

Title: HEMODYNAMIC EFFECTS OF HIGH DOSE THIOPIENTAL ANESTHESIA IN HUMANS

Authors: M.M. Todd, M.D., J.C. Drummond, M.D., H.S.U., M.D., R. Ostrup, M.D. and D.R. Stanski, M.D.

Affiliation: Departments of Anesthesia and Neurosurgery, University of California, San Diego, San Diego, California 92103 and Department of Anesthesia, Stanford University Medical Center, Stanford, California 94304

Introduction: The hemodynamic effects of thiopental (TP) anesthesia have been studied by many groups. Most have examined the changes produced by rapid injection of "small" doses (4-8mg/kg) and have made no attempt to separate myocardial effects from changes in venous pressures or ventricular preload. However, we were recently able to evaluate the effects of very large doses of TP (75mg/kg) given by infusion to 5 patients without heart disease (age 12-42) undergoing surgery for resection of giant intracranial arteriovenous malformations (AVM's). The results suggest that the direct myocardial effects of this drug may be surprisingly small.

Methods: Approval was obtained from the Human Studies committee and detailed consent was obtained from the patients (4) or parents (1). Premedication included PO diazepam or lorazepam, supplemented with IV diazepam and morphine in the OR. Monitoring included arterial and pulmonary arterial pressures (BP, RAP, PAP, PCW), cardiac index (CI-by thermodilution), heart rate (HR), EKG, expired CO₂, temperature and EEG. Calculated data included stroke volume index (SVI), systemic and pulmonary vascular resistances (SVR, PVR), and left and right ventricular stroke work indices (LVSWI and RVSWI). Blood was drawn for arterial and mixed venous blood gases and O₂ content, and for calculation of O₂ consumption (V̇O₂-Fick equation). After monitor placement, the patients rested 15 min while breathing 50% O₂ (in N₂). Control data was obtained and a 2.5% TP infusion begun at a rate of 1.25mg/kg/min. This was continued for 1 hour, with measurements made at 15, 30, 45 and 60 min. Ventilation was controlled by mask (paralysis with pancuronium/metocurine mixture, PaCO₂ 35-40mmHg) until a nasotracheal tube was placed just after the 45 min set of values (approximately 12-13min before the 60 min data, and approximately 5-10 min after EEG isoelectricity). No other stimulus was allowed during the 60 min period. To minimize the effects of changing venous pressures (preload) lactated Ringers was given at a rate sufficient to maintain PCW at control levels.

Results: Data obtained at 30 min (37.5mg/kg) and 60 min (75mg/kg) after starting the infusion are shown in the table (15 and 45 min values are similar). As planned, there were no changes in PCW. In addition, there were no changes in BP, RAP, PAP, SVR, PVR or PaO₂. At 30 min SVI had fallen by approximately 9%, and by 14% at 60 min. CI remained constant as a result of an increase in HR.

Discussion: Our data indicate that the gradual infusion of even massive doses of TP has minimal effects on vascular pressures, vascular resistance and oxygenation if venous pressures (indicated by PCW) are well maintained. Conversely, it suggests that venodilatation is an important effect (1), since 1-1.5 liters of fluid were required to hold PCW constant during induction. Some direct myocardial effect is indicated by the fall in SVI, but compensatory changes in HR were sufficient to maintain CI. These data should not be carelessly extrapolated to patients with heart disease; however, they do indicate that careful administration of large doses of TP to "normal" patients is well tolerated, and that this may represent a hemodynamically safe form of anesthesia.

TABLE (*p<0.05, paired t-test)

	CONTROL	30 MIN	60 MIN
TP DOSE	---	37.5mg/kg	75mg/kg
HR	86±9	99±9*	104±15*
BP	80±13	76±13	81±11
RAP	5.2±4.1	5.0±2.6	5.2±2.3
PAP	13.0±4.7	13.2±4.5	12.4±4.5
PCW	8.7±3.4	9.4±3.7	8.2±3.4
CI	4.2±0.4	4.4±0.5	4.4±0.7
SVI	49.1±6.2	44.6±5.4*	42.3±6.8*
SVR	11.4±1.9	10.3±2.3	11.2±2.6
PVR	0.7±0.3	0.6±2.3	0.6±0.2
LVSWI	3517±680	2934±357*	3047±469*
RVSWI	384±101	367±119*	309±147*
PaO ₂	231±37	226±40	222±50
VO ₂	155±40	122.4±48*	146±29

Legend: Hemodynamic data before, and after 30 and 60 min of the TP infusion. All data are mean±SD(N=5){Units: HR in beats/min; all pressures are in mmHg (BP, RAP, PAP, PCW); CI = l/min/m²; SVI = ml/beat/m²; SVR and PVR = mmHg/l/min, L and RVSWI = mmHg-ml/beat/m². PaO₂ = mmHg, V̇O₂ = ml/min.

Reference:

1. Conway and Ellis: Hemodynamic Effects of Short-acting Barbiturates. Br J Anes 41: 534, 1969.