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Cardiovascular Effects of Nalbuphine in Patients with Coronary or Valvular Heart Disease

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Although the hemodynamic changes produced by small doses of nalbuphine given to patients with cardiac disease are minimal, the cardiovascular effects of large doses which have been used as supplements for general anesthesia have not been investigated. Cardiovascular variables were measured after incremental doses of nalbuphine, up to 2 or 3 mg/kg in fourteen patients with coronary artery disease with normal left ventricular function and in seven patients with mitral valve disease. No significant changes in cardiac index, stroke work index, mean arterial pressure, pulmonary diastolic or wedge pressure, heart rate, or central venous pressure occurred in the preoperative period. However, nalbuphine alone did not produce surgical anesthesia and the addition of diazepam, nitrous oxide, or halothane was required in all patients. The addition of halothane coupled with surgical stimulation significantly decreased cardiac and stroke indices, increased mean arterial and pulmonary wedge pressures, and increased systemic vascular resistance in patients with coronary artery disease. In patients with mitral valve disease, following surgical incision, there were small but significant decreases in cardiac index and left ventricular stroke work index, and increases in systemic vascular resistance. Despite its lack of deleterious hemodynamic effects, the place of nalbuphine in the armamentarium of the anesthesiologist must be limited to use as a premedicant, as an adjunct to balanced anesthesia, or for postoperative pain relief. (Key words: Analgesics: nalbuphine. Anesthesia: cardiovascular. Antagonists, narcotic: nalbuphine. Heart: coronary disease; valvular disease.)

NARCOTIC ANESTHESIA is commonly used in patients undergoing cardiac surgery because of minimal or beneficial hemodynamic effects. However, at the doses used clinically, respiratory depression is common and prolonged. Nalbuphine, a narcotic agonist-antagonist, is a potent analgesic which, at low doses, is equivalent to morphine in analgesic effect and demonstrates similar respiratory depression. At doses greater than 0.45 mg/kg, there is no increase in respiratory depression with nalbuphine.[1] Since the hemodynamic effects of doses of 2 or 3 mg/kg which have been used for nitrous oxide-narcotic anesthesia** have not been investigated previously, the purpose of this study was to evaluate the effects of such doses which would be similar, although clearly not equivalent, to the high doses of morphine used in cardiac anesthesia.[2] Previous work in animals,[3] showing a plateau at only 0.3 MAC at these or higher doses, demonstrated the necessity of combining nalbuphine with other agents such as nitrous oxide or potent inhalational anesthetics to provide adequate anesthesia. However, since profound respiratory depression and apnea occur with large doses of morphine or fentanyl, but do not occur with nalbuphine, it was not compared with them since this protocol required spontaneous ventilation.

Methods

Fourteen patients (12 men and two women) scheduled for multiple coronary artery bypass grafts (CABG) and seven patients (two men and five women) for mitral commissurotomy or valve replacement (MVR) who had given their informed consent formed the study group. The protocol was approved by the Human Investigation Committee at the University of Virginia. All patients with coronary artery disease (CAD) had normal left ventricular function as evidenced by left ventricular end diastolic pressure less than 12 mmHg, normal cardiac indices, and absence of any areas of dyskinesis, akinesis, hypokinesis, or ventricular aneurysm on ventriculography. In patients with mitral valve disease, ventricular function was normal as documented by ejection fractions, cardiac outputs, or left ventriculography. The ages of the patients ranged from 41 to 74 years with a mean of 58 years in the CABG group, and from 22 to 64 years with a mean of 48.5 years in the MVR group. Eight of the fourteen CABG patients were on propranolol with the last dose given approximately 8 h prior to surgery. Two CABG patients received digitalis prophylactically immediately preoperatively, while five of the

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MVR patients were taking maintenance digoxin for treatment of congestive heart failure or control of ventricular response to atrial fibrillation. Digoxin was omitted on the day of surgery in all patients.

All patients were premedicated with 0.1 mg/kg nalbuphine and 0.005 mg/kg scopolamine intramuscularly one hour prior to arrival in the operating room. Two peripheral intravenous infusions of 5% dextrose in water were started and maintained at 30 ml/h. Radial and pulmonary artery (Swan-Ganz) catheters were placed using local anesthesia with lidocaine 2%. After the patient had breathed 100% oxygen by tight-fitting face mask for five minutes, the following control measurements were made: systolic (SBP), diastolic (DBP), and mean arterial (MAP) pressures; pulmonary artery systolic (PAS), diastolic (PAD), mean (MPAP) and capillary wedge (PCW) pressures; central venous pressure (CVP); cardiac output (CO) in triplicate, and Pa_{O_2}, Pa_{CO_2}, and *p*H. Pulmonary wedge pressures were not measured in MVR patients to avoid possibility of pulmonary artery rupture in patients with increased pulmonary artery pressures. All pressures were measured using Bentley Trantec® Model 800 transducers and Hewlett Packard® pressure modules calibrated against a mercury column. Cardiac outputs were determined with an Edwards® Laboratories Model 9520 computer and curves recorded on a Hewlett Packard® Model 7758B recorder. Rate-pressure product (RPP), systemic vascular resistance (SVR), pulmonary vascular resistance (PVR), left and right ventricular stroke work (LVSW, RVSW), and indices (SVRI, PVRI, RVSWI, and LVSWI) were calculated by means of a programmable calculator using the formulas shown in table 1. Each patient served as his own control.

In the CABG patients, 0.5 mg/kg nalbuphine was administered as a bolus through the CVP catheter, and all measurements were repeated after five minutes. This time interval was chosen for several reasons: 1) a rapid peak effect when given intravenously; 2) to simulate clinical anesthesia use; and 3) to avoid undue prolongation of the presurgical period. Additional increments of 0.5 mg/kg nalbuphine were administered to a total dose of 3 mg/kg with repeat measurements five minutes after each dose. Sedation levels were judged as follows in the CABG patients: level 1–patient awake and alert; level 2—patient sedated but arousable to vocal command; and level 3—patient asleep and unresponsive to vocal command but responsive to tactile stimuli.

As the use of an additional 1 mg/kg dose after administration of 2 mg/kg provided no further sedation (in the CABG patients), a total of only 2 mg/kg was given to the MVR patients. Patients for MVR received an initial bolus of 1 mg/kg with measurements after 5 minutes. An additional bolus of 1 mg/kg nalbuphine was then given and measurements repeated. Since the objective of the study in MVR patients was to produce anesthesia, no attempt was made to determine the sedative effects of nalbuphine in this group.

TABLE 1. Abbreviations

HR	= heart rate (beats/min)
SBP	= systolic arterial blood pressure (mmHg)
DBP	= diastolic arterial blood pressure (mmHg)
MAP	= mean arterial pressure (mmHg)
PAS	= pulmonary artery systolic pressure (mmHg)
PAD	= pulmonary artery diastolic pressure (mmHg)
MPAP	= mean pulmonary artery pressure (mmHg)
PCW	= pulmonary capillary wedge pressure (mmHg)
CVP	= central venous pressure (mmHg)
CO	= cardiac output (l/min)
BSA	= body surface area (m^2)
SV	= stroke volume (ml/min)
CI	= cardiac index ($l \cdot min^{-1} \cdot m^{-2}$)
SVR	= systemic vascular resistance ($dyn \cdot s \cdot cm^{-5}$)
SVRI	= systemic vascular resistance index ($dyn \cdot s \cdot cm^{-5} \cdot m^2$)
PVR	= pulmonary vascular resistance ($dyn \cdot s \cdot cm^{-5}$)
PVRI	= pulmonary vascular resistance index ($dyn \cdot s \cdot cm^{-5} \cdot m^2$)
RVSWI	= right ventricular stroke work index ($g \cdot m \cdot beat^{-1} \cdot m^{-2}$)
LVSWI	= left ventricular stroke work index ($g \cdot m \cdot beat^{-1} \cdot m^{-2}$)
SI	= stroke index ($ml \cdot beat^{-1} \cdot m^{-2}$)
RPP	= rate pressure product (beats/mmHg)

Formulas

$$CI = CO/BSA$$

$$SVR = \frac{MAP - CVP}{CO} \times 79.9$$

$$SVRI = SVR \times BSA$$

$$PVR = \frac{MPAP - PCW}{CO} \times 79.9$$

$$PVRI = PVR \times BSA$$

$$SWI = 0.0136\ (MAP - PCW) \times SI$$

The circulatory effects of nalbuphine in combination with halothane, diazepam, nitrous oxide, or after surgical stimulation also were determined. Since controlled myocardial depression with a potent inhalation anesthetic is desirable[14] in patients with CAD, halothane was administered to them. In patients with valvular disease, nitrous oxide with morphine or fentanyl frequently are chosen to avoid myocardial depression so nalbuphine was substituted for morphine or fentanyl. Following the administration of the incremental doses of nalbuphine and the hemodynamic measurements in the CABG patients, halothane in oxygen was added as required to induce unconsciousness as judged by the anesthesiologist in charge of the patient. No additional hemodynamic measurements were made during this period. In the MVR patients, diazepam up to 0.5 mg/kg was given slowly until patients lost consciousness and measurements repeated after two minutes. Nitrous oxide 50% in oxygen was then given and measurements repeated

TABLE 2. Cardiovascular Effects of Nalbuphine in Patients with Coronary Artery Disease

	Cardiac Index ($l \cdot min^{-1} \cdot m^{-2}$)	Heart Rate (beats/min)	MAP (mmHg)	RPP (beats · mmHg)	PCW (mmHg)	DBP (mmHg)	CVP (mmHg)	SVRI ($dyn \cdot s \cdot cm^{-5} \cdot m^2$)	PVRI ($dyn \cdot s \cdot cm^{-5} \cdot m^2$)	LVSWI ($g \cdot m \cdot beat^{-1} \cdot m^{-2}$)
Control	2.39 ± 0.09	54 ± 2.6	91 ± 4.8	7,848 ± 743	11 ± 1.1	66 ± 4.9	5 ± 0.7	2,922 ± 196	151 ± 24	48 ± 2
Nalbuphine										
0.5 mg/kg	2.37 ± 0.14	55 ± 2.4	89 ± 5.3	7,375 ± 655	12 ± 1.0	65 ± 4.9	6 ± 0.6	2,891 ± 217	168 ± 14	46 ± 3
3.0 mg/kg	2.44 ± 0.15	56 ± 3.1	98 ± 5.8	8,347 ± 911	13 ± 1.2	70 ± .5	6 ± 0.6	3,108 ± 230	171 ± 27	50 ± 3
Nalbuphine and Halothane										
2 min post-incision	1.89 ± 0.10*	64 ± 3.2*	115 ± 7.0*	10,210 ± 897*	17 ± 1.6*	90 ± 7.3*	9 ± 0.9*	4,602 ± 287*	248 ± 27	41 ± 4
2 min post-sternotomy	1.70 ± 0.11*	60 ± 2.4	98 ± 3.5	8,152 ± 545	12 ± 1.3	74 ± 4.3	7 ± 0.8	4,474 ± 347*	258 ± 62	33 ± 2*
5 min prebypass	2.15 ± 0.16	72 ± 3.3*	85 ± 4.3	8,554 ± 594	13 ± 1.1	68 ± 4.5	7 ± 0.9	3,105 ± 262	195 ± 44	31 ± 3*

Values are means ± SEM, n = 14. Statistical analysis by analysis of co-variance and Duncan's multiple range test.

* $P < 0.05$ compared with control.

in two minutes. Ventilation was controlled at any time it was necessary to maintain minute ventilation and Pa_{CO_2} near control. Metocurine, 0.3 mg/kg, was given intravenously to facilitate endotracheal intubation. Additional hemodynamic measurements were obtained at two minutes following skin incision, two minutes following sternotomy, and at the time of aortic cannulation for cardiopulmonary bypass in both CABG and MVR groups. End-tidal halothane was recorded at each time using a Beckman® LB-2 analyzer to assess the concentration of halothane required for surgical anesthesia in CABG patients.

Analysis of data for each patient group was performed by analysis of covariance using a general linear modeling procedure[5,6] and by Duncan's multiple range test,[7] comparing each of the variables with control. A P value of 0.05 or less was considered significant. A two-way linear regression was performed to determine the relationship of cardiovascular variables to different halothane concentrations using a Hewlett-Packard® 9810A calculator and STAT-PAC® III-1.

Results

PATIENTS WITH CORONARY DISEASE

All patients were awake and alert at the beginning of the study. The sedation associated with the administration of nalbuphine was quite variable. Six of the fourteen CABG patients were awake or arousable at each dose, but four of the fourteen became unconscious, unarousable to verbal command, but responsive to painful stimuli. Four other patients were unarousable at lower doses (0.5–2.0 mg/kg) but awoke by the time additional doses (1.5–2.5 mg/kg) of nalbuphine had been given. No patient was anesthetized by nalbuphine alone.

Cardiovascular variables remained stable throughout the preoperative period (table 2) in the CABG patients. There was no relation between nalbuphine dose and any cardiovascular variable; therefore, only the 0.5 and 3.0 mg/kg measurements are tabulated. Arterial blood gases also were unaffected by the administration of nalbuphine during spontaneous ventilation with 100% oxygen (table 3). An apparent large alveolar-arterial oxygen gradient was present which may reflect poor fit of the face mask prior to intubation. Ventilatory assistance was not required until metocurine was given. The inspired concentrations of halothane necessary to induce anesthesia following administration of nalbuphine varied from 0.2–1.5%. A significant rise in Pa_{O_2} and a significant drop in Pa_{CO_2} occurred, however, following the use of controlled ventilation at an FI_{O_2} of 1.0 via an endotracheal tube and the start of surgical stimulation.

Following skin incision, there was a significant decrease in CI and increases in HR, SBP, MAP, DBP, CVP, RPP, and SVRI. PCW, PAS, and PAD increased significantly. At two minutes after sternotomy, SWI was depressed and CI remained decreased while SVRI remained increased. Mean end-tidal halothane concentration at two minutes post-skin incision was 0.63% ± 0.23 (SD) indicating great variability among patients. A similar halothane concentration was found at two minutes post-sternotomy, but it had been decreased significantly to 0.36% ± 0.23 (SD) at the time of aortic cannulation as this concentration appeared adequate clinically. There was no correlation between the concentration of halothane and MAP, CI, SVRI, or SWI. All cardiovascular variables tended to return to control levels prior to cardiopulmonary bypass, except for heart rate, which remained significantly increased and stroke work index, which remained significantly decreased.

Patients with Valvular Disease

In patients with MVR, cardiovascular variables remained stable prior to surgical stimulation, except for a small but significant decrease in MAP after diazepam and nitrous oxide were added (table 4). Doses of diazepam required for unconsciousness varied from 0.08–0.41 mg/kg. LVSWI also decreased significantly after the addition of nitrous oxide. Following skin incision, significant increases in MAP and SVRI with a decrease in LVSWI and CI were noticed. The changes in CI and SVRI continued during sternotomy. PVRI increased following sternotomy. At five minutes prior to bypass, CI and LVSWI still were decreased and SVRI remained increased. Although one patient became diaphoretic after skin incision, no other signs of light anesthesia were recorded. One patient received sodium nitroprusside 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ one received halothane 0.2–0.4% inspired concentration, and one patient required both halothane or nitroprusside for control of systemic arterial hypertension or diaphoresis. Unlike the CABG patients, the MVR patients developed significant increases in Pa_{CO_2} after 1 mg/kg nalbuphine, but these changes were not worsened by the addition of either diazepam or nitrous oxide (table 5) and ventilatory assistance was not required until metocurine was given. Endotracheal intubation and controlled ventilation decreased Pa_{CO_2}. The Pa_{O_2} increased after nalbuphine and remained elevated when diazepam was added, probably due to better mask fit in a more sedated patient.

TABLE 3. Respiratory Effects of Nalbuphine in Patients with Coronary Artery Disease

	pH	Pa_{CO_2} (mmHg)	Pa_{O_2} (mmHg)
Control	7.39 ± 0.01	44 ± 1.1	245 ± 18
Nalbuphine— Spontaneous ventilation			
0.5 mg/kg	7.38 ± 0.01	45 ± 1.2	256 ± 17
3.0 mg/kg	7.38 ± 0.00	44 ± 1.1	297 ± 19
Nalbuphine and halothane with controlled ventilation via endotracheal tube			
2 min post-incision	7.50 ± 0.01*	33 ± 1.7*	338 ± 16*
2 min post-sternotomy	7.52 ± 0.02*	31 ± 2*	311 ± 23*
5 min prebypass	7.51 ± 0.01*	31 ± 1.3*	336 ± 19*

Values are means ± SEM, n = 14.
Statistical analysis by analysis of co-variance and Duncan's multiple range test.
* $P < 0.05$, compared with control.

TABLE 4. Cardiovascular Effects of Nalbuphine in Patients with Valvular Heart Disease

	Cardiac Index ($l \cdot min^{-1} \cdot m^{-2}$)	Heart Rate (beats/min)	MAP (mmHg)	PAD (mmHg)	CVP (mmHg)	LVSWI ($g \cdot m \cdot beat^{-1} \cdot m^{-2}$)	RVSWI ($g \cdot m \cdot beat^{-1} \cdot m^{-2}$)	SVRI ($dyn \cdot s \cdot cm^{-5} \cdot m^2$)	PVRI ($dyn \cdot s \cdot cm^{-5} \cdot m^2$)
Control	2.24 ± 0.22	76 ± 8.3	90 ± 4.9	19 ± 3.8	8 ± 1.6	30.9 ± 5.9	7.8 ± 1.3	3,134 ± 465	421 ± 37
Nalbuphine 1 mg/kg	2.24 ± 0.19	69 ± 6.3	87 ± 5.1	19 ± 2.8	10 ± 1.6	31.0 ± 4.3	8.4 ± 1.2	2,915 ± 432	378 ± 51
Nalbuphine 2 mg/kg	2.24 ± 0.21	67 ± 6.1	83 ± 4.8	18 ± 3.2	10 ± 1.7	31.0 ± 5.6	8.5 ± 2.0	2,828 ± 431	406 ± 63
Diazepam	2.19 ± 0.23	67 ± 3.8	79 ± 3.7*	19 ± 3.0	8 ± 1.8	27.4 ± 4.9	8.4 ± 1.8	2,754 ± 353	325 ± 47
Nitrous oxide	2.07 ± 0.15	66 ± 4.4	74 ± 3.5*	18 ± 2.4	8 ± 1.9	24.5 ± 3.5*	7.5 ± 1.3	2,649 ± 294	318 ± 38
2 min post-incision	1.61 ± 0.14*	66 ± 3.8	95 ± 4.0	22 ± 4.0	12 ± 2.3	24.5 ± 2.9*	11.0 ± 3.6	4,351 ± 476*	476 ± 84
2 min post-sternotomy	1.54 ± 0.14*	68 ± 3.7	93 ± 3.8	19 ± 3.6	11 ± 2.0	21.9 ± 2.7*	5.0 ± 1.1	4,960 ± 780*	579 ± 102
5 min prebypass	1.74 ± 0.21*	71 ± 6.5	90 ± 5.2	21 ± 2.9	10.3 ± 2.3	23.6 ± 2.5*	6.5 ± 1.5	4,005 ± 543*	442 ± 74

Values are means ± SEM, n = 7. Statistical analysis by analysis of co-variance compared with control.
* $P < 0.05$.

TABLE 5. Respiratory Effects of Nalbuphine in Patients with Valvular Heart Disease

	*p*H	Pa_{CO_2} (mmHg)	Pa_{O_2} (mmHg)
Spontaneous ventilation			
Control	7.41 ± 0.01	42 ± 1.2	233 ± 27
Nalbuphine 1 mg/kg	7.38 ± 0.01	46 ± 1.6*	307 ± 30*
Nalbuphine 2 mg/kg	7.38 ± 0.01	44 ± 0.8	350 ± 29*
Diazepam	7.38 ± 0.01	45 ± 1.7*	374 ± 26*
Nitrous oxide	7.37 ± 0.01	46 ± 1.2*	259 ± 17
Controlled ventilation via endotracheal tube			
2 min post-incision	7.52 ± 0.02*	30 ± 1.2*	185 ± 20
2 min post-sternotomy	7.53 ± 0.02*	31 ± 1.5*	188 ± 15
5 min prebypass	7.49 ± 0.02*	31 ± 1.1*	199 ± 8

Values are means ± SEM, n = 7. Statistical analysis by analysis of co-variance.

* $P < 0.05$.

Discussion

This study documents the absence of any deleterious hemodynamic changes associated with the acute administration of large doses of intravenous nalbuphine in humans. Previous workers had shown by non-invasive measurements of the circulation that nalbuphine in doses of up to 3 mg/kg is well-tolerated.†† Romagnoli and Keats‡‡ found that 10 mg nalbuphine intravenously, caused no significant changes in heart rate, right atrial pressure, pulmonary artery systolic, mean, diastolic, or wedge pressures, left ventricular end-diastolic pressure, aortic systolic, diastolic or mean pressures, pulmonary or systemic vascular resistance, cardiac index, left ventricular work index, or tension-time index in patients with coronary artery disease. In patients with acute myocardial infarction, the administration of 10 mg nalbuphine intravenously caused significant decreases in heart rate, cardiac index, and mean velocity of circumferential fiber shortening in left ventricle, but without changes in systemic arterial pressures.[8]

Morphine and fentanyl, narcotic agonists commonly used in anesthesia, are not devoid of undesirable circulatory and respiratory effects. As previously reported,[1] respiratory depression induced by nalbuphine did not increase beyond that noticed following premedication with 0.1 mg/kg, even at the 3 mg/kg dose. If nalbuphine alone provided adequate surgical anesthesia, this would be a particularly important finding when early extubation is desired following open heart surgery. With morphine[9] and fentany,[10] profound respiratory depression occurs for a prolonged period of time postoperatively, preventing early extubation. These drugs also produce rigidity of the chest wall musculature requiring small pre-induction doses of muscle relaxant for prevention. This phenomenon, not seen with nalbuphine at low or high doses, obviates the need for early administration of neuromuscular blocking agents.

In a group of patients similar to those in this study, Lappas *et al.*[11] noticed small decreases in SAP, HR, CI, and SW after 0.5 mg/kg morphine intravenously. Left and right heart filling pressures increased significantly after 2 mg/kg morphine as a result of a change in pattern of respiration to positive pressure ventilation. Likewise, 25 μg/kg fentanyl given intravenously to patients with coronary artery disease produced small, but significant decreases in MAP, MPAP, PCW, PVR, and SVR.[12] Nalbuphine produces none of these changes. While both morphine and fentanyl may decrease myocardial oxygen demand, decreases in systemic arterial pressures produced by their administration may decrease myocardial oxygen supply. Nalbuphine does not appear to affect myocardial oxygen balance adversely, since neither arterial diastolic pressure nor rate-pressure product changed significantly.

Other narcotic agonist-antagonist drugs cause detrimental cardiovascular changes in patients with coronary artery disease. Pentazocine increased SBP, DBP, MAP, PAS, PAD, MPAP, PCW, and SVR in patients during acute myocardial infarction.[13] Butorphanol increased CI and MPAP after only a single intravenous dose in healthy humans or patients with coronary disease.[14] These effects are not seen with nalbuphine.

The effects of narcotic anesthesia given to patients with valvular disease are generally favorable. Morphine decreases systemic vascular resistance and increases cardiac output.[2] In a group of MVR patients, Stanley and Webster noticed decreased MAP and HR after 20 μg/kg fentanyl, iv, without changes in CO, SVR, SV, or CVP.[15] The addition of diazepam and nitrous oxide to fentanyl or morphine produced significant cardiovascular depression.[15-17] Neither the addition of diazepam nor nitrous oxide to nalbuphine in our MVR patients produced clinically significant changes in cardiovascular variables, although MAP did decrease significantly (statistically) after addition of diazepam and nitrous oxide, while LVSWI decreased after nitrous oxide was given.

Unfortunately, nalbuphine alone is inadequate for surgical anesthesia. All patients required and received halothane (CABG) or diazepam (MVR) to induce unconsciousness. The observation of decreased sedation at doses of 1.5–2.5 mg/kg in some CABG patients may represent a manifestation of the antagonist properties of nalbuphine. Despite an increase in HR, MAP, PCW, and SVRI, and a decrease in CI with skin incision, isch-

†† Magruder MR, Christoforetti R, DiFazio CA: Balanced anesthesia with nalbuphine hydrochloride. Anesthesiol Rev 7:25–29, 1980.

‡‡ Romagnoli A, Keats AS: Comparative hemodynamic effects of morphine and nalbuphine in patients with coronary artery disease. Bull Texas Heart Inst 5:19–24, 1978.

emic changes were not seen on the EKG of the CABG patients. The fall in CI in the CABG patients may be the result of the known depressant effect of halothane alone,[18] its combination with nalbuphine, or the marked increase in systemic vascular resistance. Since the effects of halothane and nalbuphine in the absence of surgical stimulation were not investigated in this study, we can only speculate as to which of these results occurs. In patients with valvular disease, it is most likely to be the result of increased afterload.

Nalbuphine is definitely not a substitute for morphine or fentanyl as a primary anesthetic. However, in situations where an agonist-antagonist may be preferable, as in acute myocardial infarction,[8] during cardiac catheterization, and in patients with valvular heart disease or congestive failure, nalbuphine provides analgesia with sedation with no adverse hemodynamic or respiratory responses.

In summary, nalbuphine, while inadequate as the sole anesthetic in patients with cardiac disease, is devoid of deleterious hemodynamic or respiratory effects, and may be advantageous with diazepam and nitrous oxide as an induction agent in cardiac anesthesia.

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