Anaesthetic Techniques

Epidural morphine reduces the riskof post-operative myocardial ischaemia in patients with cardiac risk factors

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Perioperative myocardial ischaemia is a predictor of postoperative cardiac morbidity (PCM). Epidural anaesthesia and adequate perioperative analgesia have been shown to improve myocardial oxygen dynamics due to interruption of pain and sympathetic pathways. The aim of the present study was to compare the incidence of ischaemia after either general anaesthesia followed by parenteral analgesia with morphine or combined epidural/general anaesthesia followed by analgesia with epidural morphine. In a prospective observer-blinded analysis of the occurrence of ischaemia, 55 patients (epidural = 29/ parenteral = 26) scheduled for elective surgery with defined risks for ischaemic cardiac disease were entered and followed for 24 hr after surgery with two-lead continuous Holter monitoring. Groups were similar with respect to age, weight, modified Goldman (Detsky) risk classification and the use of cardiac medications. Fewer patients receiving the epidural anaesthesia/ analgesia had ischaemic episodes (17.2 vs 50.0%, $P = 0.01$), and tachyarrhythmias (20.7 vs 50.0%, $P < 0.05$). Epidural patients had a four-fold reduction of the relative risk for either event ($P < 0.001$). All ischaemic events were asymptomatic and unrecognized (silent). All major morbid events ($n = 5$) (MI, congestive heart failure and death) occurred in patients who had perioperative episodes of ischaemia. There were three distinct peaks in onset of ischaemia, at 1–4 hr, 9–12 hr and 22–24 hr postoperatively. One third of postoperative ischaemic events occurred within the first four hours after operation and lasted from 1 to 31 min. Forty-two percent of ischaemic episodes were associated with a heart rate > 100 bpm, or an increase of 20% over the baseline heart rate. We conclude that epidural anaesthesia/analgesia reduces but does not eliminate the risk of myocardial ischaemia and tachyarrhythmia. We were unable to determine any associated reduction in the risk of PCM.

L'ischémie myocardique périopératoire a une bonne valeur pronostique sur la morbidité cardiaque postopératoire (MCP). Il a été démontré que l'anesthésie et l'analgésie post-opératoire épidurales favorisaient l'oxygénation myocardique par interruption des voies de conductions algiques et sympathiques. L'objectif de la présente étude est de comparer l'incidence de l'ischémie après l'anesthésie générale suivie d'analgésie parentérale à la morphine à l'association anesthésie générale-épidurale suivie d'analgésie à la morphine épidurale. Sont inclus dans cette étude prospective, à l'insu de l'observateur, 55 patients (29 dans le group épidural, 26 dans le groupe parentéral) programmés pour une chirurgie réglée et présentant des risques définis de maladie cardiaque ischémique. Les patients sont monitorés continuellement pendant 24 heures après la chirurgie avec un Holter à deux dérivations. Il n'y a pas de différence entre les deux groupes pour l'âge, le poids, l'échelle de risque de Goldman (Detsky) et la médication cardiaque. Moins de patients du groupe anesthésie générale-épidurale souffrent d'épisodes ischémiques (17,2 vs 50%, $P = 0,01$), et de tachyarythmies (20,7 vs 50%, $P < 0,05$). Les patients du groupe épidural courent un risque quatre fois moins élevé de souffrir de l'une ou de l'autre complication ($P < 0,001$). Tous les épisodes ischémiques ont été asymptomatiques et sont passés inaperçus. Toutes les complications ($n = 5$) (infarctus du myocarde, défaillance cardiaque et décès) sont survenus chez des patients qui avaient présenté de l'ischémie périopératoire. On a identifié trois pointes d'incidence ischémiques postopératoires: à 1–4 hres, 9–12 hres et 22–24 hres. Un tiers des épisodes ischémiques est survenu en-deçà de quatre heures après l'opération et a duré de 1 à 31 min. Quarante-deux pourcent de ces épisodes étaient associés à une fréquence de plus de cent $b \cdot min^{-1}$ ou à une augmentation de 20% du niveau de base. Nous concluons que l'a-

Key words
ANALGESIA: postoperative, epidural;
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nesthésie/analgésie épidurale diminue mais n'élimine pas le risque d'ischémie cardiaque et de tachyarythmies. Nous n'avons pas démontré une réduction associée de la MCP.

Perioperative myocardial infarction (PMI) is an important cause of serious morbidity and mortality associated with anaesthesia and major surgery.[1] Approximately 12% of patients having non-cardiac surgery have demonstrated coronary artery disease (CAD), and 1.1% of these patients with CAD who are at risk will develop PMI. It is likely that PMI could account for at least half of all serious perioperative morbidity.[2]

Previous studies to identify predictors of postoperative morbidity suggested that ischaemia,[3–7] congestive heart failure[8,9] and other major cardiovascular events, such as arrhythmias that were present preoperatively, were indicators of patients at risk of major postoperative morbidity.

A great deal of perioperative care is driven by the hypothesis that prevention of ischaemia may reduce the incidence of serious morbidity, such as PMI. The entire perioperative period is stressful, characterized by complex autonomic,[10] hormonal[11] and physiological[12] perturbations. The response to surgical stress and pain is characterized by increased catabolism and sympathetic activity.[13] Sympathetic activation has been linked to myocardial ischaemia[14–16] and infarction, and is probably related to changes in myocardial oxygen supply and demand. Modulation of the sympathetic response reduces the incidence of myocardial ischaemia and infarction.[17–22] Blockade of the sympathetic nerves in the upper thoracic segments is possible with controlled use of epidural local anaesthesia and favourably alters myocardial oxygen supply and demand,[23,24] but is associated with a lowering of blood pressure. The perioperative stress response can also be affected by the use of epidural opiates, which attenuate the sympathetic response.[25] Since a major stimulus for the sympathetic stress response is pain, we speculate that effective control of pain could result in attenuation of the stress response.

The present study was done to compare the effects of intraoperative and postoperative epidural analgesia with parenteral morphine sulphate in patients with two or more risk factors for myocardial ischaemia sequelae. Patients were observed during the first 24 hr after surgery.

Methods

This is a prospective comparison of two methods of anaesthesia and analgesia on perioperative myocardial ischaemia and morbidity. Patients booked for elective major intra-abdominal, vascular or orthopaedic total joint surgery were eligible for study. Preoperative evaluation for coronary risk was done on all patients who were entered sequentially into the study. Allocation to anaesthesia/analgesia groups was according to the practice of the attending anaesthetist. This study was approved by the Research Advisory Group of Chedoke-McMaster Hospitals and all patients gave informed consent.

Evaluation of patient risk

Each patient was seen preoperatively by an anaesthetist and a history of myocardial infarction, congestive heart failure, arrhythmia and the use of concurrent medications was noted. An ECG, chest *x*-ray and spirometry were performed on each patient preoperatively and a modified Goldman (Detsky)[9] risk classification assigned. Usual preoperative medications (beta-blockers, calcium channel blockers or nitrates) were continued. No patients in this study received platelet inhibitory drugs.

Patients who had any two of the following risk factors for coronary artery disease (CAD) were eligible for entry into the study: high blood pressure, diabetes mellitus, chest pain on exertion, hyperlipidaemia, smoking, age greater than 70 years, or a positive family history of coronary artery disease. A positive history for angina is defined as typical anterior chest pain on exertion that is relieved by rest. A positive history for myocardial infarction is a documented ECG change with enzyme changes. Patients could also be entered if they had a myocardial infarction more than six months before surgery. No other factors were considered as entry criteria. Patients were excluded if they had: unstable angina pectoris, myocardial infarction within the past six months, bundle branch block, or were taking digitalis glycosides.

Anaesthesia

Patients were brought into the OR unpremedicated with an intravenous infusion of normal saline. The decision to use epidural anaesthesia was made by the attending anaesthetist and depended partly on the availability of suitable ward beds and individual practice. An epidural catheter was placed in a lumbar segment (usually $L_{3/4}$) and advanced to between 10 and 20 cm at the skin (i.e., 5 to 10 cm into the epidural space). Patients received a test dose of 4 ml, lidocaine 2% to confirm placement of the epidural catheter, then received epidural morphine in a dose of 0.1 $mg \cdot kg^{-1}$ followed by a further dose of lidocaine 2% (0.1–0.3 $ml \cdot kg^{-1}$) prior to the induction of anaesthesia. Sodium thiopentone (2–5 $mg \cdot kg^{-1}$) was used in all patients for induction of anaesthesia which was maintained with isoflurane up to 2%, nitrous oxide 70%, oxygen 30%, and either atracurium or vecuronium provided muscle relaxation. All patients were monitored intraoperatively for blood pressure, ECG, oxygen saturation, temperature, end-tidal carbon dioxide, and the

end-tidal inhalational agent. Ventilation was adjusted to maintain $P_{ET}CO_2$ between 36 and 44 mmHg. Temperature was maintained with warming blankets and warmed intravenous fluids. Oxygen saturation was maintained greater than 90%. Intravenous narcotics were avoided in the epidural group as this combination is associated with postoperative respiratory depression. However, the parenteral analgesic group received intraoperative sufentanil (1 $\mu g \cdot kg^{-1}$) or an equivalent dose of opioid.

Blood pressure and heart rate were controlled throughout the procedure. Heart rate was not allowed to increase above 90 bpm, by adjustment of the depth of anaesthesia, and/or use of beta-blockers. Blood pressure was maintained above a mean pressure of 70 mmHg with fluid administration or with the use of *iv* ephedrine in titrated doses of 5 mg.

Pain management

Patients who had epidural anaesthesia had this continued into the postoperative period for pain control. Each patient was commenced with epidural morphine 0.1 $mg \cdot kg^{-1}$ twelve-hourly and assessed by the attending consultant for the acute pain management service twice daily. The dose of morphine was adjusted to maintain a visual analogue pain score (VAS) of two or less on a ten point scale.

Patients who had general anaesthesia and parenteral morphine for postoperative analgesia were also followed by the attending consultant for the acute pain service. Adjustment to the dose and frequency of *iv* morphine was made after pain assessment, utilizing a VAS rating. A VAS of better than 2/10 was sought. While we were aiming for equipotent analgesia in both groups, this was not achieved. Patients with PCA analgesia accepted higher pain scores (VAS 2–5) and appeared to balance pain against specific side effects (nausea, vomiting, pruritus, and drowsiness).

ECG recording

Continuous Holter monitoring was started in the post-anaesthetic care unit (PACU) after reversal of anaesthesia and was continued for 24 hr; blood pressure and heart rate were recorded by the nursing staff at least every 30 min in the PACU, then every four hours, as per the epidural monitoring routine in our institution. Holter monitoring of the ECG used a "Cardio Data" cassette recorder system (Marlborough, Mass) and ST segment changes were analyzed with detection software (CARDIODATA MK IV) developed for this purpose. The technician and physician assessing the ECG were blinded to the pain treatment group and patient history. An ischaemic episode was defined as an ST segment depression on the ECG equal to 1 mm or greater, lasting one minute or more, occurring at least 80 msec after the J point. After an episode of ST segment depression, the baseline ST pattern was required to be stable for at least five minutes before a further event of ST segment depression was identified. Variables evaluated included heart rate, the number of supraventricular beats, ventricular arrhythmias and ectopic beats, and ischaemic episodes; the magnitude and duration of ST segment depression were recorded. The heart rate at the onset of ST segment depression and any symptoms reported by the patients were recorded. Twelve-lead ECG and cardiac enzymes were obtained and recorded if there was a clinical indication but were not routinely obtained.

Major morbid events were defined as a new onset of chest pain, shortness of breath or tachyarrhythmia, which required admission to an acute care unit; congestive heart failure; myocardial infarction or death.

TABLE I Patient characteristics

	Epidural morphine n = 29	*Parenteral morphine n = 26*
Age yr (range)	69.5 (53–88)	70.1 (49–90)
Weight kg (range)	79.6 (61–90)	84.3 (62–98)
History of ischaemia*	7 (24.1%)	7 (26.9%)
Previous MI*	3 (10.3%)	3 (11.5%)
Anti-anginal medication*	10 (34.4%)	9 (34.6%)
Median Detsky score (range)	10 (5–25)	10 (5–30)
– 0–15	25	22
– 15–30	2	2
– >30	2	2
Type of surgery		
– Orthopaedic	3	7
– Abdominal	8	6
– Vascular	18	13
Post-op ventilation	1	3

*Number of patients (%).

Statistics

Mean values for the two treatment groups were analyzed by a two-tailed unpaired t test, employing a Wilcoxon's rank test, as appropriate. Haemodynamic data were compared using analysis of variance. Categorical data were compared by Chi square test. Analysis of the frequency of ischaemic episodes used a Wilcoxon's non-paired rank test. Results were considered significant if $P \leq 0.05$.

Results

There was no difference in the preoperative demographics of the two patient populations (Table I). Patients were the same age, the same number were receiving antianginal medications in both groups. The two populations did not differ in the number of previous myocardial infarctions

TABLE II Percent incidence of cardiac events

	Epidural morphine n = 29	*Parenteral morphine n = 26*	χ^2	*P*
No. of patients Ischaemia	5 (17.2)	13 (50)	6.68	0.01
No. of episodes Ventricular tachycardia	6 (20.7)	13 (50)	5.21	<0.05
Either event	7 (24.1)	20 (76.9)	13.47	<0.001
Major morbid event*	3 (10.3)	2 (7.6)	0.08	NS

*A major morbid event was defined as documented, new MI, ischaemic, congestive heart failure, arrhythmia necessitating intensive care admission, or death.

TABLE III Characteristics of ischaemic episodes (Mean range)

	Epidural morphine n = 29	*Parenteral morphine n = 26*	
Total monitored (time hr)	687	626	NS
Number of episodes	12*	25	$P < 0.05$
Total ischaemic time (min)	136	262	$P < 0.01$
Mean duration	10.46 (1–28.5)	10.48 (1–31)	NS
Mean ST depression (mm)	2.11 (1.3–3.63)	1.89 (1.0–5.2)	NS
Onset HR	105.7 (63–145)	89.5 (54–144)	NS
No. episodes associated with tachycardia†	7	9	NS
Mean time of onset‡	11.00 (2–23)	10.00 (0.30–23)	NS

*One patient manifested seven episodes of ischaemia in the first 24 hr postoperatively.
†Defined as onset heart rate above 100 bpm or an increase of more than 20% above the 24 hr mean heart rate.
‡See circadian data, Figure 2.
42% of ischaemic episodes are associated with tachycardia.

and they did not differ with respect to their preoperative risk classification (Goldman/Detsky). In three patients in the parenteral group and in one of the epidural group, the trachea remained intubated after surgery. All patients entered, completed the study.

This report comprises 55 patients monitored for a total of 1313 hr. Thirty-seven episodes of ST depressions were seen in 18 patients. Five patients in the epidural group had ST depression, while 13 patients in the parenteral group had ST depression ($\chi^2 = 5.49$ $P < 0.02$). The total ischaemic time was 398 min, or 0.49% of the monitored time. Five patients with ischaemic events went on to experience major postoperative morbid events. No morbid events were seen in patients who did not have ST depression ($\chi^2 = 8.15$, $P < 0.01$).

Table II shows the incidence of cardiac events in each group. Ischaemia and ventricular tachycardia, alone or together, were more common in the patients who received parenteral morphine compared to those who received epidural morphine ($P < 0.001$). A major morbid event was defined as MI, ischaemic heart failure, serious uncontrolled arrhythmia necessitating admission to an acute care unit or death. No difference between the analgesia groups was found for major morbidity.

The overall risk of ischaemia was four times higher (odds ratio = 4.0) in the patients receiving parenteral morphine. The risk of ventricular tachycardia was three times higher (odds ratio = 3.0) in patients who had parenteral morphine. The risk of either of these cardiac events was also higher in the parenteral morphine group (odds ratio = 3.6).

Table III illustrates and compares the characteristics of the 37 ischaemic episodes noted in this study. The number of episodes in the epidural group was less than half the number seen with parenteral narcotics. A similar reduction was seen in the total duration of ischaemia between the two groups. There was no difference in the mean duration of ischaemia. Episodes ranged from 1 to 31 min in both groups. The degree of ST depression was similar for both groups ranging from 1 mm to 5.0 mm. The epidural patients had less change in the mean hourly heart rate than the group receiving parenteral narcotics. However, the mean heart rates at the onset of ischaemia were not different. The frequency of ischaemia associated with tachycardia did not differ. Forty-two percent of the ischaemic events were associated with a heart rate of greater than 100, or an increase of more than 20% of the mean 24 hr heart rate.

Mean hourly heart rates were not different immediately after surgery and for the first four postoperative hours (Figure 1). At hour five until 19 hrs there is a steadily increasing difference in the heart rates, the parenteral analgesic group having the greater heart rates (ANOVA $P < 0.01$). Apart from ensuring that BP was within the clinically acceptable limits, it was not further analyzed.

The timing of the ischaemic events is illustrated in Figure 2. Panel A shows the peak onset between 0900 and 1600 hr with more than 60% of episodes occurring in this period. Since this represents the peak OR times, the relationship between the end of the operation and onset of ischaemia was gleaned. Panel C shows that 65% of the ischaemia in the epidural group occurred in the first four hours postoperatively while 35% of the ischaemia in the parenteral group occurred in this time frame ($P < 0.05$). Secondary peaks emerge for both groups around 9–14 hr and 22–24 hr postoperatively. Panel B shows the timing of the onset of ischaemia when the immediate

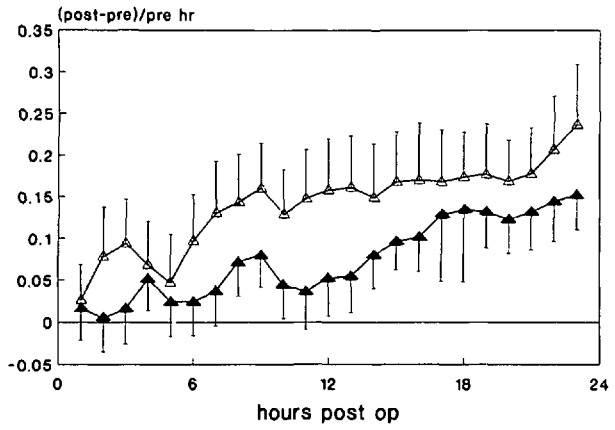

FIGURE 1 Comparison of mean hourly heart rates (Δ represents parenteral patients, Δ represents epidural patient). The heart rates are expressed as the percent change from the baseline value (mean ± SD). There was no difference between groups and the baseline heart rate. There is no statistical difference between mean hourly heart rates for the first five hours. From that point on the mean difference in hourly heart rate is statistically different (ANOVA).

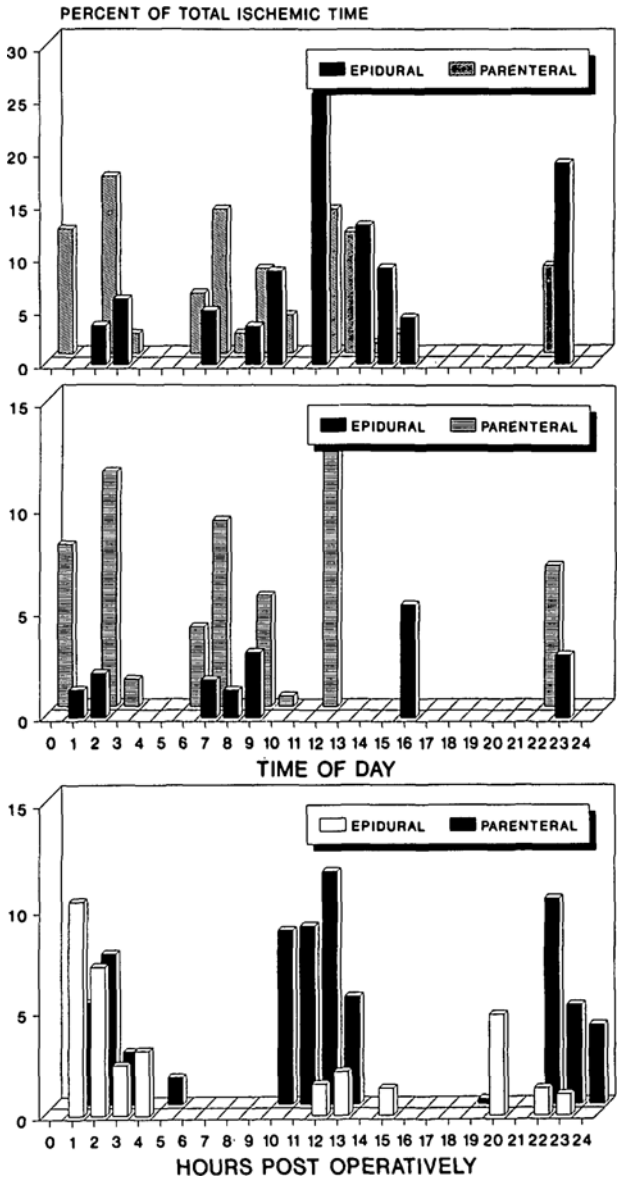

FIGURE 2 Incidence and timing of postoperative ischaemia. Panel A: Compares the incidence of ischaemia event by time of day; note the predominance of events from 0900–1600 hrs. Panel B: Examines the data after the immediate post op (hours 1–4) are eliminated. There is a predominance of ischaemia in the first four hours postoperatively (see panel C). This ischaemia is different from the ST depression which occurred later postoperatively. The ST depression occurs at a higher heart rate. This analysis was performed to see if there was any underlying rhythm to the onset of postoperative ischaemia. Panel C: Examines the same data; however, the time is changed to reflect the hours postoperatively. Three distinct peaks emerge; 0–4 hrs, 9–13 hrs, 22–24 hrs.

postoperative ischaemic episodes are excluded from analysis. Fifty percent of all remaining episodes occurred between the hours of 0600 and 1200. A secondary peak emerges between 2300–0300 hr.

Seventy-five percent of the ischaemia noted in the PACU was associated with a heart rate >100 bpm or a rise of greater than 20% over the baseline level. Thirty-four percent of the ischaemia after the sixth postoperative hour was noted to be associated with a similar change in heart rate ($\chi^2 = 3.12$, $P > 0.05$). The heart rates at the onset of ischaemia in the PACU were higher than the heart rates of the ischaemic events occurring at all other times. When the PACU ischaemic events are excluded from analysis, 25 episodes remain. Seven episodes occurred in three patients who had epidurals, and 18 episodes in nine patients receiving parenteral narcotics ($\chi^2 = 4.29$; $P < 0.02$).

All patients with morbid events manifested postoperative ST changes consistent with ischaemia, Table IV. There were three deaths. It is speculated patient one died on day ten of a pulmonary embolism. Four of the five patients had a documented previous myocardial infarction. Three of the five patients had a history of congestive heart failure. Two of the three deaths occurred in patients with a history of congestive heart failure. There was no difference between groups with respect to morbidity.

Discussion

We found a three-fold higher risk of ventricular tachycardia and a four-fold higher risk of myocardial ischaemia in patients who had *iv* morphine than in those who had epidural morphine for postoperative pain control. Moreover, the average heart rate was lower in patients who

TABLE IV Characteristics of morbid events

Patient	*Morbid event*	*Periop ischaemia*	*Risk factors (preop assess)*	*Medications*
1 Epidural total hip (died found in bed day 10)	Death ? PE	2 Episodes 1 Episode VT	Old MI Congestive failure	Captopril Nitrates Diuretic
2 Epidural aorto-bifem (failure day 4 discharge day 22)	Ischaemic failure No MI	1 Episode	Age 75 Hypertension	Dyazide
3 Epidural abdo aortic aneurysm (VF day 6, died day 8)	Death	7 Episodes	Old MI Congestive failures COPD	Captopril Lasix Prednisone Ventolin
4 Parenteral abdo aortic aneurysm (acute AMI 12 hr postop)	Death MI Asystolic arrest	1 Episode (2 hr) Arrest 12 hr	Angina Old MI Age	Nifedipine Nitrates
5 Parenteral total knee (failure day 3)	MI day 3	2 Episodes	Previous MI	Nil

received epidural morphine during the entire 24-hr period of continuous monitoring. Postoperative myocardial ischaemia is common, is usually asymptomatic, and is considered to be a reliable predictor of major morbidity, such as myocardial infarction. In this study, no morbid events occurred in patients who did not have ischaemia. This is consistent with the results of previous studies[6,7,26] which found ST segment depression to be a powerful risk indicator.

Transient episodes of silent ischaemia are common in patients with coronary artery disease. The triggering mechanism is unknown. Increased sympathetic activity, however, appears to be crucial. Two possible mechanisms of ischaemia with increases in sympathetic activity have been suggested: (a) episodic tachycardia and hypertension-induced fluctuations in myocardial oxygen dynamics and (b) episodic coronary microembolism or coronary artery spasm. Previous studies showed that the frequency of ischaemic episodes associated with haemodynamic abnormalities[27-30] ranges from 25 to 50%. The remaining ischaemia may relate to transient changes in coronary blood flow. Reversal of ischaemia with platelet deaggregation may be clinically important.[31-33]

This study also identified many similarities to ambulatory ischaemia. There was a predominance of ischaemia in the first four hours after emergence from anaesthesia, similar to the first hours of waking in the ambulatory patient.[15] The remainder of ischaemia showed a preponderance for the early morning hours. Ischaemia was predominantly silent. Finally, the bulk of ischaemia occurred with very few changes in heart rate.

The ischaemic episodes seen in this study were similar to those reported by others. The frequency, timing, and onset were similar to those seen in postoperative open heart patients.[26] The ischaemia appeared to occur predominantly at low HR and the major morbid events occurred in patients with postoperative ST depression.

Mechanism of action

The postoperative setting provides a myriad of factors which may alter the supply/demand ratio for an already compromised coronary circulation. Postoperative stresses include pain, anxiety, hypercarbia, hypoxia, medication withdrawal (notably beta-blockers and ASA) and sympathetic/parasympathetic imbalance. In this study patients receiving epidural analgesia had lower heart rates during the first 24 hr suggesting a sympatholytic effect. However, more than 50% of the patients in this study who had ischaemia did so with relatively small changes in heart rate. Similarly, ambulatory ischaemia occurs with little or no change in heart rate or blood pressure.[34] The presumption is that a change in coronary resistance is responsible. Many factors may contribute to changes in coronary resistance: platelet reactivity may cause release of vasoactive compounds. Diseased coronaries may possess less endothelium; this in turn leads to reactivity to vasocative compounds predisposing to spasm. The receptor reactivity in coronary arteries may be more sensitive to adrenergic stimuli after a time of quiescence[10] (anaesthesia); or, a combination of factors may be at play.

The results of the present study suggest that epidural morphine reduces the frequency of ischaemic events. High thoracic epidural anaesthesia with sensory blockade from T_1 to T_6, increased luminal diameter of epicardial coronary vessels which had documented severe stenosis[23] but did not change perfusion pressure, O_2 consumption or lactate extraction. The myocardial oxygen supply demand ratio is reduced throughout the perioperative period, and

is 30% lower in the early postoperative period using bupivacaine.[24] Although it is possible that the effects of local anaesthetic were carried into the first few hours postoperatively, one-third of the episodes of ischaemia occurred in the first four hours and there was no difference between groups in this time period. Further, ischaemia seen at this time is generally associated with tachycardia in both groups suggesting epidural failure in some patients.

Reiz *et al.*[35] have shown that epidural with local anaesthetic (ELA) effectively reduced the risk of ischaemia. Acute ischaemic episodes in patients with coronary artery disease were improved with ELA.[35,36] Sympathetic blockade in dogs with ELA reduced ischaemia, infarct size[36] and stroke work index.[37,38]

Epidural morphine has been shown to decrease blood pressure, and reduce the normal increase in epinephrine and cortisol levels postoperatively.[25] Further, epidural postoperative analgesia has been shown to reduce overall morbidity, including cardiac morbidity in two separate randomized trials.[39,40]

The early morning peak in ischaemia is similar to non-surgical patients.[14-16] Concomitant with this increased incidence of ischaemia is increased catecholamines,[20] heart rate, blood pressure,[20] coronary flow,[21] platelet reactivation[22] and decreased plasminogen activity.[23] It is possible that epidural morphine reduces the frequency of ischaemic episodes through its sympatholytic effects. Further, the reduction in ischaemia is seen after 5–6 hr, not in the early phases of recovery. This correlates well with the heart rate reduction. Examination of the heart rates in this study showed that our two study groups separate at five hours and continued to diverge for the rest of the 24-hr monitoring period. The effect of epidural opiates on the occurrence of ischaemia was similar to the changes in ischaemia seen with beta-blockers.[14,16] Since the episodes which do occur were identical to those of the parenteral group, it may suggest that some patients did not receive a sympatholytic effect with the dose of morphine administered. The predominance of ischaemia in the early postoperative period is curious. The events were associated with elevated heart rates (HR > 100 or a rate 20% above baseline). Several explanations may be possible. First, one epidural was clearly not working. On repositioning and injection of a local anaesthetic, the tachycardia abated and the ST segments normalized (Figure 3). (This is the only patient who received local anaesthetic in the PACU.) Further tachycardias in the immediate postoperative setting included the effects of atropine or glycopyrolate in the reversal of muscle relaxants, or similarly tachycardia may ensue with the cessation of the effect of beta-blockers due to fluid shifts.

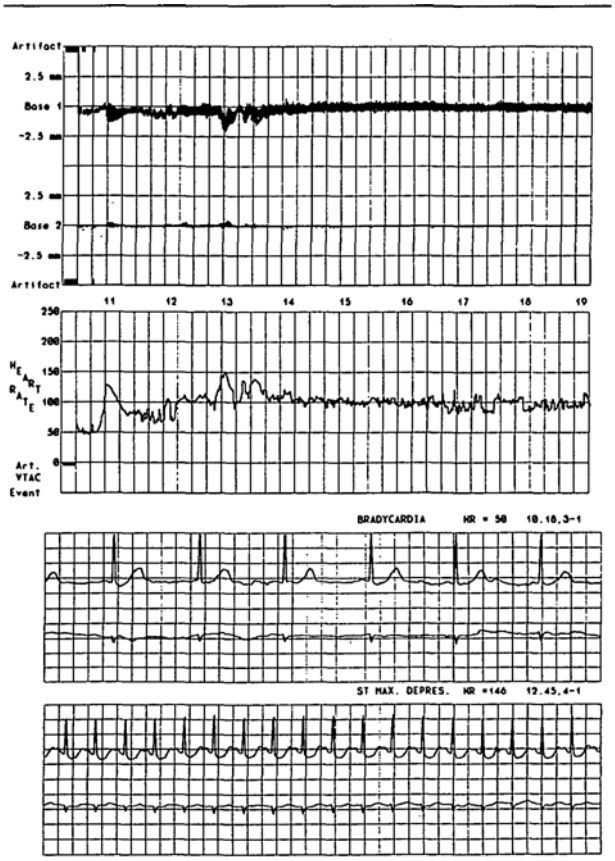

FIGURE 3 Computer output of Holter monitor data: occurrence of ischaemia in PACU (PAT OW EPI 21). Top panel shows the ST segment level by hour. Bottom panel shows the HR trend. At time 12:45 high heart rate of 146 the ST segments are depressed 2 mm. After repositioning of the catheter and injection of local anaesthetic at 1315 hrs, heart rate is reduced and ST segments were normalized. Pain score at this time was 1/10. This was the only patient in our series who required this type of intervention in the PACU.

Ischaemia is predominantly silent and occurs in normal daily life. Thus some ischaemia seen postoperatively might have occurred "normally" and is unrelated to the stress of surgery or anaesthesia. There was a considerable amount of early postoperative ischaemia in both groups. Since this was predominantly associated with tachycardia, it suggests that these episodes were almost certainly related to the stress of anaesthesia and surgery or perhaps to inadequate analgesia. The group receiving parenteral narcotics had seven episodes in five patients immediately postoperatively. The epidural group had six episodes in four patients. This incidence is not statistically or clinically different. When we excluded the early postoperative episodes from analysis, 25 episodes remained, seven episodes in three patients in the epidural group and 18 episodes in nine patients in the parenteral group ($\chi^2 = 4.29$, $P < 0.02$). Presumably, this later effect is occurring after local anaesthetics have been eliminated.

As with other studies, 48% of the parenteral analgesia group had postoperative ischaemia. All ischaemic episodes were predominantly silent. The peak incidence of ischaemic events occurs within the first four hours in the PACU as has now been seen with other studies. Secondary peaks occur at 10–13 hr and around 18–24 hr.[26]

A recent case report has suggested epidural opiates may mask ischaemia.[41] Our study showed that ischaemia was silent in both treatment groups and that the epidural group experienced less ischaemia. Since the incidence of silent ischaemia is so high, it is difficult to ascribe the "silence" to the epidural itself.

Study limitations

Patients were not randomized to type of anaesthesia/analgesia in this study. This represents what is becoming a practice bias as observations such as this combined with subjective impressions alter perioperative management. Due to the infrequency of major morbid events, a much larger study, probably multicentred, needs to be mounted using observations such as this as the rationale for its institution.

The ST segment changes are a non-specific indicator of ischaemia. Changes occur with alternative shifts in electrolyte concentrations, ventilation, drugs, position, and tachycardia. Further, many patients with ischaemic syndromes are not amenable to ST segment monitoring because of bundle branch blocks, pacemaker beats, atrial fibrillation, or chronic digitalis, all of which were exclusion criteria. Thus we have underestimated the occurrence of ischaemia in our postoperative population. However, ST segment changes, such as those we describe in this paper, are associated with ischaemia assessed by other measures.[42–44] Further, these types of ST segment changes are associated with increased cardiac morbidity in ambulatory patients,[33] and preoperative ST[6] depression and postoperative ST changes[7] are associated with increased occurrences of cardiac related morbid events. While our study was small, all morbid events occurred in patients manifesting postoperative ischaemia in the first 24 hr.

The design of this study could have been strengthened by preoperative stratification on the basis of preoperative ischaemia, as evidenced by Holter monitor detected ST depression. This was not carried out because of budgetary constraints. Secondly, we would also like to have monitored for a longer period of time postoperatively. Further studies are planned to extend the postoperative period.

While we would have liked equipotent analgesia in both groups, this is neither practical or feasible. Patients with control will accept a higher level of pain in order to limit side effects of the narcotic. We accept this fact and that it complicates the interpretation of our results. The difference in analgesia may, in fact, contribute to some of the outcome variability.

This study has shown that ischaemic events were reduced but not eliminated in patients receiving epidural/general anaesthesia plus epidural morphine analgesia. The reduction in ischaemic events is postulated to translate into fewer morbid events, but this awaits further study. Ischaemia which persists is not associated with tachycardia. It is disconcerting to find the high proportion of patients with ischaemia which goes completely undetected by patients or clinicians. Thus, if aggressive management of postoperative ischaemia, by whatever means, was to be achieved, more intensive monitoring of patients at risk is required.

Conclusions

Ischaemia occurred less frequently during epidural analgesia. Although it is logical that this effect could also reduce the risk of major postoperative morbidity such as MI or death, there were too few patients in our study for us to determine this. It seems likely from our results that the type of ischaemia that is most serious in the perioperative period could be *non-haemodynamically mediated* ischaemia.

It is disconcerting that in this study, as in others, postoperative ischaemia occurred silently, without the knowledge of the clinicians. While epidural patients experienced less ischaemia, it still occurred. Our supposition is that prevention of ischaemia will reduce cardiac morbidity. However, almost all ischaemia occurs without the knowledge of the patients. A further study is warranted to see if early detection and treatment of ischaemia does decrease long-term morbidity.

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