نامهٔ دانشکدهٔ دامپزشکی ، دانشگاه تهران ، دورهٔ (۴۱) شمارهٔ (۲) تهران (۱۳۶۴)

اثرات چاقی در بیهوشی جراحی طولانی با تیوپنتال: استفاده از گوسفندان دنبه‌دار ایرانی بعنوان یک روش نوین

دکتر مجید اجتمادی* صغری غلامی* دکتر سیف الله دهقانی*

خلاصه

از زمان معرفی باربیتوراتهای با اثر خیلی کوتاه وکاربرد آنها دربیهوشی انسانی و دامپزشکی در سال ۱۹۳۸ تیوپنتال بطور مطلوب وگسترده ای درموارد متعددی از قبیل آزمایشات مامائی و شکست بندی‌ها وغیره مصرف شده‌است. تیوپنتال همچنین دربیهوشیهای عمومی بعنوان یک عامل ایجادکننده بیهوشی قبل از مصرف بیهوشیهای استنشاقی ازقبیل هالوتان ومتوکسی فلورین بکار می‌رود. این یک حقیقتی است که تیوپنتال بعلت اثرات کوتاهش مصرف می‌شود، اما، ممکن است در بیهوشیهای طولانی با تزریق مکرر یا انفوزیون، درمواقعی که دستگاههای بیهوشی موردنظرموجودنیست، بکار گرفته شود. در جنگ جهانی دوم تیوپنتال برای ایجاد بیهوشیهای عمومی در بیمارستانهای خط مقدم جبهه که دستگاههای بیهوشی محدود بود مصرف می‌گردید.

از نقطه‌نظر فارماکوکنتیک نشان داده‌شده است، چنانچه از مقادیر مکرر تیوپنتال استفاده شود میزان غلظت پلاسمائی آن درحدود غلظت باقی دارو باقی می‌ماند. از طرف دیگر، متخصصین بیهوشیهای انسانی متوجه شده‌اند که بیمارانی که دارای ذخیره چربی زیاد *(مبتلا به چاقی)* هستند، به داروی بیهوشی بیشتری احتیاج داشته وزمان بهبودی در این بیماران بمراتب طولانی‌تر از بیمارانی است که ذخیرهٔ چربی آنها کم است. این تجربه عملی، اشاره‌ای به اهمیت *چاقی* در بیهوشیهای طولانی می‌باشد. متاسفانه، بعلت نبودن *الگوی تحقیقاتی*، تا آنجائی که بررسی نویسندگان اجازه می‌دهد، مطالعات تجربی که تجربه عملی متخصصین بیهوشی را تائید نماید، انجام نگرفته است.

در این زمینه، با توجه به اینکه گوسفندان ایرانی می‌توانند مقدار ۱۰ درصد از کل وزن بدنشان را بیشتر چربی در ناحیه دم خود ذخیره نمایند، وازهمه مهمتر اینکه می‌توان بعداز یک عمل جراحی آنرا کاملا "برداشت، فکرشد که گوسفندان ایرانی می‌توانند

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* گروه آموزشی فارماکولوژی، دانشکده دامپزشکی، دانشگاه شیراز

بهترین الگوی آزمایشگاهی برای بررسی اثرات چاقی در بیهوشی طلاونی با تیوپنتال باشد. نتیجتا" ، براین پایه پژوهشی انجام شد که نتیجهٔ آن بصورت خلاصه درزیر ارائه می‌گردد.

تعداد ده راس گوسفند نرماده به ظاهر سالم در سنین ۱۲ ــ ۱۴ ماهگی با وزنهای بین ۲۴ ــ ۳۶ کیلوگرم که از مزرعه طبیعی تغذیه می‌کردند و در ضمن علوفه خشک و آب بمیزان فراوان در اختیار داشتند ، مورد استفاده قرار گرفت . آزمایش در سه مرحله انجام گرفت : مرحله اول ، ایجاد بیهوشی با تیوپنتال در گوسفندان طبیعی ؛ مرحله دوم ، قطع دم یا برداشت بافت چربی ؛ مرحله سوم ، ایجاد بیهوشی با تیوپنتال در حیواناتی که دم آنها در مرحله دوم قطع شده بود . بیهوشی طولانی جراحی با مصرف دوز مقدماتی به مقدار ۵/۸۲±۲۶/۵۱ میلی گرم / به ازای هر کیلوگرم از وزن بدن در گوسفندان مرحله اول ایجاد و به مدت ۳ ساعت به طور موفقیت آمیزی با تزریق دوز نگهدارنده به مقدار ۵/۲۶ ± ۲۲/۹۷ ، ۵/۶۷ ± ۲۰/۳۱ و ۵/۳۱ ± ۱۴/۱۰ میلی گرم / به ازای هر کیلوگرم از وزن بدن به ترتیب برای ساعات اول ودوم و سوم نگهداری شدند ، ایجاد ونگهداری بیهوشی در حیوانات فاقد دم نیز با موفقیت انجام گرفت . دوزهای نگهدارنده در این گروه (مرحله سوم) نسبت به دوزهای نگهدارنده در گوسفندان مرحله اول به ترتیب از ۵/۲۶+۲۲/۹۷ به ۶/۳۴+۲۱/۹۹ ، از ۵/۶۷ ± ۲۰/۳۱ به ۴/۶۱ ± ۱۴/۷۵ واز ۵/۳۱ ± ۱۴/۱۰ به ۳/۲۰ ± ۸/۵۶ میلی گرم / به ازای کیلوگرم در طول ساعت اول ، دوم و سوم بیهوشی کاهش یافت . اختلاف بین دوزهای نگهدارنده در این دوگروه را می‌توان بعلت برداشت چربی در ناحیه دم گوسفندان دانست . زمان متوسط دورهٔ بهبودی در گوسفندان مرحله اول ۶۵/۷۷ ± ۳۵۸/۱۰ دقیقه بود که در گوسفندان مرحله سوم (حیوانات فاقد دم) به ۸۸/۴۹ ± ۲۰۴/۵۰ دقیقه کاهش یافت . اختلاف زمان بهبودی در این دو گروه را می‌توان به بالا بودن آهنگ متابولیسم و دفع تیوپنتال در گوسفندان مرحله سوم نسبت داد ، زیرا که میزان غلظت پلاسمائی دارو در گوسفندان مرحله سوم ، بعلت برداشت بافت چربی ، بیشتر می‌باشد و نتیجتا" طبق اصول فارماکولوژیک ، دارو سریعتر متابولیز ودفع می‌شود که اثر آن در کوتاه شدن زمان بهبودی منعکس می‌گردد .

از نتایج حاصل از این مطالعه می‌توان نقش چاقی را در بیهوشی انسانی ودامپزشکی ثابت نمود . دراین صورت بایستی به متخصصین بیهوشی پیشنهاد نمود که مسئله چاقی را بطورجدی تری در بیهوشی کاربردی موردنظر قرار دهند . سرانجام نتایج به دست آمده در این تحقیقات بیانگر این مطلب است که گوسفندان ایرانی الگوی بسیار مناسبی برای این‌گونه کارهای تحقیقاتی می‌باشند .

be attributed to fat removal in amputated tail sheep.

Average recovery time in normal animals was 358.10± 65.77 minutes. But, recovery time in tail amputed animal significantly decreased from 358.10±65.77 to 204.50+88.49 minutes. The differences could be due to higher metabol - ism and excretion rate in amputated tail sheep; since, there is higher plasma concentration of thiopental in this group of sheep, due to lack of high fat tissue, consequently, the drug gets metabolized and excreted faster and recovery period becomes shorter.

Results obtained in this study could firmly prove the important role of obesity in human and veterinary anesthesia. These data also suggest that anesthesiologist should more seriously consider the obesity at the time of practice. All this experiment proves that sheep is a good model in this kind of research.

M.EDJTEHADI; S.GHOLAMI* & S. DEHGHANI*

SUMMARY:

Anesthesiologist in human medicine noticed that patients with higher defree of fat deposit need more anesthetics and also recovery period in these patients is longer than normal patients. These indicate the important role of fat deposit that may play in prolonged thiopental anesthesia. Unfortunately, due to lack of clinical model, to the best of our knowledge, no experimental studies has been yet designed to prove the experience that anesthesiologist have obtained during clinical practice. Consequently, we thought that the Iranian fat tailed type sheep could be the best model to be used; since this kind of sheep could deposit a large amount of fat up to 10% of its body weight or more, depending on strain and age, at its tail area.

Prolonged surgical anesthesia was induced in iranian fat tailed type sheep with initial dose of 26.51±5.82 mg/kg of body weight, and maintained successfully by repeatedly injecting the maintenance dose of 22.97±5.26 mg/kg, 20.31±5.67 mg/kg and 14.10±5.31 mg/kg of thiopental for 1st., 2nd. and 3rd. hour of anesthesia respectively in this study.

Maintenance dose in tail amputed animal is decreased respectively from normal sheep 22.97±5.26 to 21.99+6.34, 20.31±5.67 to 14.75+4.61 and 14.10±5.31 to 8.56±3.20 mg/kg during 1st., 2nd. and 3rd. hour of anesthesia. The differences between maintenance dose in normal and amputated tail sheep in 2nd. and 3rd hour of anesthesia could

* Department of Pharmacology, School of veterinary Medicine, Shiraz University, Shiraz, Iran.

Table 2. Shows the begining of different reflexes after 3 hrs. of thiopental anesthesia.

Table 3. Shows the begining of voluntary movements and recovery period after 3 hrs. of thiopental anesthesia.

Acknowledgments

The authors wish to express their thanks to Mrs.P. Lalehparvar for typing the manuscript.

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time of induction anesthesia. Consequently, the variablities in initial and maintenance dose in 1st. hour of anesthesia could be attributed to physiological state of each individual at time of anesthesia.

The decrease in maintenance dose in normal sheep (stage I) indicates that thiopental probably gets to equilibrium state in fat tissue after one hour of repeated injection. Thereafter, it starts decreasing at 2nd hour onward significantly. However, the differences between maintenanoe dose in normal and amputated tail sheep in 2nd. and 3rd hour of anesthesia could be attributed to fat removal in amputated tail sheep.

The differences in recovery time in normal and amputated tail sheep could be due to higher metabolism and excretion rate in amputated tail sheep; since, there is higher plasma concentration of thiopental in amputated tail sheep, due to lack of high fat tissue, consequently, the drug gets metabolized and excreted faster and recovery period becomes shorter.

The results obtained in this study could firmly prove the important role of obesity in human and veterinary anesthesia. These data also suggest that anesthesiologist should more seriosly consider the obesity at the time of practice. All this experiment proves that sheep is a good model in this kind of research.

Legends

Table 1. Shows percent of fat removal, initial and maintenance dose and recovery period in 3 hrs. of thiopental anesthesia.

not show any undesirable sign. But, recovery time significantly decreased from 358.10 + 65.77 to 204. 50+88 $\pm$49 minutes(Table 1). The decrease was also reflected in other parameters including down time, standing and full leg coordination which were important criteria during recovery period (Table 2,3). In the recovery period of animals in stage III, recovery signs frequently were not observable or did not appear in the right order as appeared in normal animals in stage I(Table 2,3).

In general, accumulative effect of thiopental was observed. Heart rate and rhythm and respiratory pattern in tail amputated sheep (stage III) were also normal as previously reported.

Discussion

Thiopental induced surgical anesthesia was successfully maintained for three hours in normal and tail amputated sheep in this study. Accumulative effect of thiopental was also observed in animals in both stage I and II. Sixty percent of tail amputated sheep(animal in stage II) showed that they need less initial dose than before tail amputation, while other fourty percent need slightly more initial dose of anesthetic (table 1).A noticeable and significant decrease was observed concerning the maintenance dose. The decrease specially was much more statistically significant from 2nd. hour of anesthesia onward (0.02 P 0.05).

The variable results that observed in initial and maintenance dose (1st. hour of anesthesia) could be easily explained; since, thiopental does not have time to distribute in fat tissue in both group of animals at the nance of anesthesia as already described in stage I.recovery peirod and signs were also checked in these animals as described before.

The results of this experiment was statistically analysed using student "t" test.

Results

Prolonged surgical anesthesia was induced in iranian fat tailed type sheep with initial dose of 26.51±5.82 mg/Kg of body weight, and maintained successfully by repeatedly injecting the maintenance dose of 22.97 ± 5.26 mg/Kg, 20.31 ± 5.67 mg/Kg and 14.10 ± 5.31 mg/Kg of thiopental for 1st., 2nd. and 3rd. hour of anesthesia respectively in this study (Table 1). Induction of anesthesia in tail amputated animals was also successfully induced with initial dose of 22. 94 + 5.74 mg/Kg thiopental sodium. Maintenance dose in this group of animal is decreased respectively from normal sheep 22.97 ± 5.26 to 21.99± 6.34, 20.31 ± 5.67 to 14. 75+4.61 and 14.10±5.31 to 8.56± 3.20 mg/Kg during 1st., 2nd. and 3rd. hour of anesthesia (Table 1).

All animals in stage I showed no complication or undesirable sign during recovery period. Sheep obtained their eyelids, pedal, jaw movement, cough reflexes and passed through standing and walking state up to full leg coordination smoothly. Average recovery time in these animals was 358. 10±65.77 minutes. During recovery period, the animal in stage III (amputated tail sheep) also did piratory patterns were monitored. After 3 hours of anesthesia thiopental sodium injection was discontinued and animal kept under close observation during the recovery period, up to the point that animal could climb up the stairs (full leg coordination)

Stage II(Fat removal or tail amputation).

All necessary clinical precautions, including cardio vascular and respiratory examinations, were taken before induction of anesthesia for all sheep The precedure of induction and maintenance of anesthesia were the same as previously described in stage I. However, sheep were positioned on left lateral recumbancy on table. The tail and its base was clipped and shaved carefully and prepared for an aseptic operation. After drapping, a curved incision was made at the level of first and second coccygeal junction dorsally and venterally through the skin by scalple. Then, the subcutanous fascia and fat layer was dissected blindly by a pair of scissors. The fibrous attachment of first and second coccygeal junction was seperated by scalple. Effort was made to remove all deposited fat at tail area. After fat removal the subcutaneous fascia was opposed together in a simple continous suturing pattern, and skin was sutured in a simple horizontal pattern. Almost all sheep had post surgical care for 2 weeks and no complication was observed.

Stage III(Thiopental anesthesia in tail amputated animal).

The same precedure was used for induction and mainte -

Blood samples were taken from free-flowing jugular vein of each sheep for analytical determination before induction of anesthesia. The following analytical methods were used: serum glutamate-oxalacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) activities were determined spectrophotometrically (510 m) in order to see the liver function. Blood urea nitrogen (B.U.N) was determined in order to be sure of kidney function as a routine. The experiments in this study were carried out in 3 different stages; Stage I (Thiopental anesthesia), Stage II (Fat removal or tail amputation) and Stage III (Thiopental anesthesia in tail amputated animal).

Stage I (thiopental anesthesia).

For induction of anesthesia, five percent thiopental sodium solution was freshly prepared and injected via jugular vein. The nearly half dose (obtained from our previous study) of thiopental injected during first mi - mute and then continued to observe the desirable effect. Then after, trachea was intubated. The head of animal was kept in lower level than the pharynx to facilitate the gravity flow of saliva out of oral cavity. A plastic cannula was inserted into jugular vein to facilitate the anesthetic injection. However, in order to maintain the animal in deep surgical anesthesia, the absence of eyelids, palpebral and pedal reflexes which are indicative of surgical anesthesia, were checked all the way through for 3 hours. Meanwhile, heart rate and rhythm, and ressonal lab. (1,2,3,4,5). From pharmacokinetic point of view also has been shown that plasma level of thiopental sodium remains, when repeated doses of thiopental used, near that in fat tissue. On the other hand anesthesiologist in human medicine noticed that patients with higher degree of fat deposit need more anesthetics and also recovery period in these patients is longer than normal patients. These indicate the important role of fat deposit that may play in prolonged thiopental anesthesia. Unfortunately, due to lack of clinical model, to the best of our knowledge, no experimental studies have been yet designed to prove the experience that anesthesiologist have obtained during clinical practice. Consequently, following experiments were undertaken in order to show the significant effect of obesity on prolonged thiopental anesthesia.

MATERIALS AND METHODS

Due to the lack of experimental model, we thought that the Iranian fat tailed type sheep could be the best model to be used; since this kind of sheep could deposit a large amount of fat up to 10% of its body weight or more, depending on strain and age, at its tail area.

Consequently, following self control experimental design has been set. Ten apparently healthy iranian fat-tailed type sheep, aged 12-14 months and weighing 24 to 36 killograms from both sexes were kept in ranch grazing condition and were supplemented with dry hay and water ad libitum.

Effects of obestiy on prolonged thiopental surgical anesthesia:

Iranian fat tailed type sheep used as a new model.

M.EDJTEHADI * S. GHOLAMI* & S. DEHGHANI*,

Since the introduction of ultra-short acting barbiturates to human and veterinary anesthesiology in 1938, thiopental is extensively employed advantageously for numerous conditions such as gynaecologic examination and setting fracture and so on. Thiopental is also used as induction agent before administration of inhalant anesthetics, inccluding halothane and methoxyflurane. It is true that thiopental is used for its brief action, but it may be used for prolonged anesthesia by repeatedly injecting and/or infusion doses as needed in places in which anesthesiologist are short of equipments. During world war II thiopental came into wide use as a routine anesthetics in human in front-line hospitals where equipment was limitted. as a consequence of wide spread use of thiopental all over the world, a great deal of research has been carried out concerning the effects of thiopental sodium on heart, respiratory system, acid-base balance, hematological pattern and biochemical values in our per-

* Department of Pharmacology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.