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Efficacy of feverfew as prophylactic treatment of migraine

SIR,—Dr E S Johnson and his colleagues (31 August, p 569) are to be congratulated on attempting to assess the efficacy of feverfew as prophylaxis for migraine. They state that their study provides evidence that feverfew prevents attacks of migraine, but a few points need consideration.

They suggest that feverfew reduced headache frequency because the frequency increased significantly (p<0.02) in the placebo group but there was no significant change in the feverfew group. This "before and after" analysis is inappropriate to the parallel group design. The correct analysis is to compare the results for the two groups directly. When this is done for the data presented in table I the headache frequency does not differ significantly between the two groups. This is also true if the baseline values are subtracted first. The authors suggest that migraine attacks in the feverfew group were significantly (p<0.05) less likely to be accompanied by nausea and vomiting. However, the numbers of migraine attacks used as denominators in table III do not tally with the numbers calculated from table I. For example, the feverfew group appear to have had $8 \times 6 \times 1.69 = 81$ attacks, and not 93 attacks as stated in table III.

Table II shows clearly that patients could distinguish between feverfew and placebo treatments; the reason is not clear, but evidently the study was not "blind." This is particularly disturbing because the patients in the study all believed that feverfew was an effective remedy. The significant preference for feverfew shown in table V may simply be a measure of patient bias in what was in effect an open study.

It is also interesting to consider the limitations of a study which is in fact a controlled withdrawal of treatment. The authors acknowledge that the incidence of side effects caused by feverfew was probably underestimated, because patients with troublesome side effects would have discontinued feverfew and would not have been eligible for the study. For the same reason, the study would tend to overestimate the efficacy of feverfew. Those who found the herb ineffective would stop using it and Ci P C Waller Lo L E Ramsay Ci

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** The authors reply below.—ED, BMJ.

SIR,—We thank Drs Waller and Ramsay for their comments and in particular for drawing attention to our inadvertent omission from the text of the between groups analysis.

As stated, we used the Wilcoxon rank sum test for comparisons between the two treatments. The difference in headache frequency was significant (p < 0.05) when the end point was the mean of the last three months but not when it was the mean of 0-6 months. When the baseline values were subtracted significant differences (p<0.05) were also evident for both 4-6 months and 0-6 months. For the comparison of the 4-6 month end points we included the earlier values of two patients taking placebo who subsequently withdrew. This tended to understate the differences in headache frequency, as did the under-recording in cases 10, 15, and 17, so our calculations probably minimised the apparent benefit of feverfew. We now realise that errors occurred in table I: two in the 4-6 months column (the value for case 6 should have read 0.67 and that for case 8 0.67, making the mean (SEM) 1.54(0.61)) and one in the 0-6 months column (the value for case 6 should have been 1).

The apparent discrepancy for differences in the number of headaches calculated from the data in table I and the number of migraine attacks used as denominators in table III was explained in the legend of table IV. Three patients taking feverfew recorded a total of 12 episodes of visual symptoms characteristic of their migraine attacks. Although these auras were occasionally associated with nausea and vomiting, they were not followed by headaches, possibly owing to the consumption of analgesics (table IV).

The assertion that this study was not blind is untrue. Non-blindness implies prior knowledge of which treatment was active and which was placebo. Our patients knew at the outset they would receive either feverfew or placebo but, apart from breaking the capsules (and they did not), they could not discover which. In any study in which the active treatment is noticeably more effective than the placebo those patients who consider they are not benefiting would be more likely to guess retrospectively that they had not been taking placebo and those who were benefiting that they were taking the active drug. We think that the high rate of correct guessing was a true reflection of the efficacy of feverfew treatment.

The suggestion that the headaches, nausea, and vomiting suffered by the placebo takers were manifestations of the "post feverfew syndrome" is of interest, since withdrawal headaches occur when patients taking daily ergotamine suddenly stop treatment.¹ However, our patients identified their headaches as being identical with those formerly associated with their migraine attacks. The headaches were intermittent, unlike most of the other post-treatment symptoms, which lasted for several days or weeks. Furthermore, in those

who suffered from classical migraine the headaches were associated with characteristic migraine auras.

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Griffiths in action

SIR,—Dr Jack Bavin (24 August, p 543) complained about the recent appointment of the unit general manager of the mental health unit. I have no quarrel with Dr Bavin's views about the "achievements of a high order" produced by the previous teamwork and the consensus approach. He will recall that this point of view was strongly argued in Gloucester's response to the Griffiths report.

However, Griffiths is here and we have to face up to it. We have tried very hard, through consultative documents and open meetings, to explain that Griffiths is the most radical change ever made in NHS management and that the unit general manager's job is a new job and not the unit administrator's job with a new title.

It was unfortunate that the successful candidate did not meet Dr Bavin. We involved medical staff closely in the selection process and valued their views. We were faced with a situation in which the shortlist for the acute unit was considerably stronger than the shortlist for the mental health unit. It also became clear that some of the excellent candidates for the acute unit job would be willing to accept other unit general manager posts. In this circumstance we felt that we had a duty to the mental health unit to appoint the best candidate, even though he had not met the appropriate medical representative. The existing unit administrator was not dismissed; the unit general manager post was not his to lose. In fact he has now been appointed as a unit general manager in another authority.

Since 1982 we have worked closely with Dr Bavin and his colleagues to establish a clear direction for mental health services. The unit general manager and I look forward to working with everyone in the unit to provide the best possible service for the patients whom we serve.

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Improving prescribing

SIR,—I was pleased to read Dr Tessa Richards's account of the recent DHSS conference on prescribing (21 September, p 832) since this was virtually my only source of news about this meeting.

As chairman of the Association of Medical Advisers in the Pharmaceutical Industry (AMAPI) I wrote to Mr Norman Fowler to request an invitation to this meeting but received no reply or acknowledgment. This is extraordinary when one considers that it is largely AMAPI members who sign off the data sheets and advertisements for Radcliffe Infirmary,

Lancet 1983;i:431-4

Med 1985;313:675-80.

appropriate?

in pregnancy. Br Med J 1985;290:788.

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every drug and who have responsibility for each company's medical information department. I understand that the Association of the British Pharmaceutical Industry, including its medical committee, was treated in a similar cavalier fashion.

We in the AMAPI are wholeheartedly in favour of better prescribing—including not prescribing when it is not necessary—and were more than disappointed by not being asked to contribute our views at the conference. The conference was clearly a non-event. How much better it would have been if the opinions of doctors working in the drug industry had been sought or acknowledged.

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Antihypertensive treatment in pregnancy

SIR,—In their comparison of oxprenolol and methyldopa in pregnancy Dr E D M Gallery and colleagues concluded that the β blocker tested had "no adverse effects on fetal outcome" (31 August, p 563). Similarly, Dr M de Swiet stated in his recent leading article on the use of antihypertensive drugs in pregnancy that "the short term safety of β blockade has been proved" (10 August, p 365).

Leaving aside the question of whether proof of safety is ever possible in principle, reliable evidence is obviously necessary on whether such treatment might produce increases in serious adverse effects that are large enough to be of practical importance. Dr de Swiet supports his claim of safety chiefly by referring to the randomised study of Rubin et al.1 But this study was small and, although one of its aims was to find out whether β blockers were effective in decreasing fetal loss associated with hypertensive pregnancy (Rubin PC, Reid JL, unpublished protocol), the number of perinatal deaths was far too small (two controls and one treated) to establish either efficacy or short term safety. For example, even if β blockade actually doubled the probability of perinatal death, the play of chance could well produce such apparently favourable results in a study as small as this. Likewise, in the study by Dr Gallery and colleagues, there were far too few serious events to justify any claims that either efficacy or safety had been shown.

A recent review of randomised trials of diuretics in pregnancy has pointed out that reliable assessment of the effects of antihypertensive treatments on fetal loss (and other serious but rare end points) might require the randomisation of several thousand women.² De Swiet *et al*³ and Rubin⁴ have suggested that, since this would be difficult, the value of such treatment should instead chiefly be assessed on other measures of outcome, such as birth weight. This suggestion is not wholly satisfactory, however, for the medical relevance of moderate changes in such measures may be disputed.⁵

Moreover, although Rubin's study has been claimed to show an advantage for the treated group,⁶ there was no significant improvement in any of the prospectively stated end points. (The unpredicted observation that respiratory distress syndrome was less frequent in the treated group generated, but did not test, a hypothesis.)

There are substantial commercial pressures to use β blockers widely, and experience with diuretics (which were once widely used in pregnancy) suggests that they could result in many millions of mildly hypertensive pregnant women being prescribed β blockers without any good evidence for, or against, the practice. One way to get such evidence would be through widespread collaboration in multicentre randomised trials of sufficient size²⁷⁸ to detect any clinically significant differences in the frequency of important, prospectively stated end points.

If β blockers do materially reduce the net risk of an important adverse outcome then a clear result

from really large trials should greatly increase the extent to which they are used. If, however, β blockers have no material net effect (or an adverse net effect) then such studies could protect millions of pregnant women from unnecessary or harmful medication.

1 Rubin PC, Clark DM, Sumner DJ, et al. Placebo controlled trial

4 Rubin PC. Overview of randomised trials of diuretics in preg-

nancy. Br Med J 1985;290:788-9. 5 Ounsted M, Redman CWG. Overview of randomised trials of

6 Reynolds B, Butters L, Evans J, Adams T, Rubin PC. First year of life after the use of atenolol in pregnancy associated hypertension. Arch Dis Child 1984;59:1061-3.

randomised trials? Statistics in Medicine 1984;3:409-20.

Is the distribution of training practices

8 Lindheimer MD, Katz AI. Hypertension in pregnancy. N Engl J

SIR,-Dr T S Murray makes several statements

that must not go unchallenged (21 September, p

789). The question he asks is an interesting one

that he fails to answer. He bases his arguments on

two assumptions: that practices in deprived areas

are substandard and that those in areas with a high

concentration of training practices provide high

quality care. At best these views are naive; at worst

they are patronising and likely to give offence to

practitioners who work in deprived areas and are

not concerned in training. Where has it been

Dr Murray suggests several reasons why there

are fewer trainers in deprived areas: fear of

rejection, ignorance of training standards, and

anxiety that trainees will be more knowledgeable.

These paint a gloomy picture of insecure col-

leagues with limited knowledge, awareness, and

self esteem. He offers no evidence to support any of

these assertions, and what limited evidence there

Dr Murray implies that since doctors who work

in grossly deprived areas have low standards of

practice then it follows that the young principals

who join them will become disillusioned and adopt

similar professional standards. To counteract this

he suggests, firstly, that all trainees should be

attached to such a practice for one month. To do

what? He maintains that the practice would benefit

from having the trainee attached. How? Again we

Secondly, he suggests, "An educative pro-

gramme is required in the deprived areas to

identify the practices of potential and advise them

how to reach the necessary standards." If Dr

Murray equates socially deprived areas with

deprived general practice does he really under-

stand the nature of either? There is no systematic

relation between the indices of social and economic

deprivation and the pattern of care provided by

general practitioners.⁴ Does he have an adequate

grasp of the day to day problems faced by people

who are forced to live in these areas and by the

general practitioners who care for them? Before

sending his trainees across the Styx for a month

perhaps Dr Murray should make the journey

is-for example, from the Manchester study-

would tend to refute them.1-

are not told.

the patients of the practices that are chosen?

Yusuf S, Collins R, Peto R. Why do we need some large, simple

diuretics in pregnancy. Br Med J 1985;290:1079-80

of atenolol in treatment of pregnancy associated hypertension.

Rory Collins Iain Chalmers Richard Peto

himself. He may then have a clearer idea about what objectives he wants his trainees to achieve.

All, I presume, would agree that those living in areas of social and economic deprivation need high standards of medical care. The provision of that care will not be aided by indiscriminate statements, which, to say the least, are not very helpful.

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Trident versus health

SIR,—The activities of the Medical Campaign Against Nuclear Weapons described in your news item (5 October, p 976) and in the campaign's letter (p 973) will expose patients to direct political propaganda by doctors.

It is a legitimate responsibility of the medical profession to lobby the government for increased expenditure on health services and to this end inform the public (our patients) of the inadequacies of current funding. To assume that high defence spending is the cause of inadequate health care resource allocation is political opinion, and it is improper to subject patients to the political opinions of doctors under the guise of "professional concern for patients." Doctors should consider carefully the consequences of introducing their personal political opinions into their professional relationships with their patients.

W WHITROW

shown that the criteria used for selecting training practices also guarantee high standards of care for Inverness IV2 4AG

"Medical Directory (Retrospective)"

SIR,—There must be many besides myself who are irritated and frustrated by the now regular failure of the *Medical Directory* to appear until the year is almost ended.

Longman's troubles seem to date from the time they decided to move its nerve centre from Bentinck Street to Harlow. Hearsay has it that formerly it was managed by two middle aged ladies with a card index, knitting needles, and prodigious memories who declined to move to Harlow. Moved it was, nevertheless, and computerising it apparently caused a six month delay that has never been made up; since the move the directory has appeared consistently about six months late each year-that is, nearly a year after the updating forms go out to the profession. It might well these days be entitled Medical Directory (Retrospective) because, with such a lengthy lead time, those parts of it that are relatively ephemeral have already ephemed by the time it appears.

Can anyone suggest how pressure can be brought on such a monopolist? Had any alternative publisher the interest and resources to start up an alternative directory appearing by March each year one would imagine he would make a killing: he would certainly have my yearly £45 or whatever. Short of this one can but fume impotently and write letters to the medical press.

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