LETTERS TO THE EDITOR

Inhaled sodium cromoglycate

The systematic review and meta-analysis performed by Tasche and colleagues appears to have been carried out with commendable thoroughness. The results seem clear: sodium cromoglycate is ineffective as maintenance therapy in children with asthma. However, their conclusions are not objective but depend on the final analysis on their multi-variate regression model. Perhaps this is where the most important bias has crept into the analysis.

As in the case of many new drugs, clinical trials are first carried out in adults, later in schoolchildren, and finally (if ever) in infants and pre-schoolchildren. This appears to have been the case with sodium cromoglycate since, of the studies included in their review, 12 out of 14 conducted before 1981 involved schoolchildren while, of those published since 1981, nine out of 10 involved pre-schoolchildren.

I wonder if the authors could calculate the size of the treatment effect in their selected trials separately for those trials predominately involving schoolchildren and those involving predominantly pre-schoolchildren.

Systematic review and meta-analysis often lend spurious objectivity to the assessment of efficacy. In the final event statistics provide no evidence that sodium cromoglycate is more effective in schoolchildren than in pre-schoolchildren.

For both schoolchildren and pre-schoolchildren and for both outcome measures (cough and wheeze) the test of homogeneity was negative; the study results were heterogeneous in both age groups. The pooled results, using the method of Dersimonian and Laird, are shown in table 1.

These results seem to confirm Silverman’s assumption that SCG is more effective in schoolchildren than in pre-schoolchildren, although even in schoolchildren the tolerance interval for wheeze still includes zero. However, we think the conclusion of an age specific effect is as yet unwarranted. All studies in schoolchildren were performed in the early years of SCG, at a time when the quality of design, methods and reporting of trials was not much of an issue. All the studies were performed on small numbers of children, thus yielding estimators with low precision, and used a crossover design, a design which is apt to yield biased results in cases of incomplete follow up. Publication bias might also account for these findings, given the funnel plot results. To confirm these results, a trial of adequate size needs to be performed in schoolchildren.

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AUTHORS’ REPLY We appreciate the comments by Professor Silverman and have calculated the treatment effect of sodium cromoglycate (SCG) separately for trials in schoolchildren and in children of pre-school age. We excluded Silverman’s trial for the reasons given by Edwards et al in a recent letter in Thorax. 1

Table 1 Effect of sodium cromoglycate on cough and wheeze in pre-schoolchildren and schoolchildren

<table>
<thead>
<tr>
<th></th>
<th>Cough</th>
<th>Wheeze</th>
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<tbody>
<tr>
<td></td>
<td>Pooled effect</td>
<td>Tolerance interval</td>
</tr>
<tr>
<td>Pre-schoolchildren</td>
<td>0.12 (0.03 to 0.22)</td>
<td>-0.12–0.36</td>
</tr>
<tr>
<td>Schoolchildren</td>
<td>0.26 (0.17 to 0.35)</td>
<td>0.02–0.50</td>
</tr>
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</table>

BTS guidelines on TB

This excellent guideline, 1 chaired by Dr Peter Ormerod, is very welcome. However, on page 888, under the heading Public Health Law, an important Act has been omitted—namely, Section 47 of the National Assistance Act 1948, as amended in 1951. This requires a doctor (usually a public health doctor) to consider, through a legal process, the compulsory removal to hospital of a person following certain strict criteria—for example, old age and infirmity, living in insanitary conditions, unable to look after oneself.

We have been approached in the past to invoke Section 47 on a patient with tuberculosis, although such a request and actual use is, I suspect, negligible in the UK as a whole. However, its existence is still possible and will also not “be undertaken lightly” as was correctly stated for Sections 37 and 38 of the Public Health Act 1984. An attempt to use Section 47 on a patient with tuberculosis some years ago was frowned upon when a doctor pursued the


Occlusion of chest drain bottle air outlet

Treatment of a pneumothorax often requires insertion of an intercostal chest drain. Usually the tube is connected to an underwater seal which acts as a one way valve, allowing air to escape from the pleural space and thereby preventing the development of a tension pneumothorax. We wish to highlight the case of a patient who developed a potentially life threatening problem resulting from the partial occlusion of a chest drain bottle air outlet port by a plastic cap supplied with the equipment.

A 60 year old man with COPD developed a large right pneumothorax. An attempt to insert a chest drain was unsuccessful so a chest drain was inserted. This was connected to an underwater seal using a chest drain bottle supplied by Rocket Medical plc (Watford, UK). The patient’s symptoms initially improved and a chest radiograph showed the chest drain to be in a good position. The fluid in the chest tube varied with the respiratory cycle. Approximately 6 hours after insertion of the tube the patient developed dyspnoea and widespread surgical emphysema. It was also noted that the fluid in the chest drain was no longer moving with respiratory manoeuvres. A further chest radiograph showed that the position of the chest drain was unchanged. It was then noticed that a plastic cap was occluding the air outlet port of the chest drain bottle. Once the cap was removed there was an immediate release of air and surgical emphysema cleared.

The plastic disposable bottle described in this case is in widespread use in the UK and is supplied in a sealed plastic wrapping. In this case the cap had been pushed in (details available on request). In theory this rise in pressure in the bottle could impair drainage and lead to a complication which acts as a one way valve, allowing air to escape from the pleural space and thereby preventing the development of a tension pneumothorax. We wish to highlight the case of a patient who developed a potentially life threatening problem resulting from the partial occlusion of a chest drain bottle air outlet port by a plastic cap supplied with the equipment.

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was not significant in either group when (overall, aspirin, metamizole, paracetamol) of asthma and the consumption of analgesics with mild analgesic tolerant asthma (table 1). Moderate and severe asthma than in those significantly higher in AIA patients with mild, consumption and the total analgesic and paracetamol and asthma. (4.9 (7.5) v 4.1 (5.5)). The independent samples test was used to compare the severity of asthma patients could help to elucidate the difference between the analgesic consumption of patients with AIA and those without analgesic intolerance.

Paracetamol and asthma

We were interested to read the article by Shaheen et al on the relationship between paracetamol and asthma.1 We have been interested in patients with analgesic induced asthma (AIA) since 1991 and now have a total of about 238 patients who have been followed up in our allergy unit. We have previously reported some related allergic conditions and risk factors for AIA, one of which was cumulative long analgesic consumption.2 After reading the paper by Shaheen et al we re-analysed our data and compared the consumption of analgesics by patients with analgesic tolerant asthma (group 1, n=103) and those with AIA (group 2, n=191 (132 published + 59 new cases)). The mean ages of the patients were 43.1 (14.0) years and 40.9 (12.3) years and there were 89 (86.4%) and 140 (73.3%) women in groups 1 and 2, respectively. The life long analgesic consumption was evaluated by a questionnaire about the number of boxes of analgesics used before analgesic intolerance was diagnosed (each box contains 20 pills).

There was no significant difference between the two groups in the total consumption of analgesics (9.1 (12.5) v 12.1 (15.1)), aspirin (5.1 (10.3) v 4.4 (8.1)), metamizole (4.9 (7.5) v 3.3 (4.8)), and paracetamol (3.5 (4.1) v 4.3 (8.9)). The independent samples t test was used to compare the severity of asthma and the amount of analgesic consumption and the total analgesic and paracetamol consumption was found to be significantly higher in AIA patients with mild, moderate and severe asthma than in those with mild analgesic tolerant asthma (table 1). However, the correlation between the severity of asthma and the consumption of analgesics (overall, aspirin, metamizole, paracetamol) was not significant in either group when Spearman’s non-parametric correlation test was applied to the data. It is already known that the clinical course of patients with AIA is more severe than for those with analgesic tolerant asthma, and the overall consumption of analgesics and paracetamol by AIA patients has been found to be higher.3 It should also be noted that the increased consumption of paracetamol in these patients results from physicians’ analgesic preference and our re-analysis showed a weak relation. Certainly the clinical and epidemiological surveys should be evaluated separately, but our results seem to support the results of Shaheen et al. Since these retrospective surveys might include “recall bias”, prospective studies of asthma patients could help to elucidate the difference between the analgesic consumption of patients with AIA and those without analgesic intolerance.

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Table 1 Consumption of analgesics (numbers of boxes each containing 20 pills) by patients with analgesic tolerant asthma and analgesic induced asthma (AIA)

<table>
<thead>
<tr>
<th>Analgesic</th>
<th>Mild (n=56)</th>
<th>Moderate (n=43)</th>
<th>Severe (n=4)</th>
<th>Mild (n=68)</th>
<th>Moderate (n=97)</th>
<th>Severe (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>2.3 (5.3)</td>
<td>4.3 (11.3)</td>
<td>0.1 (0.3)</td>
<td>4.2 (9.9)</td>
<td>3.8 (6.5)</td>
<td>4.3 (6.4)</td>
</tr>
<tr>
<td>Metamizole</td>
<td>1.9 (4.4)</td>
<td>4.0 (7.9)</td>
<td>0.5 (1.0)</td>
<td>2.3 (5.3)</td>
<td>1.9 (3.4)</td>
<td>2.7 (3.3)</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>1.6 (2.1)</td>
<td>2.6 (5.0)</td>
<td>1.9 (1.9)</td>
<td>3.7 (7.3)*</td>
<td>4.4 (10.6)*</td>
<td>3.2 (4.5)*</td>
</tr>
<tr>
<td>Total analgesic consumption**</td>
<td>7.0 (11.8)</td>
<td>12.4 (15.8)*</td>
<td>2.8 (0.9)</td>
<td>11.8 (14.5)*</td>
<td>12.3 (16.5)*</td>
<td>12.5 (11.6)*</td>
</tr>
</tbody>
</table>

1 Reference group.
* p<0.05.
** Other analgesics not included.

4 Karakaya G, Demir AU, Kalyoncu AF. From analgesic intolerance to analgesic induced asthma: are there some determinants? Allergol Immunopathol 2000;28:229–37.

BOOK REVIEW


This is the third edition of the standard textbook on high altitude medicine. Although it is only five years since the second edition appeared, the book has been extensively revised to take into account the recent explosion of interest in high altitude medicine. As the authors mention in their preface to the third edition, there have been over 1500 publications since 1995 on altitude related topics. All the chapters in this edition have been updated to take into account these recent publications and additional sections on commercial activities at altitude have been added.

I was interested to receive this new edition because, by chance, the first edition of this book was the first medical textbook I ever bought. At the time I was a student planning a trip to the Himalayas and wanted to learn more about the aetiology of the life threatening forms of acute mountain sickness, high altitude pulmonary oedema, and high altitude cerebral oedema. The book provided an excellent overview of the subject and introduced me to other interesting topics. Comparing the first and third editions, it is interesting to note that relatively little advance has been made in terms of understanding the pathophysiology of high altitude pulmonary and/or cerebral oedema, despite their increasing importance given the greater numbers of individuals travelling to high altitude now compared with 20 years ago. Those advances which have been made are well summarised in the relevant chapters of the third edition. High Altitude Medicine and Physiology remains the standard textbook in its subject area. It is comprehensive and well referenced and yet remains eminently readable. This is not a handbook of emergency medicine for the use of doctors or mountaineers travelling to altitude, but a book which covers a much broader subject area. It should be on the bookshelves of all individuals interested in the effect of altitude on the human body. —IH
Paracetamol and asthma

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