Comparison of ampicillin and amoxycillin in acute on chronic bronchitis

Sir,—Since my observations on the comparative efficacy and cost of ampicillin and amoxycillin in acute bronchitis[1] are quoted in the article by Anderson and colleagues,[2] I hope you will permit me to comment on its contents and conclusions.

There is no explanation in the article as to why the authors selected a dose of 4 g per day of ampicillin for their study. That this was unnecessarily large should have been evident from three articles published from this unit.[3–5] In these double-blind controlled comparisons of ampicillin with various other antibacterial agents in acute on chronic bronchitis the mean times for clearance of sputum purulence were 3·5 and 3·9 days respectively with 1 g of ampicillin per day, and 3·5 days with 2 g per day, compared with four days for 4 g per day, as reported in the study by Dr Anderson and his colleagues. I would not dispute their conclusion that ampicillin and amoxycillin were, *in the doses they employed,* of approximately equal efficacy and cost. Nevertheless, I wonder if it is sensible in terms of economical prescribing to compare a dose of ampicillin which is four times greater than one shown to be equally effective, with a dose of amoxycillin which is twice that recommended by its manufacturers.

The contrived conclusion that amoxycillin is no more expensive than ampicillin will no doubt delight the manufacturers of Amoxil, but only by ignoring reliable evidence that equally good results in the treatment of acute on chronic bronchitis can be obtained with 1 g of ampicillin per day. This would cost the National Health Service only about £1·25 for one week's treatment, as compared with £5 for the authors' two extravagant regimens and £2·50 for amoxycillin in the manufacturers' recommended dose of 250 mg thrice daily.

Would it be wrong to suggest that in these times of financial stringency the potential economic consequences of publishing certain articles in medical journals now have important ethical implications? If doctors in the National Health Service are persuaded to expend twice or even four times as much money as is necessary on drugs used for the treatment of common illnesses, this may well deprive other patients of facilities and equipment vital to their survival.

Finally, I would question the propriety of accepting, without evidence of independent verification, a statistical analysis prepared by a pharmaceutical company with a vested interest in promoting preferentially one of the drugs being investigated in a comparative clinical trial.

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References

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2 Anderson G, Jariwalla AG, Sadur J. A comparison of ampicillin and amoxycillin in acute on chronic bronchitis. *Thorax* 1979; **34**:814–6.
3 Aitchison WRC, Grant IWB, Gould JC. Treatment of acute exacerbations in chronic bronchitis. *Br J Clin Pract* 1968; **22**:343–5.
4 Malone DN, Gould JC, Grant IWB. A comparative study of ampicillin, tetracycline hydrochloride and methacycline hydrochloride in acute exacerbations of chronic bronchitis. *Lancet* 1968; **2**:594–6.
5 Willey RF, Gould JC, Grant IWB. A comparison of ampicillin, erythromycin and erythromycin with sulphamethopyrazine in the treatment of infective exacerbations of chronic bronchitis. *Br J Dis Chest* 1978; **12**:13–20.

Sir,—Dr Grant's comments are entertaining but lack logic. The dose of ampicillin of 4 g daily was based upon the demonstration by May and Delves[1] that ampicillin 1g and 2 g daily gave sputum ampicillin levels likely to achieve bacteriostatic levels in only one-quarter and one-half of patients respectively. These dosage schedules would certainly not achieve bactericidal levels, and May and Delves found that after treatment with 1 g and 2 g a high proportion of patients still had purulent sputum or grew *Haemophilus influenzae*. We have always used 4 g daily as our standard treatment of acute exacerbations of chronic bronchitis. In separate trials Dr Grant's group have shown similar times to achieve clearance of sputum purulence with 1 g and 2 g of ampicillin, but he really cannot assume that the result would be the same with 4 g. It is not permissible to compare his results with ours because our patients might have been more ill and with initially more purulent sputum. As he correctly states, we were careful to indicate that the conclusions only applied to the doses studied.

So much for scientific argument but Dr Grant proceeds to use this shaky logic as a foundation to attack the pharmaceutical industry. His final paragraph is frankly offensive to a group of professional colleagues. The best refutation is the conclusion that ampicillin, whose manufacture is no longer protected by patent, is as good as amoxycillin. This result was a commercial disappointment to the firm concerned, yet the results were provided very quickly and they gave me every help with the study. Dr Grant is employed in a teaching hospital where statistical advice may be freely available. No such facility is provided by my Area Health Authority. I have often sought statistical and other help from the pharmaceutical industry and have always found it unbiased and beyond reproach.

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Reference

1 May JR, Delves DM. Ampicillin in the treatment of *Haemophilus influenzae* infections of the respiratory tract. *Thorax* 1964; **19**:298–305.

Sir,—We write to support the recent report by Dr Anderson and his colleagues.[1] We have carried out a similar study.

Twenty-four patients admitted to hospital and found to have greater than 50% pus in the sputum were treated randomly with either ampicillin 1 g qds or amoxycillin 500 mg qds for 10 days. The drugs were contained in plain capsules and administered double-blind.

Patients were recruited regardless of diagnosis but excluded if (i) they were receiving oral corticosteroids, (ii) sputum culture showed bacterial resistance, or (iii) they had a known drug allergy.

Initial clinical assessment of severity was made in conjunction with changes on the chest radiograph. Sputum purulence was measured using a simple scale according to the estimated percentage of pus in the first 24-hour specimen. Four gradings were used from "trace" to "mucopurulent" (MP) +++, and 24-hour sputum specimens were examined on each of the 10 days by the same physician. Patients were examined daily and questioned about skin and gastrointestinal symptoms.

On day 10 a final clinical assessment was made and the initial investigations repeated. Patients were then issued with a special one-month diary card and instructed to estimate their sputum purulence from day to day and also note any symptoms or requirement for further antibiotic treatment.

The two groups were comparable on the basis of age, smoking habits, initial sputum purulence, fever, FEV_1, 24-hour sputum volumes, and final diagnosis. Sputum culture was positive in 10 patients, five in each group. The mean number of days to sputum clearance for the 13 patients in the ampicillin group was 6·5 against 5·6 in the amoxycillin group. One patient in the ampicillin group and three in the amoxycillin group failed to clear after 10 days treatment.

No cases of bacterial resistance were seen and adverse effects were confined to only one case of oral candidiasis in the amoxycillin group. During the follow-up period no bacteriological tests were carried out but recurrence of sputum purulence was seen in 10 patients, five from each group. All 10 required further antibiotic treatment.

The patients selected were those with *heavily infected sputum*, and under the conditions of this study ampicillin and amoxycillin were equally effective.

In our study there is a significant saving with ampicillin since the hospital cost for this treatment was £4.20 per patient compared with amoxycillin at £9.75 per patient.

We are indebted to Beecham Research Laboratories for the supply of ampicillin and amoxycillin.

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Reference

1 Anderson G, Jariwalla AG, Sadur J. A comparison of ampicillin and amoxycillin in acute on chronic bronchitis. *Thorax* 1979; **34**:814–6.