NERVE CONDUCTION IN CHRONIC RENAL FAILURE TREATED BY DIALYSIS*

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The occurrence of peripheral neuropathy in association with chronic renal failure has recently assumed increased clinical importance since the introduction of treatment by periodic dialysis. The clinical features of the neuropathy have been discussed by Asbury, Victor and Adams (1963). It is usually a mild sensory neuropathy with numbness and tingling in the feet and sometimes also in the hands. In more severe cases, motor signs may also develop. The neuropathy may appear for the first time or a pre-existing neuropathy may deteriorate in the early stages of treatment by dialysis and may subsequently impede rehabilitation.

A number of authors have described slowing of nerve conduction in patients with chronic renal failure, in particular Funck-Brentano et al. (1963), Versaci et al. (1964) and Tenekhoff et al. (1965). These authors, and also Preswick and Jeremy (1964), observed that abnormalities of nerve conduction may exist in patients who show no clinical evidence of neuropathy.

In this communication, the results of serial nerve conduction studies on 20 patients currently under treatment by periodic haemodialysis or peritoneal dialysis are reported. These comprise 13 men and 7 women ranging in age from 17 to 57 years. All had severe chronic uraemia, the average pre-treatment blood urea being 394 mg/100 ml. Creatinine clearances were 5 ml/min. or less. Renal failure was due to chronic glomerulonephritis, chronic pyelonephritis or polycystic kidneys. Patients with renal failure due to diseases that of themselves might affect the peripheral nerves such as diabetes mellitus, amyloidosis or systemic lupus erythematosus were excluded.

Before the start of dialysis, 15 patients had clinical evidence of neuropathy. In two patients, deterioration of the neuropathy occurred shortly after treatment by dialysis was commenced. The symptoms were usually purely sensory, and confined to or maximal in the feet. The neuropathy subsequently cleared in all except three patients, but later recurred in two others. The clinical features of these cases have been described in greater detail elsewhere (Konotey-Ahulu et al., 1965).

Methods

Motor nerve conduction was measured in the median and lateral popliteal nerves, recording from the abductor pollicis brevis and extensor digitorum brevis muscles respectively, by the technique described by Thomas, Sears and Gilliatt (1959). Sensory nerve conduction was examined in the digital nerves of the index fingers, recording percutaneously from the median nerve at the wrist by the method described by Gilliatt and Sears (1958). Skin temperature over the distal part of the limb at the time of the recording was 32–34.5 °C.

Results

Nerve conduction studies were performed on 11 of the patients at the time dialysis was started and will be referred to as Group I. Ten had clinical evidence of neuropathy when nerve

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conduction was first examined. In the remaining 9 patients (Group II), treatment by dialysis had already been in progress for 6-22 months before nerve conduction was studied. In this group, there was no clinical evidence of neuropathy at the time nerve conduction was first examined.

The results of the initial measurements of motor nerve conduction velocity, expressed in m/sec, are shown in Table I, and have been compared with control observations from Thomas et al. (1959). Conduction velocity was found to be significantly reduced in the median and lateral popliteal nerves in both groups.

| TABLE I |
|-----------------|-----------------|-----------------|-----------------|
|                | Abductor pollicis brevis | Extensor digitorum brevis |
| Controls       | 57.2 ± 4.2       | 49.7 ± 7.1      |
| Mean (with S.D.) | 51.8 — 67.1      | 35.6 — 63.5     |
| Patients       |                  |                  |                  |
| I              |                  |                  |                  |
| Mean (with S.D.) | 49.2 ± 4.4       | 37.9 ± 7.4      | 41.2 ± 7.2      |
| Range          | 40.9 — 54.0      | 29.5 — 54.8     | 32.7 — 51.4     |
| II             |                  |                  |                  |
| P              | < 0.001          | < 0.001         | < 0.001         |

Serial recordings of nerve conduction are being made on these 20 patients and so far follow-up results over periods of 6-11 months have been obtained. The results for motor nerve conduction are shown in Table II. For the median nerve, conduction velocity has not changed significantly, either in the group examined before the start of dialysis, or in those already treated for some time before being examined. For the lateral popliteal nerve, the follow-up results for Group I do not include two patients in whom the extensor digitorum brevis muscle became completely denervated on both sides subsequent to the initial examination. One patient deteriorated shortly after dialysis was started and the other showed a recurrence of the neuropathy after having been dialysed for several months. The remainder display no statistically significant change as compared with the initial values.

| TABLE II |
|-----------------|-----------------|-----------------|-----------------|
|                | Abductor pollicis brevis | Extensor digitorum brevis |
| Initial        |                  |                  |                  |
| Mean (with S.D.) | 49.2 ± 4.4       | 37.9 ± 7.4      | 41.2 ± 7.2      |
| Range          | 40.9 — 54.0      | 29.5 — 54.8     | 32.7 — 51.4     |
| Follow-up      |                  |                  |                  |
| Mean (with S.D.) | 53.1 ± 6.6       | 39.1 ± 5.7      | 36.7 ± 3.5      |
| Range          | 43.3 — 60.7      | 30.5 — 45.7     | 32.2 — 40.6     |
| P              | > 0.05           | > 0.05          | > 0.05          |

The results of the sensory nerve action potential recordings have been compared with the control results given by Gilliatt and Sears (1958). At the initial examination, the amplitude of the potentials mostly fell within the lower part of the normal range, the mean value being 11 \( \mu \text{V} \). In five, the amplitude was below the lower limit of normal and in three patients, who
showed a persisting sensory neuropathy, no potential could be recorded. The latencies tended to fall within the upper part of the normal range, being abnormally prolonged in only one instance. Little change was observed in the follow-up period except that small potentials of 3 and 5 μV were seen in two of the cases where they had previously been absent.

Conclusions

These results confirm previous reports of slowing of nerve conduction in patients with severe chronic uraemia, and have demonstrated abnormalities in both motor and sensory nerve fibres. Although in the majority, treatment by periodic dialysis was followed by disappearance of the neuropathic symptoms, the nerve conduction studies have so far failed to show a commensurate improvement. It is possible that the follow-up period is as yet too short. Tenckhoff et al. (1965) reported improvement in motor nerve conduction only in patients treated by dialysis for periods of longer than a year.

The cause of the slowing is uncertain. Its magnitude is not great and values of the order encountered in neuropathies in which segmental demyelination occurs were not observed in this investigation. Asbury et al. (1963), in a study on the post-mortem changes in uraemic neuropathy, reported that destruction of both axons and myelin sheaths is found, the anterior horn cells showing chromatolytic changes of the type associated with axonal damage. It has yet to be established whether the slowing of nerve conduction is merely the result of loss of the larger and faster conducting nerve fibres or whether a disturbance of the conducting mechanism is involved.

REFERENCES

DISCUSSION

The Chairman: Before opening these two papers for discussion, it is perhaps just worth making the point that the subjects in the first paper had not undergone dialysis, whereas the subjects in the second paper had, I think, all undergone dialysis. This provides one obvious, but not necessarily correct, explanation for the discrepancy between the two sets of results. Now these papers are open for general discussion.

Dr. R. S. Willison (Institute of Neurology, Queen Square): Figure 1. I should just like to show this slide because we have had the opportunity at the National Hospital of examining 21 patients from Professor de Wardener's unit. Dr. J. McLeod, Dr. M. Hasan and I have seen these patients over a period of about a year. Eight of these patients were on chronic dialysis but I have not separated them in this summary of the findings.

![Diagram of Nerve Conduction in Uraemic Patients]

**Fig. 1.** 25 year old man with terminal chronic glomerulonephritis.
DISCUSSION

I should like to support Dr. Thomas' findings. For instance, from the slide you can see that in the case of motor conduction velocity, which was measured in both the median and lateral popliteal nerves, there are a large number of the cases outside the control ranges (shaded areas).

We did not find, in the case of median nerve action potentials, much abnormality of amplitude, but I should draw your attention to the action potentials which can be recorded from the lateral popliteal nerve at the head of the fibula in which we have 8 patients with values below the normal range.

In 4 patients this was the only abnormality; the recording of nerve action potentials at this site is one of the most sensitive tests for neuropathy.

The other point that I should like to reaffirm is that, in the case of motor conduction, we have not seen any severe slowing except in one instance in the lateral popliteal nerve. This would support Dr. Thomas' view that the degree of slowing is quite compatible with the drop out of the larger and faster fibres.

This is of some practical importance because it might well be that the measurement of motor conduction velocity is not the most suitable test of progress. It might be more valuable to measure the amplitudes of the muscle action potentials which are elicited by stimulation of the nerve at the ankle and at the head of the fibula.

Dr. D. N. S. Kerr (Newcastle): I should like to have the views of the speakers and any other experts in the audience on a syndrome we have encountered in 3 of our chronic dialysis patients. We are not certain if it is, in fact, a neuropathic manifestation or not. All of these patients have been dialysed for more than one year. They are all apparently well-controlled by most people's criteria with a pre-dialysis blood urea below 150. All in the last 6 months have developed pain in the feet which is not present at rest and is only present on walking, similar to claudication, but lasting for a rather longer time. Two of them are osteoporotic on X-ray of the feet but have not responded to vitamin D. To our examination, they have no other manifestations of neuropathy, and no other explanation for the pain. I should be interested if other people have seen it and can explain it.

The Chairman: I ask the two opening speakers to note that comment in their final statements.

Dr. H. Tenckhoff (Seattle): To Dr. Coomes' question concerning the patient difference between Lindholm's and Versacci's report and his patients I think, if I remember right, Dr. Lindholm reported on chronic dialysis patients or patients just about to be started on chronic dialysis. This certainly would explain the difference between the population groups because in our chronic dialysis patients the incidence is very high.

I am not quite sure right now about Versacci's patients. One explanation for the high incidence of neuropathy would be the unusual way of measuring nerve conduction velocities. He measured to the peak of the action potential rather than to the 'take off' which could give him longer conduction times unless the ascending slopes were identical.

Dr. Kerr's question—we have seen patients who have had exactly that sort of pain. I recall two right now, one on peritoneal dialysis and one on haemodialysis. We found in both patients elevated alkaline phosphatases and radiological evidence of osteopathy. With treatment with vitamin D and calcium—calcium gluconate in addition to dietary intake—the alkaline phosphatase came down and the pain disappeared. The treatment had to be continued for many months before any change in pain occurred.

Dr. E. N. Coomes (Manchester): I think this illustrates the point that there are two differing populations of patients. My memory does not serve me right as to whether the patients of
Versacci and Lindholm were all having dialysis at the time of examination and I cannot give you that data, but perhaps Dr. Berlyne, who is right behind you can tell you.

Dr. G. M. BERLYNE (Manchester): Lindholm’s group—all 7—went on to chronic dialysis. Six of them were suffering from neuropathy before going on. They were clearly patients very severely affected.

Dr. J. L. FUNCK-BRENTANO (Paris): I have two points to emphasize and one question to ask.

The first point concerns the fact that early reduction of conduction velocity has been observed in our patients by measurements made on the very distal part of the lateral popliteal nerve, though, at the same time, no reduction of the conduction velocity could be found on the proximal part of the nerve and a fortiori on the median nerve.

The second point concerns the use of this test to follow-up the nerve condition of patients treated by repeated haemodialysis. One of our patients is very illustrative for this purpose. He has been treated during 8 months by repeated haemodialysis. Clinical signs of polyneuritis progressed to complete paraplegia. During the same time the conduction velocity decreased from 40 m/sec. to zero. Then he had a successful renal transplantation. His neurological condition improved. The pain in the limbs and the feet disappeared, he became able to walk though he was completely paralytic before the transplantation. The conduction nerve velocity improved much more slowly than the apparent clinical signs. Thirteen months after renal transplantation it is 30 m/sec. which, coming from zero, is much better but not normal.

The question I have to ask is: what was the vascular condition of your patients having neurological symptoms of polyneuritis?

The CHAIRMAN: The time has now come to ask the opening speakers if they have any closing remarks to make.

In that case we will move on to the next pair of papers. Both of them concern the problems of dialysis of chronic patients preparatory to transplantation procedure. I suppose in a way they are a bridge to to-morrow morning’s exercise.