Administration of a crystalloid fluid preload does not prevent the decrease in arterial blood pressure after induction of anaesthesia with propofol and fentanyl

R. J. TURNER, S. P. GATT, P. C. A. KAM, I. RAMZAN, M. DALEY

Summary
Anaesthesia was induced in 58 women (ASA I or II) undergoing elective gynaecological procedures, using propofol 2.5 mg kg\(^{-1}\) and fentanyl 1.5 µg kg\(^{-1}\). Patients were allocated to receive 20 ml kg\(^{-1}\) of crystalloid fluid preload over 20 min or to receive no fluids before induction of anaesthesia. A significant decrease in systolic arterial pressure (<75% of baseline value) occurred in both the fluid-loaded and the control groups, and was similar in both groups. Administration of a fluid preload did not attenuate the decrease in systolic arterial pressure after induction of anaesthesia with propofol and fentanyl. (Br. J. Anaesth. 1998; 80: 737–741)

Keywords: anaesthetics i.v. propofol; complications hypotension; fluid balance fluid therapy

Propofol (2,6 diisopropylphenol) is a rapidly acting i.v. anaesthetic agent that has gained wide acceptance for the induction and maintenance of general anaesthesia. Propofol is ideal for short and ambulatory surgical procedures requiring general anaesthesia, as recovery is rapid with fewer unwanted side effects, such as drowsiness on recovery, disorientation and nausea, when compared with other agents such as thiopentone. The induction of general anaesthesia with propofol, however, has been associated with a decrease in systolic arterial blood pressure.\(^1\)\(^{-3}\) While this decrease in blood pressure is rarely clinically important in young and healthy individuals, this may not be the case in patients who are elderly, medically unwell or pregnant, in whom hypotension may critically reduce tissue perfusion and oxygenation.

The aim of the present study was to determine whether preloading patients with crystalloid fluid would prevent or attenuate this decrease in blood pressure.

Patients and methods
After obtaining approval from the regional ethics committee and informed consent we studied 58 women, ASA I or II, undergoing elective gynaecological procedures. Patients were allocated according to month of birth to receive 20 ml kg\(^{-1}\) of crystalloid fluid preload over 20 min (group F) or to receive no fluids before induction of anaesthesia (group NF). To achieve blinding, the fluid preload was given outside the operating theatre by one investigator, and the empty fluid bags replaced with fresh fluid bags. Thus all patients arrived in theatre with full fluid bags attached to the i.v. fluid administration sets, and the anaesthetist was unaware whether the patient had received a fluid preload. Exclusion criteria included a history of taking vasoactive medications, hypertension, cardiovascular disease and a body weight greater than 90 kg.

The patients received no premedication. In the anaesthetic room, i.v. access was established using local anaesthetic and a 16 gauge cannula in a superficial left forearm vein. Patients allocated to receive a fluid load were infused over 20 min with Hartmann’s solution, 20 ml kg\(^{-1}\) warmed to 38 °C. Patients in group NF received minimal fluids, to keep the vein open, until the end of the study, when fluid therapy was left to the discretion of the attending anaesthetist.

Blood pressure was measured using the Finapres (Ohmeda) automated continuous non-invasive blood pressure monitor. An appropriately sized cuff was applied to the right-hand forefinger and baseline blood pressure measurements were recorded. The monitor was serviced and calibrated twice by Ohmeda during the study.

Fentanyl 1.5 µg kg\(^{-1}\) was given 1 min before induction, and propofol 2.5 mg kg\(^{-1}\) injected over 20–30 s. After induction, haemodynamic variables were recorded at 15-s intervals for 4 min. End-tidal carbon dioxide was continuously monitored and the patient ventilated with 70% nitrous oxide and 30% oxygen via a face mask to maintain end tidal carbon dioxide at 34–40 mm Hg. Muscle relaxants were not given and no movement or surgical stimulation was permitted during the study period.

After completion of these measurements, the anaesthetic continued as normal with a further incremental dose of propofol or other agent given if clinically indicated. The treatment of hypotension was left to the discretion of the attending anaesthetist. No therapeutic interventions were required for any patient in this study.

The number of patients required for the study was calculated from an earlier study on the...
haemodynamic effects of propofol. Using Altman’s nomogram for a study with a power of 0.90, 50 patients would be needed to detect a difference in mean arterial blood pressure of 10 mm Hg at the 0.05 level. Patient characteristics were analysed statistically using Student’s unpaired t test. The haemodynamic data were analysed using ANOVA for repeated measures for differences between groups and for changes within groups. The method of summary measures as described by Matthews and colleagues was used to compare haemodynamic variables at 1 and 4 min. Statistical analysis was performed using a package designed for personal computers (Number Cruncher Statistical System, JL Hintze, Kaysville, UT, USA). The data are presented as mean (95% confidence intervals).

Results

There were 26 patients in group F and 32 patients in group NF. The two groups were comparable with respect to age, weight and fasting times (table 1). The mean fluid load for group F was 1222 (87) ml. There were no statistical differences in baseline blood pressures between the groups.

Systolic arterial pressure (SAP) decreased significantly ($P<0.001$) in both groups after induction of anaesthesia. Blood pressures recorded at 4 min were 75% of baseline values in group NF and 74% of baseline values in group F. The SAP decreased from 132 mm Hg to 99 mm Hg ($P<0.001$) at 4 min and from 129 mm Hg to 96 mm Hg ($P<0.001$) at 4 min in groups NF and F respectively. The decrease in SAP over time was similar for both groups. There was no significant difference between the two groups (fig. 1). Decrease in mean arterial blood pressure (MAP) and diastolic blood pressure (DAP) was also compared. MAP and DAP were similar in both groups. There were no significant differences in MAP and DAP (fig. 2) between the two groups.

Baseline heart rates were similar in both groups. Initially heart rates increased in both groups, reaching a peak at 15 s. Heart rates recorded at 15 s from induction increased by 116% in group NF and

| Table 1 | Patient characteristics in the two study groups (mean (95% CI)). Group NF = no crystalloid fluid preload. Group F = crystalloid fluid preload with 20 mg kg$^{-1}$ of Hartmann’s solution |
|-----------------|-----------------|-----------------|
| Group NF        | Group F ($n=26$) |
| Age (yr)        | 33.3 (3.3)      | 31.3 (3.1)      |
| Weight (kg)     | 63 (6.8)        | 62 (4.3)        |
| Fasting time (h)| 11.4 (1.5)      | 11.1 (1.5)      |
| Fluid preload (ml) | 0              | 1221.5 (86.7)   |

Figure 1 Changes in systolic arterial pressure (SAP) (mean (95% CI)) after propofol administration in groups NF (no fluid preload) and F (fluid preload). Values at 0 min indicate baseline blood pressures.

Figure 2 Changes in systolic arterial pressure (DAP) (mean (95% CI)) after propofol administration in groups NF (no fluid preload) and F (fluid preload). Values at 0 min indicate baseline blood pressures.
120% in group F. This corresponded to an increase of heart rate from 77 to 90 beats min\(^{-1}\) (P<0.01) and 75 to 92 beats min\(^{-1}\) (P<0.01) at 15 s in the groups NF and F respectively. After the initial increase, heart rate gradually declined to a level below baseline. Heart rates recorded at 4 min from induction were 91% of baseline values in group NF and 88% of baseline values in group F. Overall the heart rate decreased from 77 to 70 beats min\(^{-1}\) (P<0.01) and 75 to 66 beats min\(^{-1}\) (P<0.01) at 4 min in groups NF and F respectively. From 30 s to 4 min after propofol was given, the heart rate in group F was significantly less than the heart rate in group NF (P<0.001). The average difference between mean heart rate in both groups was 6.4 beats min\(^{-1}\) (fig. 3).

**Discussion**

This study demonstrates that the infusion of 20 ml kg\(^{-1}\) of crystalloid preload does not prevent or attenuate the decrease in blood pressure after induction of anaesthesia with propofol and fentanyl. For the purposes of this study we defined clinically significant hypotension as a decrease in blood pressure of greater than 20% below baseline measurements.

Clinically, hypotension becomes important when end-organ blood flow is reduced. The degree of hypotension required to reduce end-organ blood flow will depend on the health of the patient and the ability of the vascular beds of individual organs to autoregulate blood flow. In a young, fit individual, during deliberate hypotensive anaesthesia, a mean arterial blood pressure as low as 50–65 mm Hg appears to be tolerated, but at this blood pressure renal blood flow is significantly reduced. Renal blood flow is impaired when the mean arterial blood pressure falls below 80 mm Hg. An elderly, pregnant or medically compromised patient will not tolerate hypotension to the same degree as a young, healthy patient and it is difficult to predict the level at which end-organ blood flow is reduced. When considering these factors a decrease in arterial blood pressure of greater than 20% below baseline indicates a clinically significant fall in arterial blood pressure, but is unlikely to result in end-organ hypoperfusion, particularly in the healthy patient. The Finapres continuous non-invasive blood pressure monitor was used to measure arterial blood pressure.

This useful instrument allows continuous measurement of arterial blood pressure without the discomfort and potential complications of arterial catheter placement. The Finapres has been extensively evaluated and compared with invasive arterial pressure monitoring. While recordings made using the Finapres correlate well with invasive arterial pressure monitoring, discrepancies have been reported between the two methods of blood pressure measurement, particularly when arterial blood pressure is high.

Fentanyl was used to supplement induction of anaesthesia with propofol. The cardiovascular effects of low-dose fentanyl are minimal. In combination with propofol there is some evidence that the addition of low-dose fentanyl may accentuate hypotension and cause a slower heart rate when compared with that in patients who have received propofol only for induction of anaesthesia. In this study the haemodynamic effects of fentanyl would apply equally to both groups. Similarly, the use of nitrous oxide was required to ensure anaesthesia during the duration of the study. While nitrous oxide may influence the haemodynamic variables, this effect would also apply to both groups equally.

Hypotension after induction of anaesthesia with propofol is well recognized. This observation was supported by the present study and occurred equally in both groups. While fluid preloading did not prevent hypotension it did affect the cardiovascular response to propofol induction of anaesthesia, reducing the overall heart rate in the fluid-preloaded group. However, fluid preloading did not reduce the initial tachycardia seen in both groups immediately after propofol administration. The mechanism of propofol-induced hypotension is unresolved. While many studies have demonstrated a significant decrease in systemic vascular resistance that would account for the decrease in arterial blood pressure, the effect of propofol on the myocardium is more controversial. Some studies suggest that propofol causes a significant reduction in contractility while others demonstrate only minimal depression of contractility. Other studies attribute the decrease in blood pressure to both a decrease in systemic vascular resistance and a decrease in myocardial contractility.
The use of a crystalloid fluid preload to prevent hypotension after induction of anaesthesia with propofol has not been extensively evaluated. Several mechanisms may be postulated to explain the failure of fluid loading to attenuate hypotension after the induction of anaesthesia with propofol. The crystalloid fluid administered may be rapidly distributed into the interstitial and intracellular spaces with only a little remaining in the systemic circulation. Previous studies have suggested that the increase in pulmonary artery pressure after rapid infusions of crystalloid may be quite transient, with modest increases in pulmonary pressures returning to baseline values within 15–20 min.\textsuperscript{20} Measurement of central venous or pulmonary artery pressures would help further to define the degree of fluid redistribution. Colloidal solutions may be more effective in attenuating the decrease in blood pressure because a greater proportion is retained in the intravascular space. We propose that an alternative explanation may be found in the pharmacodynamic effects of propofol. If the predominant mechanism for hypotension is loss of arteriolar tone and reduced systemic vascular resistance, then fluid administration would be less effective in reducing hypotension than if the predominant mechanism is reduced myocardial contractility or venous dilation. Further investigation with monitoring of central venous pressure and cardiac output would help to define these cardiovascular changes.

The use of a fluid load to treat hypotension during anaesthesia has been well established. In the healthy patient, fluid preloading is associated with minimal risk. In the elderly or medically compromised patient, fluid preloading requires cautious administration to avoid complications such as pulmonary oedema. The healthy obstetric patient, however, is able to tolerate a fluid load, and it is generally believed that fluid preloading is beneficial for these patients under some circumstances. Fluid preloading is practised routinely in many obstetric units to prevent hypotension before central neuraxial block.\textsuperscript{21} Recent studies have questioned the value of this practice.\textsuperscript{22,23}

Heart rate increased immediately after propofol injection. This is best explained by the arterial baroreceptor response to arterial hypotension. Subsequently the baroreceptor response appears to be inhibited, with heart rate slowing to below preinduction levels. Depression of the baroreceptor response has been documented in previous studies.\textsuperscript{1,2} These studies have demonstrated similar changes in heart rate over time, after induction of anaesthesia with propofol. In the fluid-loaded group heart rate was lower when compared with that in the control group. It is possible that fluid loading produces an increase in myocardial preload, leading to an increased stroke volume and therefore maintains cardiac output at a lower heart rate without increasing blood pressure. This supports our hypothesis that decreased systemic vascular resistance is the predominant mechanism for hypotension following propofol administration. Further studies are required fully to evaluate the mechanisms causing hypotension after propofol administration.

In conclusion we found that the i.v. administration of crystalloid fluid does not prevent the decrease in arterial blood pressure after induction of anaesthesia with propofol and fentanyl. This practice cannot be recommended as a satisfactory technique to prevent hypotension following induction of general anaesthesia with propofol.

Acknowledgements

We thank Dr Judith Walker, Department of Physiology and Pharmacology, University of New South Wales, for advice on statistical analysis.

References


