102 (4): 249–50; 255–7and 261(abstract)
21. Said, G.; Boudier, L.; Selva, J.; Zingraff, J. and Drueke, T.(1983): Different patterns of uremic polyneuropathy: Clinicopathologic study. Neurology, 33:567 –575.
22. Sethi, R.K. and Thompson, L.L. (1989): The electromyographer's handbook, 2nd edit., Little, Brown and Company, Toronto, 67 – 75 and 101 – 6.
23. Tenchhoff, H.A.; Jebsen, R.H. and Honet, J.C. (1967) : The effect of long term dialysis treatment on the course of uremic neuropathy . Trans. Am. Soc. Artif. Organs, 13 : 58 – 61 .
24. Thomas, P.K.; Hollinrake, K.; Lascelles, R.G.; O'Sullivan, D.J.; Baillod, R.A.; Moorhead, J.F. and Mackenzie, J.C. (1971): The polyneuropathy of chronic renal failure. Brain, 94: 761 – 80.
25. Tzamaloukas, A.H. and Agaba, E.I. (2004): Neurological manifestations of uraemia and chronic dialysis., Niger. J. Med., 13(2):98-105.
26. Yu, Y.L.; Cheng, I.K.; Chang, C.M.; Bruce, I.C.; Mok, K.Y.; Zhong, W.Y. and Chan, Y.W. (1991): A multimodal neurophysiological assessment in terminal renal failure. Acta. Neurol. Scand., 83: 89 – 95.