pofol are manifested as systemic hypotension resulting from a reduction in systemic vascular resistance. Cardiac output is not consistently affected," is definitely misleading. In most of the studies where cardiac output was "not consistently affected," there was significant respiratory acidosis. In particular, the study of Claeys *et al.*,[2] which Sebel and Lowdon repeatedly refer to, was conducted during spontaneous ventilation during propofol infusion with significant respiratory acidosis. Even the potent inhalation anesthetics show minimal cardiovascular effects when patients are allowed to breathe spontaneously and develop respiratory acidosis.[3-5] Stephan *et al.*[6] demonstrated after induction with 2 mg/kg propofol, 0.1 mg/kg pancuronium, and tracheal intubation that hypercarbia (Pa_{CO_2} = 50 mmHg) resulted in no depression of cardiac output, while normocarbia (Pa_{CO_2} = 40 mmHg) and hypocarbia (Pa_{CO_2} = 30 mmHg) produced significant decreases in cardiac output. Thus, if patient's lungs are ventilated during propofol anesthesia (and as Sebel and Lowdon point out, the drug is a potent respiratory depressant), then the usual cardiovascular response in almost all studies has been a decrease in cardiac output.

They also state that in the studies from Prys-Roberts' group,[7,8] "cardiac output decreased but the decrease was significant in only two studies and only during steady-state anesthesia before surgical stimulation." In all of the Prys-Roberts' studies, surgical stimulation resulted in an increase in arterial pressure, but with either no change in the significantly decreased cardiac output or further decrease. Although Sebel and Lowdon do not comment on the effect of propofol on cardiac output and stroke volume in the study by Larsen *et al.*[9] this group also showed major effects on cardiac output produced by propofol anesthesia. Again, I think they are misleading when they compare the study of Claeys *et al.*[2] to that by Larsen *et al.*,[9] both as far as the patient population is concerned and the conditions of the study.

It is important when a drug is introduced that the practitioner be well aware of the cardiovascular effects. In the case of propofol, if anything, the cardiovascular effects are more pronounced than those of the usual iv anesthetics we are accustomed to using and in patients with cardiovascular compromise, the drug must be carefully titrated to effect.

ROBERT G. MERIN, M.D.
Professor of Anesthesiology
Department of Anesthesiology
The University of Texas
Health Science Center at Houston
6431 Fannin, 5.020 MSMB
Houston, Texas 77030

REFERENCES

1. Sebel PS, Lowdon JD: Propofol: A new intravenous anesthetic. ANESTHESIOLOGY 71:260–277, 1989
2. Claeys MA, Gepts E, Camu F: Hemodynamic changes during anesthesia induced and maintained with propofol. Br J Anaesth 60:3–9, 1988
3. Bahlman SH, Eger EI II, Halsey MJ, Stevens WC, Shakespeare TF, Smith NT, Cromwell TH, Fourcade H: The cardiovascular effects of halothane in man during spontaneous ventilation. ANESTHESIOLOGY 36:494–501, 1972
4. Calverley RK, Smith NT, Jones CW, Prys-Roberts C, Eger EI II: Ventilatory and cardiovascular effects of enflurane anesthesia during spontaneous ventilation in man. Anesth Analg 57:610–621, 1978
5. Cromwell TH, Stevens WC, Eger EI II, Shakespeare TF, Halsey MJ, Bahlman SH, Fourcade H: The cardiovascular effects of compound 469 (Forane) during spontaneous ventilation and CO_2 challenge in man. ANESTHESIOLOGY 35:17–25, 1971
6. Stephan H, Sonntag H, Schenk HD, Kohlhausen S: Einfluß von Disoprivan (Propofol) auf die Durchblutung und den Sauerstoffverbrauch des Gehirns und die CO_2-Reaktivität der Hirngefäße beim Menschen. Anaesthesist 36:60–65, 1987
7. Monk CR, Coates CP, Prys-Roberts C, Turtle MJ, Spelina K: Haemodynamic effects of a prolonged infusion of propofol as a supplement to nitrous oxide anaesthesia. Br J Anaesth 59:954–960, 1987
8. Coates DP, Monk CR, Prys-Roberts C, Turtle M: Hemodynamic effects of infusions of the emulsion formulation of propofol during nitrous oxide anesthesia in humans. Anesth Analg 66: 64–70, 1987
9. Larsen R, Rathgeber J, Bagdahn A, Lange H, Rieke H: Effects of propofol on cardiovascular dynamics and coronary blood flow in geriatric patients. A comparison with etomidate. Anaesthesia 43(Suppl):25–31, 1988

(Accepted for publication November 16, 1989.)

Anesthesiology
72:394–395, 1990

Propofol Causes Cardiovascular Depression. II.

To the Editor:—We disagree with the description of cardiovascular effects of propofol recently summarized by Sebel and Lowdon.[1] While there is no doubt that propofol causes a significant decrease in arterial blood pressure by focusing on the results reported by Monk *et al.*,[2] Coates *et al.*,[3] and Claeys *et al.*,[4] the authors seem to accept the conclusion that the observed decrease in arterial blood pressure following administration of propofol is caused by a decrease in systemic vascular resistance without changes in cardiac output or stroke volume.

In fact, the reported effects of propofol on the cardiovascular system are conflicting. Some authors describe a decrease in systemic vascular resistance with no change in cardiac output,[4] whereas others report a decrease in cardiac output with an unchanged systemic vascular resistance.[5-7] Furthermore, a negative inotropic action has been demonstrated in humans[5,8] and in dogs.[9] The observed decrease in systemic vascular resistance in the experiments by Claeys *et al.*[4] and Monk *et al.*[2] may not necessarily reflect an effect of propofol but may be the result of a concomitant increase in Pa_{CO_2} in their patients.[7] Cullen *et al.*[10] have shown that an increase in Pa_{CO_2} causes an increase in cardiac output, stroke volume, and a decrease in systemic vascular resistance.[10]

Finally, we are concerned with the authors statement that, "the combination of propofol and opioids may constitute safer anesthesia practice." Although such therapy may blunt the sympathetic response to laryngoscopy and tracheal intubation, it will also enhance cardiovascular depression and lead to even greater hypotension.[5,8] This potentiation may in part be explained by the higher plasma propofol concentrations that occur if propofol is used together with opioids.[11] Furthermore, bradycardia as seen in some patients[12] after the administration of propofol is more likely to develop with the additional cholinergic action of opioids.

In conclusion, we think that the cardiovascular effects of propofol are profound, unpredictable in their severity, and not easily treated

Downloaded from http://asa2.silverchair.com/anesthesiology/article-pdf/72/2/394/635719/0000542-199002000-00036.pdf by guest on 13 March 2024

by fluid resuscitation as they are the result of both a decrease in systemic vascular resistance and a negative inotropic effect. By no means are these side effects negligible, and we therefore would like to advise our colleagues to use propofol with the utmost care in patients with cardiovascular disease, peripheral vascular disease, and those with hypovolemia.

HUGO VAN AKEN, M.D., PH.D.
Professor of Anesthesiology
University Hospitals
Katholieke Universiteit Leuven
Herestraat 49
B-3000 Leuven, Belgium

THOMAS BRÜSSEL, M.D.
Klinik und Poliklinik für Anästhesiologie
Westfälische Wilhelms-Universität
Albert-Schweitzer Straße 33
D-4400 Münster, West Germany

REFERENCES

1. Sebel PS, Lowdon JD. Propofol: A new intravenous anesthetic. ANESTHESIOLOGY 71:260–277, 1989
2. Monk CR, Coates DP, Prys-Roberts C, Turtle MJ, Spelina K. Haemodynamic effects of a prolonged infusion of propofol as a supplement to nitrous oxide anaesthesia. Br J Anaesth 59: 954–960, 1987
3. Coates DP, Monk CR, Prys-Roberts C, Turtle M. Hemodynamic effects of infusions of the emulsion formulation of propofol during nitrous oxide anaesthesia in humans. Anesth Analg 66: 64–70, 1987
4. Claeys MA, Gepts E, Camu F. Haemodynamic changes during anaesthesia induced and maintained with propofol. Br J Anaesth 60:3–9, 1988
5. Van Aken H, Meinshausen E, Prien T, Heinecke A, Lawin P. The influence of Fentanyl and tracheal intubation on the hemodynamic effects of anesthesia induction with propofol/N_2O in humans. ANESTHESIOLOGY 68:157–163, 1988
6. Stephan H, Sonntag H, Schenk HD, Kettler D, Khambatta HJ. Effects of propofol on cardiovascular dynamics, myocardial blood flow and myocardial metabolism in patients with coronary artery disease. Br J Anaesth 58:969–975, 1986
7. Carlier S, Van Aken H, Vandermeersch E, Thorniley A, Byttebier G. Does nitrous oxide affect the hemodynamic effects of anesthesia induction with propofol. Anesth Analg 68:728–733, 1989
8. Lepage J, Pinaud ML, Hélias JH, Juge CM, Cozian AY, Farinotti R, Souron RJ. Left ventricular function during propofol and fentanyl anesthesia in patients with coronary artery disease: Assessment with a radionuclide approach. Anesth Analg 67:949–955, 1988
9. Brüssel T, Theissen JL, Vigfusson G, Lunkenheimer PP, Van Aken H, Lawin P. Hemodynamic effects of propofol and etomidate. Negative inotropic properties of propofol. Anesth Analg 68: 35–40, 1989
10. Cullen DJ, Eger EI, Gregory GA. The cardiovascular effects of carbon dioxide in man, conscious and during cyclopropane anesthesia. ANESTHESIOLOGY 31:407–413, 1969
11. Cockshott ID, Briggs LP, Douglas EJ, White M. Pharmacokinetics of propofol in female patients. Br J Anaesth 59:1103–1110, 1987
12. Thompson SJ, Yate PM. Bradycardia after propofol infusion. Anaesthesia 42:430, 1987

(Accepted for publication November 16, 1989.)

Anesthesiology
72:395–396, 1990

Propofol Causes Cardiovascular Depression. III.

To the Editor:—In the recent review of propofol,[1] Sebel and Lowdon stated that administration of propofol to patients with good left ventricular function undergoing myocardial revascularization was reported to cause consistent, significant decreases in blood pressure, variable changes in heart rate, and no statistically significant changes in cardiac output or cardiac index. These data were obtained from earlier European reports, but Kaplan *et al.** found that even in patients with good left ventricular function (ejection fractions of 30% or better and no previous myocardial infarctions within 3 months of their study), propofol produced significant decreases in MAP, SVR, and LVSWI as well as an increase in heart rate. The addition of other agents during anesthesia (halothane and pancuronium) further accentuated these effects prior to intubation. The authors indicated that their results imply that these decreases may be due to some degree of myocardial depression in addition to some vasodilatory effect. Lippmann *et al.*† found noncardiac elective surgical patients (ASA physical status 2–3) that LVSWI decreased by 35%, cardiac index by 18%, and MAP by 23%, respectively, with no significant decreases in PVR and SVR. Heart rate remained stable. Other studies,[2] also showed the cardiodepressant effect of propofol.

Further in their article, Sebel and Lowdon[1] stated that administration of propofol in combination with a potent opioid may constitute "safer practice" and offer more effective blunting of autonomic sympathetic responses. This may be correct in managing the hypertensive reaction to laryngoscopy in most patients but not in the poor-risk patient, patients with poor cardiac reserve, or even in patients about to undergo cardiac surgery with good left ventricular function. Vermeyen *et al.*[3] in their investigations found that propofol depressed the heart and the addition of fentanyl accentuated this depressant effect. Therefore, the combination of potent opioid with propofol does not offer a "safer practice" and should be used with due caution. The cardiovascular depressant effects of propofol must be borne in mind when this drug is being used in clinical practice.

MAURICE LIPPMANN, M.D.
MARTIN S. MOK, M.D.
Department of Anesthesiology
UCLA School of Medicine

* Kaplan JA, Guffin AV, Mikula S, Dolman J, Profeta J: Comparative hemodynamic effects of propofol and thiamylal sodium during anesthetic induction for myocardial revascularization. Journal of Cardiothoracic Anesthesia 2:297–302, 1988.

† Lippmann M, Paicius R, Gingerich S: A controlled study of the hemodynamic effects of propofol vs thiopental during anesthesia induction. Seminars in Anesthesia 7:116–122, 1988.

Downloaded from http://asa2.silverchair.com/anesthesiology/article-pdf/72/2/394/635719/0000542-199002000-00036.pdf by guest on 13 March 2024