Table 1. Hemodynamic Response to Anesthesia and Surgery

<table>
<thead>
<tr>
<th>Preoperative treatment</th>
<th>Before Induction</th>
<th>Intubation</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>MAP</td>
</tr>
<tr>
<td>Nifedipin</td>
<td>13</td>
<td>67</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>14</td>
<td>59</td>
</tr>
<tr>
<td>Nifedipin + beta-blocker</td>
<td>35</td>
<td>61</td>
</tr>
</tbody>
</table>

| Nifedipin              | 13 | 70  | 15   | 79  | 13 | 11  | 4    | 2.38 ± 0.47 |
| Beta-blocker           | 16 | 65  | 12   | 87  | 10 | 11  | 4    | 2.45 ± 0.53 |
| Nifedipin + beta-blocker| 35 | 63  | 10   | 80  | 9  | 10  | 4    | 2.16 ± 0.43 |

HR = heart rate (beats/min); MAP = mean arterial pressure (mmHg); PCWP = pulmonary capillary wedge pressure (mmHg); CI = cardiac index (l·min⁻¹·m⁻²). Values are means ± standard deviation. * = significantly different from the beta-blocker group (p < 0.05).

between preoperative long-term calcium channel blockade and anesthesia and intraoperative stress, we analysed retrospectively, 70 consecutive patients (age 56 ± 8) with coronary heart disease and angina pectoris, scheduled for aortocoronary bypass surgery. Sixty-four per cent of the patients had three-vessel disease, 66% were in functional class 3–4, and the preoperative LVEDP was 20 ± 6 mmHg. Preoperatively 13 patients were taking nifedipin, 16 were taking beta-blockers, and 35 were taking both nifedipin and beta-blockers. Two patients were being maintained on verapamil, and four were on long-acting nitrates only. The average nifedipin dose was 44 ± 20 mg daily, and the last dose was given orally 1 h before anesthesia. All other medication was continued up to the night before surgery. For anesthesia, flunitrazepam, fentanyl, pancuronium, and nitrous oxide were used and nitroglycerin added iv when required.

Table 1 shows the hemodynamic data prior to, and 10 min after, induction and the peak response to intubation and sternotomy in the patients on nifedipin and beta-blockers.

Except for lower arterial pressure under anesthesia in the nifedipin groups, the analysis of variance did not reveal any significant differences between the groups. Up to now we have not seen any adverse effects that could be attributed to preoperative nifedipin treatment.

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REFERENCES

(Accepted for publication March 8, 1983.)

Methadone Titration to Avoid Excessive Respiratory Depression

To the Editor:—It is unfortunate that for the past several decades the excellent clinical properties of methadone largely have been ignored by American anesthesiologists. In this regard, Gourlay et al.¹ are to be commended for their excellent article in which they comprehensively ascertained the pharmacokinetics and pharmacodynamics of this narcotic in the perioperative period. They were able to produce satisfactory analgesia with 20 mg of methadone given upon induction with the analgesic effect lasting well into the postoperative period.

It is the potential for prolonged respiratory depression, however, that deters most anesthesiologists from using this narcotic. While this problem does exist, we believe that the risk has been overstated: in particular, we have found that titrating the drug before induction

Anesthesiology
59:363–364, 1983
for its respiratory-depressant effect eliminates individual variability and the possibility for prolonged respiratory depression.

Our usual sequence involves administering 8–12 mg of methadone to the awake patient until the threshold for respiratory depression (respiratory rate of 6–8/min) is reached. An additional bolus of methadone amounting to half the initial dose then is given just before the incision. Using this method of administration we have obtained clinical results similar to those observed by Gourlay et al. and have had no instances of excessive respiratory depression postoperatively. We believe that this is a superior method of administration for methadone and one that is necessary, given the prolonged half-life of the drug.

In reply—The clinical experience of Wangler and Rosenblatt, with regard to prolonged postoperative analgesia with methadone, is similar to that reported in our ANESTHESIOLOGY article. We also have not observed any significant respiratory depression following a 20-mg intravenous bolus dose administered after induction of anesthesia as previously reported. However, we share the concern expressed by Wangler and Rosenblatt for the potential prolonged respiratory depression following large methadone doses, and we support the need for a titration method. This is particularly important in the situation where the initial dose is insufficient for adequate pain control and supplementary doses of methadone are required.

We recently have completed a further study (submitted) in which supplementary intravenous methadone doses (5 mg) were administered in the immediate postoperative period (in addition to the 20 mg of methadone intraoperatively) when the following criteria have been satisfied:

1. The patient complained of significant postoperative pain,
2. No significant respiratory depression (rate less than 10 breaths/min) was observed, and
3. There was no marked depression of the level of consciousness.

We elected to use the intravenous route because there is complete bioavailability, and the pharmacodynamic response can be monitored immediately. Our previously reported pharmacokinetic data indicate that the mean distribution half life is 6 min and therefore at least 30–40 min (that is five to six times the distribution half-life) should elapse between supplementary doses so that a thorough assessment of the previous dose can be made. One to three additional 5 mg intravenous doses have been administered in the Recovery Ward to achieve satisfactory analgesia to a series of patients undergoing surgical procedures involving upper abdominal incisions. The duration of analgesia from the time it was achieved by titration of additional methadone doses was similar to that in our previous report (mean SD 21 ± 13 h). A further 5 mg methadone dose administered when pain returned after this resulted in an adequate analgesia for a similar duration. Under these conditions there was no significant respiratory depression assessed by measuring unstimulated respiratory rate.

Wangler and Rosenblatt and our group independently have arrived at essentially similar titration methods with minor differences in the dose of methadone administered and the time of administration. In addition, our recent results suggest a safe and effective method of administering additional methadone postoperatively, should this be indicated.

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(accepted for publication April 7, 1983.)