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(Accepted for publication April 8, 1993.)

Anesthesiology
79:198–199, 1993

In Reply:—We agree with Johnstone and Martinec that it would be highly desirable for anesthesia studies involving new drugs to include a cost evaluation.[1] Unfortunately, information on the cost of new drugs is not available at the time phase 3 studies are conducted.[2–4] Given the high cost of drug development (variously estimated at $150–250 million), it is not surprising that new drugs, such as ketorolac and ondansetron, are more expensive than the drugs they are replacing.

Determining the cost of a new therapeutic agent is a complex process because consideration must be given to direct and indirect costs (table 1). We also agree with Johnstone and Martinec that the inclusion of drug-company employees as coauthors may raise concerns regarding the objectivity of the authors' presentation of favorable data. However, the inclusion of drug-company employees as coauthors did not prevent Wong *et al.* from concluding that the use of ketorolac (as an alternative to the opioid analgesics) was not associated with a difference in the overall "quality of life" or the time to resumption of normal activities.[2] These authors suggested that the lack of a global "outcome difference" between ketorolac and opioid analgesics needs to be weighed against the cost differential between ketorolac and the standard analgesic drugs. Other recently published studies[5–7] suggested that ketorolac offers only minor advantages over fentanyl in the ambulatory setting. Nevertheless, patients at risk for opioid-related side effects (*e.g.*, respiratory depression, nausea, vomiting, ileus, pruritis) may benefit from the use of nonsteroidal antiinflammatory drugs, such as ketorolac.

The drug cost calculations performed by Johnstone and Martinec for the studies by Scuderi *et al.*[3] and McKenzie *et al.*[4] raise concerns regarding the potential impact of drug packaging (unit *versus* multidose vials) and waste on the cost of drugs, including ondansetron. However, even if a minimally effective dose of ondansetron was prescribed, the costs of this drug likely would be higher than droperidol. Yet, preliminary studies would suggest that ondansetron is more efficacious than either droperidol[8] or metoclopramide* in the prevention of postoperative nausea and vomiting. As suggested in our editorial, the cost of a new drug (or therapy) should include a thorough analysis of indirect costs (*e.g.*, postanesthesia care unit stay, unanticipated hospitalization, resumption of normal activities).

Table 1. Factors Determining the Costs of Anesthetic Drugs

Direct Costs	Indirect Costs
Anesthetic drugs	Preparation and set-up time
Adjuvant agents	Excess operating room turnover time
Equipment and supplies	Recovery room stay
Drug waste	Postoperative "rescue" treatments
	Unanticipated hospitalizations
	Equipment maintenance

Johnstone and Martinec correctly pointed out the high cost of indiscriminant use of expensive drugs, such as ondansetron. Because more than 60% of patients undergoing ambulatory surgery will not experience postoperative nausea and vomiting,[9] routine prophylaxis with ondansetron cannot be recommended at this time. Yet, for selected high-risk patient populations undergoing surgical procedures associated with a high incidence of postoperative emesis, antiemetic prophylaxis may be both efficacious and cost-effective.

With the impending changes in our health-care reimbursement system, it will be important to examine our drug-usage patterns. Information on medication costs and alternative therapeutic agents is essential if we are going to practice more cost-efficiently.[10] The cost of expensive new drugs and monitoring techniques (*e.g.*, brainstem evoked potentials, esophageal echocardiography) will be scrutinized more closely in the future. Provisions for providing the cost information requested by Johnstone and Martinec should aid anesthesiologists in making informed decisions regarding the choice of drugs during the perioperative period.

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(Accepted for publication April 10, 1993.)

Anesthesiology
79:199–200, 1993

Intrathecal Baclofen in Tetanus: Alternative Methods of Administration

To the Editor:—Saissy *et al.*[1] reported the efficacy of flumazenil in counteracting the central nervous system depression induced by intrathecal administration of baclofen. As in a previous report from this group,[2] large boluses of baclofen were given intrathecally to control the rigidity and spasms of tetanus, favoring this method of drug administration over continuous infusion in view of "simplicity, safety, and low cost." Although recognizing that these benefits support the use of intermittent intrathecal administration of baclofen in certain economic and demographic settings, we urge caution in using this method of intrathecal baclofen administration because of the increased risk of overdose.

Experience with the use of continuous intrathecal infusion of baclofen in the treatment of intractable spasticity due to multiple sclerosis, spastic paraplegia, and traumatic spinal cord injury established the safety of this method of drug administration. Baclofen shows significant variability in its pharmacokinetics following intrathecal injection, with an elimination half-life between 0.9 and 5 h reported in a study on four patients.[3] After lumbar intrathecal administration, Penn and Kroin[4] reported that the lumbar to cervical baclofen ratio was 4.1:1, and therefore, the concentration of baclofen that reached the brain was not large. After bolus administration, however, higher concentrations would be expected centrally, with resultant increased toxicity, as demonstrated by Saissy *et al.*,[1] and as other authors report following inadvertent or intentional bolus therapy.[5]

Current recommendations for intrathecal administration of a baclofen test dose in patients with causes of spasticity other than tetanus are doses of 25–50 μg, although we have not encountered problems using test doses of 50 μg followed by 75 or 100 μg. This is to avoid precipitating an overdose in patients who may be unduly sensitive to the drug. In tetanus, the sensitivity to intrathecal administration of baclofen is decreased, because larger bolus doses are well tolerated. However, because most medical centers in developed countries have the facilities available for continuous intrathecal administration through a lumbar intrathecal catheter connected to an external infusion pump, it is difficult to justify the increased risk associated with a large bolus.

Of reported cases[6] that used intrathecal baclofen infusion in the management of tetanus, a dosage range of 600–2,000 μg/day by continuous intrathecal infusion was effective. Müller *et al.*[6] also used large boluses of up to 1,000 μg baclofen given intrathecally in tetanus. However, an initial bolus of 200 μg baclofen, with consideration of the intrathecal half-life of baclofen when increasing the infusion rate or giving additional boluses, should allow for safer use of this therapy.

Practical considerations are the risk of infection with an external infusion device and the cost of an implantable infusion device. A compromise would be the use of a subcutaneous port to allow regular (every 6 h) intrathecal injection, which carries a smaller risk of infection (than the external infusion device), significantly less cost (than the implantable infusion device), and through the use of more frequent and smaller doses of baclofen, less risk of overdose (than the intermittent lumbar puncture technique).

The experience of Saissy *et al.*[1] in treating tetanus with baclofen given intrathecally is far greater than ours; however, like Müller *et al.*,[6] we believe that, when facilities are available for continuous infusion, this may be preferable. Intermittent intrathecal injection through a subcutaneous port also should be considered as an ac-