COMPARISON OF THE CARDIOVASCULAR EFFECTS OF BOLUS V. INCREMENTAL ADMINISTRATION OF THIOPENTONE

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SUMMARY

Twenty unpremedicated patients (ASA grade I) were assigned randomly to receive thiopentone in 50-mg increments every 15 s until loss of lash reflex (group I) or as a 4-mg kg\(^{-1}\) bolus (group II). Arterial pressure, heart rate, systolic time intervals and end-tidal carbon dioxide were measured in the control state and then every 30 s. The mean dose of thiopentone in group I was 5.58 ± 1.24 (SD) mg kg\(^{-1}\) which was significantly larger than in group II (P < 0.001). Both groups exhibited similar decreases in arterial pressure and increases in heart rates. The degree of cardiac depression revealed from measurement of the systolic time intervals, indexed for heart rate, was equal in the two groups.

Fieldman, Ridley and Wood (1955) have stated that the incremental administration of thiopentone, at a rate of 50 mg min\(^{-1}\), will induce general anaesthesia without producing decreases in arterial pressure. However, their conclusion is open to question. Their patients were premedicated and were receiving nitrous oxide while the thiopentone was being administered and the measurements made. In addition, carbon dioxide tensions were neither measured nor controlled.

In clinical practice, thiopentone is injected usually as a bolus of 4–6 mg kg\(^{-1}\) or given at a more rapid incremental rate than was used in Fieldman’s study. We have compared the cardiovascular effects of a bolus of thiopentone with those of an incremental injection technique.

METHODS

This study was approved by The Committee for the Protection of Human Subjects at our institution and written informed consent was obtained from each patient. Twenty unpremedicated patients (ASA grade I) were assigned randomly to receive thiopentone incrementally at a rate of 50 mg per 15 s (group I) or as a bolus of 4 mg kg\(^{-1}\) (group II). Control measurements of arterial pressure (BP) by the Riva–Rocci method, heart rate (HR) as determined by the R–R interval on the e.c.g., systolic time intervals (STI) and end-tidal carbon-dioxide (\(FE'_{CO_2}\)) were recorded while the patients breathed 100% oxygen from a face-mask. Measurements of STI were made from a simultaneous 100-mm s\(^{-1}\) recording of the e.c.g., phonocardiogram and carotid arterial pulse tracing. Recordings were made on a Hewlett-Packard (HP) 78308A recorder. The phonocardiogram was obtained with an HP 2105A contact sensor placed in that area of the precordium which produced the finest tracing. An HP 2105D pulse-wave pickup was placed on the neck to record the carotid pulse tracing. \(FE'_{CO_2}\) were obtained from a precalibrated Beckman LB-2 Medical Gas Analyzer.

Group I patients received thiopentone 50 mg every 15 s until the lash reflex was abolished. Group II patients received thiopentone 4 mg kg\(^{-1}\) as a bolus injected as rapidly as possible through an 18-gauge i.v. cannula. Haemodynamic measurements were recorded in each group when a total of thiopentone 4 mg kg\(^{-1}\) had been given and every 30 s thereafter. Recordings were continued for 5 min or until the patients showed signs of wakening. Oxygen 100% was continued and ventilation of the lungs was assisted if necessary to maintain a \(FE'_{CO_2}\) between 4.5% and 5.5% throughout the study.

Total electromechanical systole (QS\(_2\), left ventricular ejection time (LVET) and HR were averaged from three to five sinus heart beats in each measurement period. The pre-ejection period (PEP) was calculated as QS\(_2\) minus LVET and all values were indexed for HR (Weissler, Harris and Schoenfeld, 1968). From the indexed values of QS\(_2\) (QS\(_2\)-I) and LVET (LVET-I), 1/PEP\(^2\)-I and PEP-I/LVET-I were calculated to determine the effect of the thiopentone on myocardial function. The maximum changes in BP, HR, 1/PEP\(^2\)-I and PEP-I/LVET-I

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were compared between the two groups using a two-tailed unpaired \( t \) test.

**RESULTS**

Comparison of the control states in both groups showed no differences (table I) and control values of STI were consistent with accepted values (Weissler, Harris and Schoenfeld, 1969). In every patient, a decrease in arterial pressure and a depression of cardiac function, as indicated by STI, occurred during the study period, with subsequent recovery towards control values. The mean dose of thiopentone in group I was 5.58 ± 1.24 (SD) mg kg\(^{-1}\) which represented a significantly larger dose than the 4 mg kg\(^{-1}\) received by group II (\( P < 0.001 \)). All but one patient in group II lost the lash reflex with the 4-mg kg\(^{-1}\) bolus. Table II shows that both groups experienced similar decreases in arterial pressure and increases in heart rate. No significant difference in the degree of cardiac depression, as revealed by changes in \( \frac{1}{PEP^2} \) and \( PEP-I/LVET-I \), was evident between the groups. The period during which the patients in both groups remained unconscious varied. Group I patients slept for 150-300 s with a mean of 264 ± 60 s. Group II slept for 60-300 s with a mean of 222 ± 94 s. The difference between groups was statistically (\( P < 0.05 \)) but probably not clinically significant.

**DISCUSSION**

Several groups of investigators have described the effect of thiopentone on myocardial function as determined by STI (List, 1975; Dauchot et al., 1976; Filner and Karliner, 1976; Becker and Tonnesen, 1978). In all these studies the patients received atropine. In two, either diazepam (Filner and Karliner, 1976) or pethidine (List, 1975) was administered also before the study period. In none of these studies were various modes of administration of thiopentone compared.

Externally measured STI have been shown to correlate well with invasively obtained indices (Martin et al., 1971). Prolongation of PEP has been shown to correlate with decreases in stroke volume and cardiac output (Weissler, Harris and Schoenfeld, 1968, 1969) while \( \frac{1}{PEP} \) has been compared with peak ascending aortic blood-flow acceleration and has been shown to have a good correlation with the latter (Reitan et al., 1972). Therefore, a decrease in \( \frac{1}{PEP^2} \) indicates a decrease in myocardial contractility. An increase in the ratio of PEP/LVET indicates a decrease in left ventricular function (Weissler, Harris and Schoenfeld, 1969). In subjects without valvular disease, shunts or cor pulmonale Ahmed and colleagues (1972) demonstrated a good correlation of PEP/LVET to ejection fraction and cardiac index and excellent correlation to measurements of myocardial contractility.

In spite of the fact that the patients in group I received about 40% more thiopentone than those in group II, we could not demonstrate any significant difference in the cardiovascular effects of these two modes of administration of thiopentone. A possible explanation for the larger dose given to group I is that the blood concentration necessary to abolish the lash reflex is reached more slowly as a result of constant redistribution of the incremental doses. When the blood concentration was obtained, it was probably very close to that obtained with the bolus and, therefore, the cardiovascular side-effects were similar. It is likely that a larger bolus (6 mg kg\(^{-1}\))
would produce greater peak blood concentrations which would lead to further myocardial depression. If so, a difference might be demonstrated between this large bolus (6 mg kg$^{-1}$) and the type of incremental induction described.

As our results are based on findings in healthy patients, we caution against extrapolation of these results to high-risk patients such as those who are hypovolaemic or in heart failure. Hypovolaemia would allow anaesthetic blood concentrations to be reached after a much smaller dose of thiopentone than is described here. List (1975) has shown that digitalis improves STI measured after thiopentone when compared with measurements made in the same patients 1 week before receiving digitalis. One can infer from List’s work that patients with various degrees of left ventricular dysfunction show a greater degree of myocardial depression following thiopentone than those with normal myocardial contractility.

We conclude that inducing anaesthesia to the point of abolishing the lash reflex in healthy patients by giving thiopentone incrementally at a rate of 50 mg per 15 s produces cardiovascular depression similar to that seen following a 4 mg kg$^{-1}$ bolus.

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REFERENCES


COMPARACION DE LOS EFECTOS CARDIOVASCULARES DE UN BOLO DE TIOPENTONA CON LA ADMINISTRACION PROGRESIVA DE TIOPENTONA

RESUME

Vingt malades n’ayant reçu aucun prétraitement (ASA grade 1) ont été désignés au hasard pour recevoir des doses de thiopentone augmentant progressivement par paliers de 50 mg toutes les 15 s, jusqu’à ce qu’ils perdent le réflexe ciliaire (groupe I) ou sous la forme d’un bol de 4 mg kg$^{-1}$ (groupe II). On a mesuré la pression artérielle, la fréquence cardiaque, les intervalles des systoles et le gaz carbonique en fin d’expiration à l’état témoin et ensuite toutes les 30 s. La dose moyenne de thiopentone du groupe I a été de 5,58 ± 1,24 (écart type) mg kg$^{-1}$, ce qui a été sensiblement plus important que dans le groupe II (P<0,001). On a constaté dans les deux groupes des baisses de pression artérielle et des augmentations de fréquence cardiaque similaires. Le degré de dépression cardiaque qui est ressorti de la mesure des intervalles des systoles indéxés pour la fréquence cardiaque, a été le même pour les deux groupes.

VERGLEICH DER HERZKREISLAUFWIRKUNGEN BEI BOLUS- ODER SCHRITTWEISER VERABREICHUNG VON THIOPENTON

ZUSAMMENFASSUNG

Zwanzig nicht vorbehandelte Patienten (ASA grade 1) wurden willkürlich ausgewählt, Thiopentone 50 mg alle 15 s zu erhalten, bis Verlust des Lidreflexes auftrat, (gruppe I), oder als Bolus zu 4 mg kg$^{-1}$ (gruppe II). Arterieller Druck, Herzfrequenz, systolische Intervalle und Ausatmungs-Kohlendioxidgehalt wurden im Kontrollstadium und dann alle 30 s gemessen. Die mittlere Thiopentone-Dosis in gruppe I betrug 5,58 ± 1,24 (SD) mg kg$^{-1}$, was wesentlich mehr war als in gruppe II (P<0.001). Beide Gruppen zeigten ähnliches Absinken des arteriellen Druckes und Anstieg der Herzfrequenz. Das Ausmass der kardialen Depression, festgestellt durch Messung der systolischen Zeitintervalle gemäss der Herzfrequenz, war in beiden Gruppen gleich.

COMPARACION DE LOS EFECTOS CARDIOVASCULARES DE UN BOLO DE TIOPENTONA CON LA ADMINISTRACION PROGRESIVA DE LA MISMA

SUMARIO

Se designó a veinte pacientes que no habían recibido premedicación (ASA Grado 1) al azar para recibir tiopentona en incrementos de 50 mg cada 15 s hasta pérdida del
reflejo ciliar (grupo I) o como un bolo de 4 mg kg$^{-1}$ (grupo II). Se llevó a cabo la medición de la presión arterial, del ritmo cardíaco, de los intervalos sistólicos y el dióxido de carbono terminal-respiratorio en el estado de control y después cada 30 s. La dosis media de tiopentona en el grupo I era de 5,58 ± 1,24 (SD) mg kg$^{-1}$, lo que representa una dosis significativamente mayor de la del grupo II ($P<0,001$). Ambos grupos manifestaron similares diminuciones de la presión arterial y aumentos de los ritmos cardíacos. El grado de depresión cardíaca arrojada por la medición de los intervalos sistólicos puestos en índice para el ritmo cardíaco era igual para los dos grupos.