HIGHLIGHTS

Computer-controlled Infusion of Alfentanil for Postoperative Analgesia: A Pharmacokinetic and Pharmacodynamic Evaluation

Marjolein C. O. van den Nieuwenhuyzen, M.D., Frank H. M. Engbers, M.D., Anton G. L. Burm, M.Sc., Ph.D., Harry J. M. Lemmens, M.D., Ph.D., Arie A. Vletter, B.Sc., Jack W. van Kleef, M.D., Ph.D., James G. Bovill, M.D., Ph.D., F.F.A.R.C.S.I.

ALFENTANIL'S rapid elimination half-life should permit an anesthesiologist to provide profound intraoperative analgesia followed by rapid recovery. In theory, administration of alfentanil by infusion rather than as repeated boluses should minimize fluctuations from the desired concentration, decreasing the administered dose and speeding recovery. Several studies have examined whether computer-controlled infusion devices, programmed with pharmacokinetic parameters obtained from a representative population, could be used to administer alfentanil effectively during anesthesia. Although the studies have demonstrated that the computer-driven devices can achieve target plasma concentrations of alfentanil with reasonable accuracy, the devices have not yet proliferated in anesthetic practice. Whether the development of more "user-friendly" infusion devices will facilitate the use of computer-controlled infusion regimens remains to be established.

In the present issue, van den Nieuwenhuyzen *et al.* (page 481) examine whether computer-controlled infusions can provide analgesia during the postanesthetic period. After administering alfentanil and nitrous oxide intraoperatively, these investigators waited until the patients awakened sufficiently to complain of pain, then administered alfentanil for 36 h, adjusting the target concentration frequently according to the patients' needs. Plasma concentrations of alfentanil were measured and compared to the target concentrations; pain was assessed using a visual analog scale. Plasma alfentanil concentrations varied markedly for each individual and between individuals; the former because pain changed over time, the latter because of differences in tolerance to pain. Measured plasma concentrations were similar to target concentrations. The regimen provided effective pain relief for most subjects and was rated by the patients as providing adequate pain relief.

The performance of the infusion device represents a significant finding that the pharmacokinetic parameters programmed into the device continue to predict plasma alfentanil concentrations over a longer period than that tested in previous intraoperative studies. Thus, van den Nieuwenhuyzen *et al.* demonstrate the accuracy (and, to a limited extent, the efficacy) of computer-controlled infusion regimens in a new setting. Yet, the study raises an important (and unanswered) question: Will administering opioids *via* this regimen improve outcome or provide any particular benefit? Certainly, new modalities to provide postoperative analgesia warrant attention from our research and clinical colleagues.

Dennis M. Fisher, M.D.

Autologous Platelet-rich Plasma Does Not Reduce Transfusion of Homologous Blood Products in Patients Undergoing Repeat Valvular Surgery

Mark H. Ereth, M.D., William C. Oliver, Jr., M.D., Froukje M. K. Beynen, M.D., Charles J. Mullany, M.B.M.S., Thomas A. Orszulak, M.D., Paula J. Santrach, M.D., Duane M. Ilstrup, M.S., Amy L. Weaver, M.S., Kenneth R. Williamson, M.D.

MORE than a decade has passed since the identification of platelet defects as a major contributor to excessive bleeding after cardiopulmonary bypass. Efforts to limit postbypass bleeding have explored both pharmacologic and mechanical interventions, including autologous prebypass collection of platelet-rich plasma with readministration after bypass. This technique appeals in theory to the clinician wishing to spare a portion of the patient's platelets from the disruptive effects of bypass. Although previous studies demonstrated a bene-

ficial effect of this pheresis technique, their unblinded designs raised serious questions about flawed methodology: physician bias can easily influence intraoperative hemostasis efforts, altering blood loss, as well as subjective decisions governing transfusion.

Ereth *et al.* (page 540) employed a double-blinded design to reassess the benefit of autologous platelet-rich plasma collection and administration. To blind all clinicians, the investigators isolated the harvesting equipment with curtains and substituted an unblinded anesthesia team during harvesting (study group) or sham procedure (control group). They found no salutary hemostatic effect of this technique. Coagulation studies did not differ at the end of operation, although the group undergoing platelet-rich plasma harvesting experienced prolongation of the prothrombin time and decreases in platelet count and fibrinogen concentration during operation.

Is autologous platelet-rich plasma collection following the same evolution as desmopressin, *i.e.,* initial enthusiasm followed by ultimate disappointment? Ereth *et al.* rightly point out that platelet-rich plasma harvesting may yet prove beneficial in perioperative blood conservation, perhaps in combination with a pharmacologic therapy, such as fibrinolytic inhibitor administration, or in a more specific subpopulation. However, their results indicate no hemostatic benefit of autologous platelet-rich plasma collection alone for patients undergoing repeat valve replacement.

Jan Charles Horrow, M.D.