Spinal Cord (1997) 35, 189–191

Letters to the Editor

Traumatic Spinal Cord Injuries in Istanbul

I read with interest the letter of Mr Robert Pringle (*Spinal Cord* 1996; **34:** 498) on Dr Karamehmetoglu's paper, the reply given by Dr Karamehmetoglu, also the article written by him (*Paraplegia* 1995; **33:** 469–471).

Mr Pringle asked 'Is Turkish wrestling only restricted to Central and Eastern Turkey?' and this was not answered by Dr Karamehmetoglu.

The answer is 'no'. Wrestling is carried out all over the country and the famous and oldest championship is held every year in a western border city named Edirne. There are also several locations around Istanbul which are famous for traditional wrestling.

The second question asked was whether there are changes in the rules or not. There are no changes in the rules but most trainees are simultaneously trained for international wrestling games.

I wish to add further to the criticisms of Dr Karamehmetoglu concerning my paper entitled 'Wrestling causing paraplegia (*Paraplegia* 1990; **28:** 265–268). That paper was written in order to discuss the mechanisms responsible for spinal cord injury during wrestling, not to prove wrestling's role in spinal cord injury as it should be very well known. This is why cases of wrestling between friends was included. The fourth wrestler was injured in a traditional Turkish wrestling contest. There are two main types of wrestling: the first one is that mentioned by Dr Karamehmetoglu where the wrestlers wear tight leather pants and cover themselves with olive oil. The other is the type which is called Karakucak. In this type, wrestlers do not use oil. Our fourth patient was injured in such a Karakucak match. No matter what type of Turkish wrestling is undertaken the main cause for spinal cord injury is a sudden supine fall in a twisted position.

Finally, to my surprise, although Dr Karamehmetoglu mentions in his paper (*Paraplegia* 1995; **33:** 469–471) that his study included 'all of the hospitals of Istanbul'. I did not see in the list, as well as in the article, the names of several university, state, military and private hospitals of Istanbul.

The lack of such information may restrict the value of an epidemiological study.

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Omental Transposition in Chronic Spinal Cord Injury

A recent article was published in *Spinal Cord* titled 'Omental Transposition in Chronic Spinal Cord Injury' (Clifton, G.L. *et al*, *Spinal Cord* **34:** 193–203, 1996). Based on their personal surgical experience the authors concluded that the operation was ineffective with 'no justification for further clinical trials for the procedure in patients who have complete or sensory incomplete lesions'. For the surgical investigators to make such a sweeping statement that would be expected to dissuade other surgeons from evaluating this procedure, it is essential that the experimental design and performance of their surgical trial be precise since these factors would directly reflect subsequent neurologic, neurophysiologic and statistical verification of the operation.

Clifton began his interest in using the omentum for spinal cord injuries in 1989 by operating on four patients with two being available for long-term follow-up. One of these two patients had 'slight improvement for the first 12 months after surgery and then neurologically plateaued'. The second patient developed 'improved truncal control, decreased spasticity, increased sensation beginning at 8 months after surgery and normal at 2 years after surgery'. These clinical findings were sufficiently intriguing for Clifton and his associates to embark in 1992 on a study of 11 patients to determine if omental transposition in spinal cord-injured patients was an effective surgical treatment where evidenced by careful postoperative examinations with associated statistical analysis.

Patients in the study were neurologically and neurophysiologically evaluated prior to surgery and at 4, 8 and 12-month intervals. The results at one year were to be compared to the patient's own preoperative status and to a comparable non-operated group of spinal cord-injured patients. The article in *Spinal Cord* stated that in order to carry out the study, 11 patients underwent 'transposition of pedicled omentum to the area of spinal cord injury.' Unfortunately this was not accomplished since only five of the 11 patients had a pedicled omental graft placed on their injured spinal cord while the other six patients, as stated in the paper, had 'free omental grafts taken rather than creating a pedicle for blood supply'. This free graft technique is more technically demanding than simply placing a pedicled omental graft on the spinal cord since the free omental grafts that were fashioned required microsurgical anastomoses of the gastroepiploic artery and vein to the external carotid artery and internal jugular vein. Creating these free omental grafts markedly changed the surgical trial since this major variation in the operation completely altered the experimental design of the study. A free omental graft is not only more technically difficult to develop than a pedicled graft, but a free graft eliminates one of the major characteristics of the omentum, namely, its enormous edema-absorptive capacity. The loss of this absorption capability is a reflection of a non-functioning omental graft probably because all lymphatic vessels are divided in taking an isolated piece of omentum and making it into a free graft. Such a critical loss of omental function may well be seen in three of Clifton's 11 patients who 'developed persistent CSF accumulations 4–8 months after surgery, with all requiring lumbo-peritoneal shunts 8 months after surgery for their problem'. Performance of these L-P shunts further changed the experimental design of this surgical trial and must bring into question any critical evaluation of the effectiveness of omental transposition of a pedicled omentum to an injured spinal cord as measured by the statistical analysis of the neurological results.

Although Clifton's paper is long and detailed, its soundness as a scientific study is open to question. For example, it was stated that all 11 patients had an MRI at 12 months but only nine of the 11 patients were found to have had their omentum in contact with the dorsum of the spinal cord. One of the two patients without omental-spinal cord adherence had to have his omental graft removed 6 months after surgery at which time it 'was not found to be anatomically connected to the cord'. How could two of 11 patients (18%) in which the omentum was being evaluated for its effect on the spinal cord be studied neurologically and neurophysiologically as determinates in a group evaluation for statistical purposes one year after surgery, when the omentum was not even adjacent to the spinal cord? What would be the significance of ASIA neurological scores, MRI's, SEPS, etc when there are such major flaws in the surgical design and performance of the study?

Clifton and his associates are to be congratulated for searching for new procedures to help patients with chronic spinal cord injuries since there has always been a tendency in medicine to question new ideas and techniques. The purpose of their experimental surgical study was to learn the effectiveness of omental transposition in patients with chronic spinal cord injury using precise neurological and neurophysiological examinations with results being confirmed by sophisticated statistical analysis. Such a careful study is needed since the procedure is being performed in several countries with more than 3000 cases of omental transposition to the injured spinal cord in humans being reported from China alone.[1]

Clifton's study would be expected to reflect directly the manner in which the experimental design of the operation was carried out and the technical manner in which it was performed. He and his colleagues have reported negative clinical results which support their personal hesitation to perform additional omental operations on patients with chronic spinal cord injury. However, it is unreasonable for them to recommend to other spinal cord investigators, that based on their surgical endeavors, there be 'no further clinical trials'.

References

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Reply from Dr Guy L. Clifton

Dr Goldsmith's argument is that the surgical procedure was flawed, not the methodology of assessing its effect. Omental Transposition is a major procedure with major risk. Our conclusion was that further clinical trials in complete and sensory incomplete patients was not justified without compelling new laboratory data.

We did not conclude that there should be a moratorium on further clinical trials in motor incomplete patients. We had no data to make such a statement on motor incomplete patients. If the procedure should be effective for complete or sensory incomplete patients and since it is being widely performed, then data contradicting ours should be put forward using the same methodology.

If clinical data refuting our conclusion does not exist after the length of time the procedure has been in use then compelling animal studies should be done before any more complete or sensory incomplete patients are subjected to this procedure in our opinion. In its absence, we see no reason to alter our conclusion.

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Exaggerated neurological side-effects of oral and intravesical oxybutynin in a patient with multiple sclerosis

Sir, We wish to discuss a practical problem with the use of oxybutynin in a 42-year old frail female who has had multiple sclerosis (MS) since 1972. About 3 years ago, she was prescribed oxybutynin by mouth, 5 mg tablet one, three times a day for urinary urgency. She developed a dry mouth, vision was affected; and she became drowsy. These side-effects occurred within a couple of hours of taking oxybutynin by mouth; the dose of oxybutynin was then halved; but the same side-effects still occurred, although to a lesser degree. Therefore it was discontinued. Two days after stopping the drug she was doing well with us, free of the drug-induced side-effects. During this period, there was no relapse of MS.

About a year ago, when an intravesical sterile 'ready for use' solution (not crushed tablets) of oxybutynin became available for prescription on a named-patient basis, she was prescribed oxybutynin 5 mg in 30 ml (manufactured by Leiras Oy, Finland), instilled intravesically three times a day as adjunctive pharmacotherapy to intermittent self-catheterisation. There was no concomitant medication except for vitamins and minerals which she had been taking for many years. With intravesical oxybutynin therapy, she could retain 350–400 ml of urine whereas prior to oxybutynin therapy, she could hold only 150–200 ml of urine. Similarly, before commencing intravesical oxybutynin therapy, she was catheterising herself about 10 times a day whereas subsequent to that therapy, she could reduce the number of catheterisations to six a day and remain dry. With intravesical oxybutynin, she did not develop a dry mouth, and there was no effect on her bowels or on sweating, but she had difficulty in focusing and could not read small print. After a month of intravesical oxybutynin therapy, she noticed that the bladder area and the 'top of her legs' became numb five minutes after intravesical instillation of oxybutynin, and this adverse effect occurred after each instillation of oxybutynin. Neurological examination revealed diminished touch and pain sensation in the sacral 2, 3 and 4 dermatomes. Initially, the numbness and somato-sensory loss lasted for a couple of hours; but later lingered on for progressively increasing periods. Because of these side-effects, the dose of intravesical oxybutynin was halved (2.5 mg three times a day). Two days later there was only slight improvement. As she felt numbness in her lower extremities after each instillation of oxybutynin, she

realised that it would be unsafe to walk with her walking frame. She therefore, discontinued the intermittent catheterisation regime and adjunctive intravesical oxybutynin therapy, and resorted to indwelling urethral catheter drainage. During this period, there was no relapse of MS. Two months after stopping the intravesical oxybutynin therapy, the degree of numbness in the 'top of her legs' was only 10–20% as compared to her status prior to commencing intravesical oxybutynin therapy. Neurological examination revealed diminished touch and pain sensation in the sacral 2, 3 and 4 dermatomes, albeit to a lesser degree.

This patient developed an exaggerated *sedative* effect after oral administration of oxybutynin. When oxybutynin was administered intravesically, she noticed numbness in the sacral dermatomes corresponding to the visceral (urinary bladder) autonomic innervation. Clinical examination revealed objective sensory changes which were transient to begin with, coinciding with intravesical oxybutynin instillation. However, over a period, the subjective sensory changes and the sacral dermatomal somato-sensory loss observed during the clinical examination became persistent. Although oxybutynin may be implicated because of temporal coincidence, it is recognised that MS is such a variable disease that sacral numbness coinciding with intravesical oxybutynin administration is not, by itself, a definite evidence of its causation. If the numbness was due to systemic absorption of oxybutynin after its intravesical instillation, the side-effect would be expected to happen 2 to 3 h after intravesical administration, i.e. during maximum serum concentration. But this patient developed numbness 5 min after intravesical administration. Similarly, any dose-effect of oxybutynin subsequent to its systemic absorption following intravesical instillation, should occur from the first day of treatment. But, this patient developed neurological symptoms and signs a month after beginning intravesical treatment. Thirdly, her neurological symptoms and signs persisted even after stopping the intravesical treatment. Oxybutynin has a short elimination half-life; there should not be any detectable serum concentration of oxybutynin 2 days after stopping the treatment. These apparently contradicting clinical observations may be explained in a rational manner if we consider the possibility of neurotoxicity of oxybutynin in a patient with demyelinating disease. In molecular structure, oxybutynin resembles those amines with a local anaesthetic effect, such as lidocaine, and is purported to share this property. *In vivo* animal data showed that oxybutynin has twice the anaesthetic potency of lidocaine when administered intradermally.[1] It was proposed that demyelination may render the neural tissue to become more susceptible to potential neurotoxic effects of local anaesthetic agents.[2] A higher concentration of the drug, over a longer period of time, may produce a neurotoxic effect in the presence of demyelination, and such an adverse neurological side-effect may not be observed in a spinal cord injury patient, as such patients do not have a demyelinating pathology. Indeed, none of the spinal cord injury patients in this Centre who have been using intravesical oxybutynin therapy to their great advantage, observed numbness in the sacral dermatomes after its intravesical instillation.[3]

Elderly tetraplegic patients who are frail and relatively immobile, should receive a smaller dose of oxybutynin than the dose recommended to a young, active, traumatic paraplegic patient because the bio-availability of oxybutynin is greater in frail, elderly patients due to altered pharmacokinetics.[1] While using oxybutynin intravesically in patients with demyelinating diseases, they should be forewarned to the rare possibility of the development of numbness in the sacral dermatomes which may persist to some extent after discontinuing the medication.

We thank Dr. Eeva Lukkari, Clinical Research, Leiras Oy, Helsinki, Finland for her valuable advice.

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