ABNORMAL ALFENTANIL PHARMACOKINETICS

Sir,—In a recently published study of alfentanil pharmacokinetics during prolonged infusion in the intensive care unit (Yate et al., 1986) we described one patient who demonstrated grossly abnormal alfentanil kinetics. The kinetics in this patient (patient No. 15 in the paper) were an elimination half-life of 720 min, a volume of distribution of 0.6 litre kg\(^{-1}\) and an estimated clearance of 0.66 ml kg\(^{-1}\) min\(^{-1}\) after a dose of alfentanil 25 mg given over 17 h.

We have recently had the opportunity to restudy this patient as a volunteer. The patient, a 64-yr-old female weighing 55 kg, was given a single i.v. dose of alfentanil 700 µg. Venous blood samples were taken before the injection and then at 2, 5, 11, 15, 30, 60, 120, 180, 240, 300 and 360 min afterwards for estimation of plasma alfentanil concentrations—which were measured by radioimmunoassay. On this occasion the calculated kinetic variables were \(T_{1/2} = 6.9\) min, \(T_{1/2} = 161\) min, \(V_D\) 458 ml kg\(^{-1}\) and clearance 1.96 ml kg\(^{-1}\) min\(^{-1}\).

The elimination half-life found was at the upper end of the range normally quoted for alfentanil and was attributable to a low clearance rather than to an increase in the volume of distribution. The possibility of an identifiable group of patients with a prolonged elimination half-life of around 160 min has been previously suggested (McDonnell et al., 1982), and it may be that this patient belongs to this group.

We do not know the reason for the differences between the kinetics found this time and previously; however, there are various possibilities. The total dose administered on the first occasion was larger by a factor of 34 and it may be that, in this patient, alfentanil kinetics could be better described by a Michaelis–Menten model similar to that seen with high-dose thiopentone infusions (Stanski et al., 1980). Alternatively, after major surgery there would almost certainly be alterations in hepatic blood flow although, as alfentanil has a low hepatic extraction ratio, changes in liver blood flow should have little effect. As alfentanil excretion can be described as binding sensitive capacity limited, changes in protein binding could have a profound effect and alfentanil is bound to acute phase proteins which are known to increase after cardiac surgery.

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REFERENCES


SPINAL NEEDLES, GAUGE AND HEADACHE

Sir,—Gauge standards evolved before the international metric system. British Imperial Standard Wire Gauge (SWG) became a legal standard in England in 1883 (Camm, 1965). Some gauge standards are based on successive doubling or halving of an initial diameter, while others are multiples of unknown origin. Certain standards have survived as measurements for thickness of needles. Without referring to which standard is used, the gauge concept is very inaccurate. To demonstrate this inaccuracy, we have examined needles supplied for dural puncture from two companies: Braun (German) and Becton & Dickinson (British). From both companies 25-gauge needles are orange, 26-gauge needles are brown, without reference to the gauge standards used. Macroscopically, one can easily see and feel differences in the thicknesses of the needles.

A total of 40 needles were examined: 10 needles of each size (25-gauge and 26-gauge) from Braun (Spinocan), and 10 of each from Becton & Dickinson. The examination was performed by the State Institute of Technology in Oslo. The thickness of the needles was measured with length-measuring equipment SIP MUL-1000 connected to a laser measuring system HP 55 28 A. The maximum and minimum diameter

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>Braun 25-gauge (orange)</th>
<th>Braun 26-gauge (brown)</th>
<th>Becton &amp; Dickinson 25-gauge (orange)</th>
<th>Becton &amp; Dickinson 26-gauge (brown)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum</td>
<td>0.5675</td>
<td>0.4608</td>
<td>0.5207</td>
<td>0.4718</td>
</tr>
<tr>
<td>Maximum</td>
<td>0.5536</td>
<td>0.4950</td>
<td>0.5113</td>
<td>0.4606</td>
</tr>
</tbody>
</table>
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TABLE II. Reference dimensions of nominal diameters for U.S. Standard and Standard Wire Gauge

<table>
<thead>
<tr>
<th>Size in gauge</th>
<th>U.S. Standard</th>
<th>Standard Wire Gauge</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-gauge</td>
<td>0.556</td>
<td>0.508</td>
</tr>
<tr>
<td>26-gauge</td>
<td>0.476</td>
<td>0.457</td>
</tr>
</tbody>
</table>

anywhere along each needle were found. The measuring precision was 10⁻⁵ mm. The results are shown in Table I. The maximum diameter of 25-gauge needles from Braun could be 0.0468 mm larger than the needles from B & D (9%). For the 26-gauge needles, those from B & D could have a maximum diameter 0.011 mm greater than those from Braun (2.4%).

The two companies (Braun and Becton & Dickinson) follow two different gauge standards. Braun follows U.S. standard, while B&D follows SWG. The nominal diameters in millimetres (mm) for the two standards are shown in Table I. Comparing the measured diameters (Table I) with the standards (Table II), it is evident that Braun's 25-gauge and 26-gauge needles both fulfill the criteria for the U.S. standard. Likewise, B&D needles fulfill the criteria for 25-gauge and 26-gauge according to the SWG. On the other hand, Braun 25-gauge needles do not fulfill the SWG standard; indeed, they are close to the 24-gauge SWG. Therefore, the incidence of headache after spinal anaesthesia may well differ depending on the actual needle (of the same nominal size) used.

Our investigation demonstrates how imprecise the gauge concept is. We recommend a change from gauge to millimetres for sizes of needles used in medicine.

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REFERENCE


GUIDELINES FOR PATIENTS RECEIVING LITHIUM TREATMENT WHO REQUIRE MAJOR SURGERY

Sir.—One person out of every 1000 in the general population is receiving long-term prophylactic treatment with lithium for recurrent manic-depressive illness. When such patients require surgical intervention it is important that the anaesthetist is aware of the attendant risks and can take the appropriate precautions. We wish to draw attention to a few points which, we believe, are particularly relevant.

Discontinuation of lithium in connection with major surgery. Lithium is eliminated through the kidneys. A decrease in glomerular filteration rate, or a negative fluid and/or sodium balance may lead to a reduction in the renal clearance of lithium with resultant accumulation of lithium and risk of lithium poisoning. Lithium poisoning is dangerous and has, occasionally, led to death. Lithium treatment should, therefore, be discontinued 2–3 days before major surgery (the elimination half-life of lithium is about 24 h), and it should not be resumed until renal function and fluid-electrolyte balance are again normal. The treatment need not be discontinued for minor surgery. There is no clinical evidence of interaction between lithium and anaesthetic agents, although lithium may prolong the action of neuromuscular blocking drugs.

Resumption of lithium treatment. Prophylactic lithium treatment effectively prevents manic and depressive relapses. Discontinuation of the treatment involves risk of recurrences, sometimes with catastrophic results. It is, therefore, important that the interruption of lithium treatment—in connection with major surgery—it as short as possible. Difficulties arise if the lithium treatment is not restarted again after the surgery. This is illustrated by the following case history.

A female patient with a history of several severe depressions and one episode of mania started prophylactic lithium in 1974 and on this treatment remained free of episodes for 8 years. In 1982 lithium was discontinued because the patient had to undergo hip-joint surgery. Ten days later the patient became restless and tense and she herself suggested that the lithium treatment should be resumed. This was, however, disregarded, the intensity of the mania increased, and 5 weeks after the operation the patient had to be admitted to the closed ward of a psychiatric Unit. She was then violently manic, dysphoric, irritable and aggressive, and she lacked insight completely. Treatment with neuroleptic agents brought her mania under control, and lithium maintenance treatment was resumed. The patient has been free of symptoms since then.

Preoperative parenteral fluid administration. In some patients lithium treatment decreases the renal concentrating ability, with consequent development of polyuria and polydipsia. These side effects may be troublesome for the patient, but they do not decrease the elimination of lithium and are not in themselves dangerous. However, owing to the reduced concentrating ability these patients become dehydrated rapidly if fluid intake is restricted or additional fluid lost. Dehydration may reduce the lithium clearance and increase the risk of lithium poisoning. If patients with lithium-induced polyuria must abstain from drinking before surgery, they should be given parenteral fluids the night before the operation. This point is illustrated by the following case history.

A female patient developed pronounced polyuria and polydipsia during lithium treatment, but decided that she could live with these side effects, because the treatment removed her manic and depressive episodes very effectively. She was, however, admitted to a surgical ward for uterine curettage and was forbidden food and fluid intake during the night before the operation. Under this regimen she developed symptoms of dehydration and slight lithium poisoning with malaise, hand tremor and dysarthria. When she was admitted for another curettage 1 year later, she protested against being deprived of fluid before anaesthesia, but the nursing staff clearly felt that this insistence on having something to drink was merely the whim of a psychiatric patient. Finally, she screamed so loudly that a psychiatrist was brought in, and he advised the administration of fluid i.v. before anaesthesia. In this way the patient avoided symptoms of dehydration and lithium poisoning.

Parenteral fluid administration may also be required for lithium-treated patients who vomit copiously, or who are unconscious for many hours.

In summary:

(1) Lithium should be discontinued 2–3 days before major surgery.

(2) The treatment should be resumed as soon as possible after the operation—that is, when kidney function and fluid-electrolyte balance have become normal.