Sir,—We wish to comment on the article by Dahl and colleagues [1], who investigated the effects on postoperative pain and analgesic requirements of starting a 72-h continuous infusion of extradural bupivacaine and morphine either before surgical incision or immediately after surgery. The results showed that the two main outcome measures did not differ significantly between the preincisional and the postsurgical groups.

We congratulate the authors on their continuing work aimed at reducing postoperative pain [1–3]. Their pioneering studies are a welcome addition to clinical practice. Dahl has demonstrated that timely preventive measures in combination with aggressive postoperative treatment can reduce postoperative pain significantly, to near zero levels. The results of these studies raise the possibility that “painless surgery” may soon become a reality.

Animal studies by Woolf and Wall [4] and others have led to the idea that noxious intraoperative events (surgical incision, wound retraction) may contribute to postoperative pain long after surgery if, at the time of surgical trauma, primary (or visceral) afferent fibres are capable of transmitting their message centrally, and spinal cord cells receive the “afferent barrage” signalling the presence of injury. It has been hypothesized that one effect of the afferent barrage is to alter central processing so that, after surgery, inputs from the wound impinge on sensitized spinal cord cells which amplify the peripheral signal and contribute to enhanced postoperative pain. The implication is that postoperative pain can be reduced by pre-emptive analgesia [5] which would prevent the development of central sensitization, and Dahl and colleagues have tested this hypothesis by comparing treatments administered before incision or after surgery.

One issue concerns the potential pre-emptive effects of systemic opioids [6, 7]. The possibility cannot be excluded that the preoperative administration of fentanyl 0.1–0.2 mg to patients in both preincisional and postsurgical groups at induction may have attenuated the afferent barrage and contributed to non-significant intergroup differences in postoperative pain. The minimum effective dose of preoperatively administered systemic opioids that significantly attenuates or prevents the central consequences of noxious perioperative events is not known. However, we do know from animal studies [4] that the dose of systemic morphine required to abolish established noxious stimulust-induced central hyperactivity is an order of magnitude greater than the dose required to prevent it. Until this has been established in clinical studies of pre-emptive analgesia, opioid administration as one component of the general anaesthetic procedure will confound the main outcome measures that are assessed.

Moreover, in the study by Dahl and colleagues [1], the time between induction and skin incision may have differed for the groups. It is clear that 40 min elapsed between induction and skin incision in the group that received the extradural block before incision, but it is not clear from the methodology if the onset of surgery also occurred 40 min after induction in the other group. If not, then the effects of the induction dose of fentanyl on postoperative pain could have been different in the two groups of patients. A second related issue concerns the timing of the test dose of bupivacaine (2 ml of 0.75 %) relative to incision in the control group. This may be important, in that even a small test dose (of a very potent concentration) may afford some degree of block when surgical incision is made shortly after. As noted above, it is unclear from the methodology how much time elapsed between the test dose and incision.

The final issue concerns the balance between achieving the clinical objective of abolishing postoperative pain and the theoretical objective of evaluating whether the trauma associated with surgery may have a prolonged effect on postoperative pain. These two objectives may run at cross purposes because, in order to demonstrate the latter, the former may be compromised in some study designs. In the study by Dahl and colleagues [1], postoperative VAS pain scores at rest were near zero in both groups, making it virtually impossible to demonstrate an advantage of pre-operative postoperative analgesic administration. The postoperative regimen was fixed in both groups. This regimen does not appear to have been titrated to analgesic effect by either patients or staff, and thus may have been so effective as to block nociceptive processing at the spinal level in both groups. This appears to be confirmed by the minimal requirements for supplementary morphine in both groups during the 72-h period studied.

As we see it, the issue of theoretical importance in pre-emptive analgesia is not whether or not postoperative pain can be abolished regardless of the timing of administration of analgesics relative to surgical incision—although abolishing postoperative pain is a clinical objective that we all should strive to achieve. Studies that examine the efficacy of pre-emptive analgesia must allow patients to demonstrate their level of pain either directly, through verbal report (e.g., VAS pain scores) or indirectly, through their consumption of postoperative analgesics. When postoperative pain levels are near zero, one must then rely on analgesic consumption to provide the crucial measure. However, if the postoperative analgesic regimen is fixed (i.e., not titrated to patient need) and pain is near zero, it may not be possible to detect if the afferent barrage produced by the surgical trauma had a prolonged central effect.

In summary, the conclusion [1] that the timing of onset of the extradural regimen relative to skin incision is not of “major clinical importance” must be evaluated with the knowledge that, in the control group, the combined effects of the induction dose of fentanyl and the extradural test dose of bupivacaine may have attenuated the surgery-induced afferent barrage. We would also caution readers about overgeneralizing the results to other anaesthetic procedures. Pre-incisional administration of analgesics may be more effective than postincisional (or postoperative) administration for certain combinations of analgesic agents, routes of administration and types of surgery [8, 9].

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