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EVALUATION OF SOME LIVER AND KIDNEY FUNCTIONS FOLLOWING THIOPENTAL INJECTION IN DOGS

(With 2 Tables)

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تأثير حقن جرعات مختلفة من الثيوبنتال على وظائف الكبد والكلى في الكلاب

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أجريت الدراسة على ١٢ كلب سليم من الناحية الاكلينيكية . حيث تم حقن الحيوانات بجرعات مختلفة من الثيوبنتال، كل مجموعة تشمل ٦ كلاب. هذا وقد تعرض الحيوان في المجموعة الأولى لجرعة واحدة من المخدر وفي المجموعة الثانية لجرعتين متتاليتين من المخدر .

أوضحت النتائج أنه: لايستحب حقن مخدر الثيوبنتال أكثر من جرعة واحدة لما له من تأثير ضار على الكبد والكلى. وللحصول على فترة تخدير أطول من ساعة يستخدم الثيوبنتال كبداية فقط بحقنه جرعة واحدة ثم يكمل بإستخدام طريقة إستنشاق المخدر المناسب.

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SUMMARY

Twelve clinically healthy dogs of both sexes (2-3 years age, 10-15 Kg B.wt) were used in this study. The animals were divided into 2 groups (each of 6 dogs). Animals were anaesthetized by using single and repeated doses of thiopental by intravenous injection. From each animal two blood samples were collected before injection of anaesthetic solution and 24 hours after. Blood serum total protein, cholesterol, glucose, urea, creating, potassium, sodium, and chloride levels were estimated. Results revealed that intravenous injection of thiopental must be used only for induction of general anaesthesia. Complete anaesthesia could be reached by using the inhalation anaesthesia for prolongation the time of surgical stage more than one hour and to avoid its toxicity on the liver as well as on the kidnies.

INTRODUCTION

Thiopental an ultra short-acting thiobarbiturate, is widely used in both human and veterinary medicine as an intravenous anaesthetic agent usually in conjunction with inhalation agents *(GHONEIM and SPECTOR, 1982)*. The brief duration of anaesthetic action is due to the rapid decline in the central nervous system concentration of the drug. This can be attributed to further distribution of the drug and to a lesser extent hepatic biotransformation *(GOLDSTEIN and AARON, 1960)*.

Renal and hepatic functions are important in the fate of barbiturates because malfunction of the liver can influnce bitransformation of the drugs and renal malfunction can influence its elimination *(KEW et al., 1971)*.

GREENE (1968) cited that since most intravenous anaesthetics are quite lipid soluble, they cannot be excreted often by the kidneys and must be metabolized to more polar molecules in the liver before they can be removed from the 48 hours in sheep after thiopental anaeesthesia. They attributed this decrease to a transient renal dysfunction and increased protein breakdown.

The present study had been carried out to throw light upon the influence of different doses of thiopental, as an

anesthetic, on some blood serum parameters namey total protein, albumin, cholesterol, glucose, urea, creatinine, potassium, sodium and chloride levels in dogs. This may evaluate the effect of therapeutic and repeated doses on both liver and kidney functions.

MATERIAL and METHODS

Twelve clinically healthy dogs of both sexes (2-3 years age, Kgs B.wt) were used in this study. Animals were divided into into 2 groups (each of 6 dogs). First one: Each animal was anaesthtized by using single dose of intravenous injection of thioental (20-30 mg/Kg b.wt) till the main reflexes disappeared. Second group: Repeated intravenous injection with exceedin doses untill the reflexes are abolished. Same anaesthtic was used again at the begining of recovery to prolong the period of the surgical stage. All the injections were carried out very slowly in the cephalic vein.

From each dog, two blood samples were taken one before injection of anaesthetic solution and the other 24 hours after. Blood samples were then centrifugated and blood serum was separated. These samples were analysed for some serum parameters; Total protein by *WEICHSELBAUM (1946)*, Cholesterol by *HUSDAN and RAPAPORT (1968)*, Creatinine by *HUSDAN and RAPAPORT (1968)*, Glucose by *HULTMANE (1959)*, Urea by *HAURY and NAUMANN (1965)*, Potassium and Sjodium by using (flame photometer [Corning 400] and Chloride by using Chloridemeter [model 925].

RESULTS

Signs of general anaesthesia were characterized by loss of the main reflexes and the surgical stage of anaesthesia was develope and lasted for 30-45 minutes then the animal recovered (group 1). In group 2, with repeated injection with exceeding doses until the reflexes are abolished again, the animal was still anaesthetized for 2-3 hours, with depression for 24 hours post injection.

Results of biochemical analysis of blood serum samples are illustrated in Tables 1 & 2.

DISCUSSION

Regarding thiopental it is well known that its short action is due to the rapidly declining level of the drug in the brain *(GOLDSTEIN and ARONOW, 1960)*.

After general anaesthesia all measures of urinary function are temporarily depressed, including renal blood fluid (ABF), glomerular filteration rate (GFR), urinary flow rate and electrolyte excretion *(PRIANO, 1984)*. When anaesthesia is prolonged, secondary endocrine effects may be manifested by impaired ability to excrete water or concentrate urine; these effects may persist for several days *(HAYES and GOLDENBERG, 1963)*. The alteration in renal function induced by anaesthetic agents is due to indirect effects on the circulatory, sympathetic nervous and endocrine systems and direct effects upon tubular transport mechanisms *(BASTRON, 1980)*. Anaesthesia may induce major distrbances in the circulation, resulting in equally major alteration in renal hemodynamics and tubular function.

Elimination of the drug takes place slowely by hepatic biotransformation *(BRODIE, 1952)*. Furthermore, *MARK (1966)* declared that following a single injection of thiopental, recovery was primarily due to redistribution of the drug from the visera and the blood to the muscles.

Thiopental has a great affinity for binding to plasma proteins especially albumin *(MORSY, 1985)*. The obtained data revealed a slight increase in the total protein in dogs given single, and repeated dose of thiopental. Values reached 11.0±1.57, 9.21±0.57 g/l, respectively. However, cited literature showed that the eventual changes in the total protein can be caused by the capillary inflow of the fluid and by redistribution of proteins from the intravascular space. This is probably due to increased capillary permeability and/or decreased lymphatic return of proteins. *(FINSTERER et al., 1975)* in dog kept in equilibrium between input and renal output by continous infusion of saline. Such decrease in the total protein level was also previously recorded by *KUMAR et al. (1974)*. This decrease was previously interpreted *KUMAR (1974)* as a result of the transient renal dyfunction and the increased protein breakdwon.

Hyperglycaemia was evident in dogs given single and repeated dose of thiopental. Values amounted 108.13±9.51 and 138.40±6.99 mg%, respectively. General anaesthesia is considered as severe stress consequently this leads to elevation on Adenocortico trophic hormons which leads to hyperglycaemia *(COLES, 1983)*. The anaesthetics act directly on the adrenal gland to cause aldosterone release; or probably act indirectly by inducing vasopressin release that subsequently stimulates ACTH release, with resultant nervous system

stimulation. This induces renal vasoconstriction leading to renin and ultimately angiotensin body. Approximately 30% of the cardiac output is directed through the liver. Therefore, after an intravenous injection, 30% of an injected drug is exposed to liver enzxymes on the first circulation. Intrinsic activity of the microsomal enzymes, protein binding and hepatic blood flow affect the metabolic clearance of drugs by liver; furthermore, barbiturates are biotransformed almost completely and less than 1% is excreted unchanged in the urine *(GREENE, 1968)*.

Metabolism occurs primarily in the endoplasmic reticulum of the hepatic cell and a major step is oxidation of one of the alkyl side chains to yield a carboxylic acid *(BRODIE et al., 1950)*. *MARK (1966)* stated that the consensus that following a single injection of thiopental, recovery is primarily due to redistribution of the drug from the viscera and the blood to muscles.

Metabolism occurs at a much slower rate with 10% to 20% of the drug being metabolized by the liver each hour *(ATKINSON et al., 1977)*. Most of the drug is metabolized with only 0.3% unchanged in the urine *(BRODIE, 1952)*.

The effect of thiopental on the kidney result from the decrease in systemic blood pressure, renal artery constriction and antidiuretic hormone secretion resulting in a decrease in the urine output.

The normal values of total protein ranged from 5.5 to 9 gm/dL in dog but when received a single dose of thiopental it reached 7.68±0.13 gm/dL and blood urea normal level was 20-40 mg/dL, but in single dose reached 19.9±0.88 mg/dL *(MORSY, 1985)*.

Blood glucose levels in other species were increased after induction either by using Nesdonal or ketamine *(DOWIDAR et al., 1984)*. Expoing of an animal or humanbeing for anaesthetic solutions might be considered as stress factor which leads to haematological and biochemical changes, which might stimulate the hypothalamus with subsequent release of many important factors, the most important of them is the corticotropin-releasing factor which stimulate the production of ACTH with subsequent production of glucocorticoids *(FABER, 1970)*. Moreover the hyperglycaemia could be induced by the increased level of cortisol.

It was observed that the total blood serum protein contents were decreased following i/v anaesthesia of Nesdonal and reach their maximal reduction after 15 minutes, then the level begin to rise somewhat towards normalization *(HASSAN et al., 1984)*.

KUMAR et al. *(1974)* and *EL-GUINDI* et al. *(1981)* showed a momentary decrease in the total serum protein that returned again to its normal levels after about II formation, which inturn leads to peripheral vasodilation that via bioreceptor reflexes leads to activation of the renin-angiotensim system *(priano, 1984)*. So it is not possible to separate the effects of anaesthesia appear to be dose-related and ameliorated by adequate replacement of extracellular fluids *(COUSINS* et al., *1983)*.

Slight elevation was observed in the values of blood serum urea in the anaesthetized dogs. Single, repeated and over dose of thiopental increased blood serum urea to reach 29.05±2.51, and 28.11±2.52 respectively. Such elevation was in accordance with that reported by *KUMAR* et al. *(1974)*. Our interpretation of this behaviour can be offered on the basis that the level of serum urea is expected to be affected as far it is produced in liver and could indicate transient renal dysfunction. Severe stress (i.e., general anaesthesia) decrease RBF and FGR through increased sympathetic nervous activity. It appears therefore, that the decrease in RBF and GFR induced by general anaesthesia is a result of increased sympathetic tone *(COUSINS* et al., *1983)*. Decreased renal excretion of urea is, however, the most common cause of an increased BU. Such decreased phenomena may appear through decreased renal flow and or kidney failure *(MICHEAL and LARRY, 1987)*.

A transient variation was also noticed in the level of blood serum creatinine by all doses of thioental. It seems in our view that creatinne excretion behave in a similar manner as urea nitrogen under the stress caused by thiopental anaesthesia.

There was a slight increase in the serum potassium levels in both groups (4.72±0.37, and 6.99±1.21 mmol/1, respectively). The increase of serum potassium concentration due to the injection of thiopental may be caused in the view of *(MICHAEL and LARRY, 1987)* by increased intake, decreased excretion (mainly renal) or redistribution of potassium from cells into the extracellular fluid. The obtained data revealed also a hyponatremia in anaesthetized dogs and values reached 155.7±9.24 mmol/1 in single dose, and 157.50±9.86 mmol/1 in repeated dose respectively. Such variation in the concentration of narium and potassium is also expected under anaesthesia and this may reflect in each case; the condition of the patient at time of receiving the respective drug. Morevoer, an increase in choloride levels was observed in our data (129.96±9.59, and

136.00±8.45 mmol/1 ins single, and repeated dose). Simalar results by *TACLOB and NEEDLE (1973)* were also noticed; however, *TEVIL et al. (1968)* who found no signicicant electrolyte changes with anaesthesia.

In conclusion, the intravenous injection of thiopental must be used induction of general anaesthesia. In addition there is a need to prolonge the time of surgical stage more than one hour, the inhalation anaesthesia using Halothan or fluthan is prefered to avoid thiopental toxicity on the liver as well as on the kidnies.

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Table (1):The mean values, the standard deviation and the range of some blood serum parameters in dogs injected with Thiopental sodium single dose.

Parameters	Unite	Before injection	24 hr.after injec.
Total protein	g/dL	11.2633±1.0914 (9.4100-12.490)	11.0650±1.5704 (7.4900-12.580)
Cholesterol	mg%	46.3167±5.8755 (39.9000-55.000)	121.3333±5.7155 ** (112.0000-129.00)
Glucose	mg%	72.1033±6.8662 (65.1500-92.300)	108.1383±9.5185 ** (97.9200-153.84)
Urea	mg%	27.6850±0.8918 (26.2100-28.330)	29.0550±2.5133 (26.5500-32.520)
Creatinine	mg%	1.9053±0.0547 (1.8500-2.0100)	1.5058±0.3248 ** (1.1400-1.9000)
Potassium	mmol/l	5.1217±0.3884 (4.4000-5.5000)	4.7250±0.3791 * (4.3000-5.2500)
Sodium	mmol/l	161.2333±9.2999 (164.9500-179.50)	155.7267±9.2486 (143.3000-173.26)
Chloride	mmol/l	128.1667±9.4441 (117.1300-137.20)	129.9667±9.5994 (122.5000-154.50)

Table (2):The mean values, the standard deviation and the range of some blood serum parameters in dogs injected with Thiopental sodium repeated dose.

Parameters	Unite	Before injection	24 hr.after injec.
Total protein	g/dL	11.2633±1.0914 (9.4100-12.490)	9.2133±0.5733 ** (8.7400-9.9100)
Cholesterol	mg%	46.3167±5.8755 (39.9000-55.000)	136.0000±5.4558 * (168.0000-183.00)
Glucose	mg%	72.1033±6.8662 (65.1500-92.300)	138.4017±6.9946 ** (99.3800-199.30)
Urea	mg%	27.6850±0.8918 (26.2100-28.330)	28.1183±2.5258 (25.3200-32.250)
Creatinine	mg%	1.9053±0.0547 (1.8500-2.0100)	1.8117±0.3721 (1.2500-2.1900)
Potassium	mmol/l	5.1217±0.3884 (4.4000-5.5000)	6.9900±1.2164 ** (4.9000-8.4500)
Sodium	mmol/l	161.2333±9.2999 (164.9500-179.50)	157.5000±9.8642 (147.2000-170.00)
Chloride	mmol/l	128.1667±9.4441 (117.1300-137.20)	136.0000±8.4558 (158.0000-183.00)

* Significant at (p<0.05). ** Highly significant at (p<0.01).