Correspondence

Transient ischaemic attacks

Sir,

In his editorial on transient ischaemic attacks (June 1998) Dr Peter Sandercock provided a well-balanced and scholarly account of the diagnosis and treatment of patients with transient ischaemic attacks. Concerning the antiplatelet treatment of transient ischaemic attacks, he correctly states that all patients should be started on a reasonable dose of aspirin. He then discussed whether there is any antiplatelet regime superior to aspirin alone, but concluded that there is no convincing evidence at present favouring an alternative or combined antiplatelet regime. The positive evidence from the European Stroke Prevention Study (ESPS) 2 trial was partially discounted by the earlier anti-platelet trialists overview, which concluded that dipyridamole did not add to the benefit of aspirin. Finally, the author suggested that the ESPS 2 data should be included in a further overview before practical conclusions could be drawn.

Is this suggested line of enquiry less than fair to the ESPS 2 trial? This trial was a substantial multicentre, placebo-controlled, double-blind trial, carried out by an independent organization, in which 6602 stroke or TIA patients were allocated to one of four groups; placebo, aspirin, dipyridamole, dipyridamole plus aspirin combination. The primary end points were stroke, death and stroke or death together, and patients were followed on treatment for 2 years. Analysis demonstrated that the combination of aspirin and dipyridamole was significantly more effective than either aspirin or dipyridamole prescribed alone. The combination therapy yielded a significant 23.1% reduction in stroke risk over aspirin alone (p = 0.006), translated into a saving of 30 strokes per 1000 patients treated over 2 years. Thus, a well-designed trial of a size sufficiently large to achieve meaningful end points showed the combination aspirin/dipyridamole therapy to provide truly additive benefit, better than aspirin alone. Rather than consigning this trial to further meta-analysis, where its impact would be diluted by several heterogeneous and early trials, would it not be better to conclude that this trial has achieved an advance in knowledge of practical use to clinicians and patients?

I appreciate that no trial can stand alone, however large and well-designed. The onus on clinicians is either to accept that the results of the ESPS 2 trial are correct or press for a second similar trial to be carried out, of sufficient size to prove or disprove it convincingly.

To take an example from trials in myocardial infarction, the case for thrombolytic therapy after myocardial infarction was firmly demonstrated by two large trials (GISSI 1 and ISIS 2), which showed virtually identical results. In stroke and TIA treatments should we not press for further large trials, rather than more meta-analysis? The title of Dr Sandercock’s editorial was ‘Transient ischaemic attacks: new treatments, new questions’. Perhaps if we accepted some of the existing treatments we should not have to ask so many new questions.

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References

Correspondence

Sir,

Professor Prentice’s letter raises a general point about how to evaluate treatments. Should one base one’s estimate of treatment effect on the results of a single trial or on a systematic review of all the randomized evidence? There are proponents—such as Professor Prentice—who are keen to highlight the positive or perhaps negative effects of a single trial. There are others (such as the ESPRIT group) who have preferred to look at all the available randomized evidence and find it unconvincing. The fact that the many clinicians around Europe in ESPRIT are sufficiently unconvinced by the data to undertake a further randomized controlled trial comparing aspirin plus dipyridamole with aspirin alone in patients with stroke suggests that there is some continuing uncertainty amongst clinicians.

Professor Prentice then goes on to mention the example of thrombolysis for acute myocardial infarction. Of course the ISIS 2 trial was prompted by a systematic review of all the then available evidence from randomized trials, which suggested that thrombolytic therapy for acute myocardial infarction reduced early mortality by about one fifth. The proportional reductions in death observed in ISIS 2 and GiSSI2 were almost identical. The mega trial confirmed the results of the previous systematic review.

The Antiplatelet Trialists’ Review of all of the available randomized evidence suggested that dipyridamole did not definitely add additional benefit to aspirin alone.1 The ESPS 2 trial produced somewhat different estimates of the benefits of adding dipyridamole to aspirin. Since the trial is not concordant with the previous systematic review, it is therefore not surprising that there is so much debate. The debate will probably not be silenced until further randomized evidence from the ESPRIT trial is available.

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References

Self-limiting abdominal wall herniation and constipation following herpes zoster infection

Sir,

Herpes zoster is caused by a neurotropic virus with a predilection for the posterior root ganglia. Thus the majority of neurological complications are sensory ARAR.3 However, motor complications, both visceral and somatic, sometimes occur in the segments corresponding to the involved sensory dermatomes.2 We describe a case of abdominal wall herniation and constipation, following herpes zoster infection of the T11/12 segments. Both conditions resolved fully over a period of 6 months.

An 84-year-old man presented with a large hernia of his right flank. He had a background of chronic lymphatic leukaemia, which was in remission for over 6 months, following treatment with chlorambucil. Three months prior to his presentation, he developed shingles of the T11/12 dermatomes on the right side. A swelling appeared in his flank 2 weeks after the herpetic eruption which enlarged dramatically over the following few days. He also developed severe constipation at this time, having had a regular bowel habit all his life. This lasted for 2 months, and resolved fully thereafter.

On examination, a reducible swelling, measuring 15 cm by 10 cm, protruded through an area of flaccid muscle in the right lumbar area. It was made prominent by coughing. A healed herpetic rash ran obliquely across its surface along the T11/12 dermatomes. Superficial abdominal reflexes were absent on the right side and this area was hyperaesthetic. The patient had an incidental and long-standing right inguinal hernia.

Concentric needle electromyography of the right external oblique and paraspinal muscles confirmed motor axonal loss in the T11/12 segments, with some reinnervation, consistent with involvement of the anterior horn cells by shingles. A corset was fashioned to maintain reduction of the hernia in anticipation of resolution. Six months following the onset of shingles, his bowel habit had returned to normal and the hernia had almost vanished.

Segmental zoster paresis is rare. It predominantly affects the elderly, especially patients with underlying haematological malignancies.1 The involved myotomes and dermatomes correspond. Segmental reflexes are reduced or absent. Somatic neuropathy includes cranial and peripheral lesions. Cranial neuropathies, such as the Ramsay Hunt syndrome, are the best recognized zoster palsy, occurring in up to 12% of cephalic herpes zoster infections.3 Peripheral neuropathies include segmental paresis of the limbs, diaphragm and abdominal musculature. The incidence of clinically detectable weakness is 0.3% when the skin lesions are between the T2 to L1 dermatomes, due to overlap in the innervation of the trunk muscles. We are aware of only four previous reports of actual abdominal herniation associated with shingles, all of which resolved spontaneously.4–7

Visceral neuropathy has also been described, affecting the urinary and gastrointestinal tracts, resulting variously in urinary retention, cystitis and
colonic pseudo-obstruction. The latter was usually diagnosed by colonoscopy or barium enema, coupled with its self-limiting clinical course. Our patient did not have colonic investigations because his constipation was resolving at the time of presentation. However, given the chronology of this episode of constipation, and its spontaneous resolution, it is likely to have resulted from visceral motor involvement by shingles. This patient therefore represents the first described case of shingles simultaneously involving the sensory, somatic motor and visceral motor nervous systems. Awareness of these entities may help to avoid unnecessary surgery for lesions which usually recover fully in time.

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**References**