

EFFECTS AND RISKS OF THORACIC EPIDURAL ANESTHESIA FOR CARDIAC SURGERY

Mohammad Ali Sheikhi¹, Ahmad Ebadi^{2*}, Behnam Gholizadeh¹, Khosrow Sharifi¹

¹Assistant Professor of Cardiovascular Surgery MD, Department of Cardiac surgery, Atherosclerosis Research Center Golestan Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

²Professor of Cardiac Anesthesiology MD, Department of Cardiac Anesthesiology, Atherosclerosis Research Center Golestan Hospital and Pain Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

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*Correspondence for Author

Ahmad Ebadi

Professor of Cardiac
Anesthesiology MD,
Department of Cardiac
Anesthesiology,
Atherosclerosis Research
Center Golestan Hospital
and Pain Research Center,
Ahvaz Jundishapur
University of Medical
Sciences, Ahvaz, Iran.

ABSTRACT

The use of epidural techniques in patients undergoing cardiac surgery has increased in the past decade. Thoracic Epidural Anesthesia (TEA) compared with techniques base on narcotics in different types of surgeries, have points for the extra anesthetic and respiratory function. TEA provides good hemodynamic control and provides possible removal of the primary tube with better pulmonary function and a much milder pain after surgery.

KEYWORDS: THORACIC epidural anesthesia, Cardiovascular, Effects, Risks, Cardiac surgery.

INTRODUCTION

The popularity of local anesthesia has increased due to better understanding of the physiology of afferent nerve biopsy in the function of different organs, during the past 20 years. Epidural thoracic anesthesia (TEA) has some advantages over the previous anesthesia, and provides better pulmonary function compared with

narcotics techniques in a variety of surgeries. TEA due to these benefits has obtained high popularity in heart surgery, despite the possible risks. And the epidural techniques have been expanded in the recent decades, in patients undergoing cardiac surgery. TEA possible

benefits include improve of anesthesia after surgery, reduction of stress respond to surgery and are derived from cardiac thoracic sympathectomy.

In summary, numerous clinical studies including the use of epidural techniques in those patients undergoing cardiac surgery show that the use of thoracic epidural opioids or local anesthesia for patients before and after the cardio- pulmonary bypass, provides anesthesia after surgery, circulation, oral food intake and reliably gastro- intestinal function to relieve stress respond and improve of lung function after surgery.

2. Sympathetic block and thoracic epidural anesthesia

Given to the impact of thoracic epidural anesthesia on the postoperative output and pathophysiology, this kind of anesthesia has studied frequently. In scientific discussion, temporarily sympathetic piece block, considered to be a desirable outcome.

Although clinical and experimental data on sympathetic activity are rare during TEA and require careful interpretation, the embedding surface of catheter, volume and concentration of anesthetics and also methodological limitations of measuring the sympathetic activity are needed to be considered. Microneurography is the only technique that allows quantitative measurement of abnormal sympathetic activity. However, this method has various limitations in spatial resolution and is just limited to experimental studies on animals. Many data of indirect techniques based on performance measurement of surgery affected limb are obtained during the sympathetic block. Of course theses parameters are susceptible to the influence of the anatomy of capillary, emotional state and adjustment of temperature or existence of general anesthesia.

It is assumed that the TAE induces the piece sympathetic blocks which cover a minimum surface of sensory blocks. This block depending on the amount of insertion, and quality of the cervical epidural anesthesia and splanchnic sympathetic nerves and in the case of thoracic and mid- thoracic epidural anesthesia are performed of various cardiac sympathetic fibers in the high TEA. The sympathetic block should be limited to one piece and is associated with a compensatory increase of the sympathetic activity at its lower part.

Contrary to this perception, clinical studies failed to show the thoracic sympathetic block in the sensory block in TEA by using 4.2 ml of 0.75% of injected bupivacaine into Th6- Th9. Despite these negative findings, lately a thoracic sympathetic block before the surgery with

thermography in induced TEA is shown at low concentration and high volume of local anesthesia. During the mid- thoracic TEA, the decrease of skin temperature in Th4- Th12 compared with artificial group, was significantly lower which is shown a decrease in inducing- contraction of the sympathetic activity. Similarly, in the TEA continues model of rat, is recorded early and sustained increase at skin temperature of Th6, Th1 and Th12 dermatomes. In another rat model, the amount of 30 micro liter of 2% lidocaine was injected into the Th6 epidural surface and as the quality was determined by thermography, shows the increase in the temperature of the thoracic and abdominal skin.

Although it remains unclear that whether a piece of a high sensory thoracic block is associated with limited sympathetic block or not, in the experimental TEA on cats, the high TEA associated with the amount of 0.1 ml/kg of 1% lidocaine causes an induced cardiac sympathetic block (Th1- Th4). But it increases the sympathetic nervous activity (Th8), as recoded by the microneurography. In a similar study, lumbar epidural anesthesia caused renal sympathetic block and increased obstruction sympathetic block. Clinical data about limited obstruction piece of sympathetic activity in TEA has been inconclusive until now. In human sensory thoracic block which reaches to Th6, is observed during the high induced TEA by 75.0 percent of bupivacaine. Although in these patients, skin temperature in legs is also increased, that shows unlimited sympathetic block including visceral parts. In contrast to these findings, the amount of 4 ml bupivacaine 5.0% in Th4 causes sensory block less than Th8, but had no effect on sympathetic activity in the lower organs. Consequently, the concentration of local anesthesia may determine not only the intensity but also the extent of the sympathetic block. Greater volume of 25% bupivacaine is injected at the mid- thoracic surface and causes sympathetic block including complete reversing of sympathetic of legs.

3. Effects on heart beating and heart rhythm

A major protein from chronotropic and inotropic cardiac control are shipped by various vector fibers through the heart reflex arc in the five upper pieces of spine column. Animal studies have demonstrated the obvious effect of TEA on the cardiac electrophysiology. Hatvedet et al (1983) have shown increased ventricular effect and functional resistant periods, and also prolonged single phase action potentials in dogs. It is not clear that the sympathetic nervous system directly acts as a cardio-accelerator, or indirectly is doing its work by modifying the parasympathetic tone. Messner et al (2001), studied the isolated cardiac sympathectomy by TEA in conscious dogs, and have found the prolong repolarization

and prolong refractory period in the ventricular location in compared with atrium. Slight but outstanding decrease in the heart beating by TEA can be observed in healthy volunteers and undergoing surgery patients. Takashima and Dohi (1985) have shown in healthy volunteers that the cervical epidural blocks are created only slightly in baroreflex; these results are similar to the results obtained by Bonet et al (1989) in patients who have undergone carotid artery surgery, and in them the nerve stimulation block of cardiac sympathetic reduces baroreflex activity without completely disabling. High TEA (T1- T5) which has deprived the lower thoracic areas and has not blocked lumbar regions of heart circulation response-mediated sympathetic to various pressures such as tracheal intubation and hypercarbia. Although the overall reduction in sympathetic tone and obstruction of cardiac accelerator fibers can reduce the risk of observed dysrhythmia during the cardiac surgery and cardiopulmonary bypass and randomized controlled experiments despite a dramatic reduction in sympathetic activity, cannot create reduction in the incidence of sustained atrial fibrillation after surgery.

In the same way the direct temporal relationship is not provable between the presence and absence of TEA and incidence of atrial arrhythmia.

4. Coronary blood flow

The large epicardial coronary artery is densely filled by adrenaline nerve fibers. Heart stimulation of cardiac sympathetic either in animals and human causes vasoconstriction of the normal and sick coronary segments. In a model of canine experimentally from local anemia of induced myocardial, cardiac sympathectomy by TEA has shown to improve local blood flow. Epidural severe blocking is re-distributed the coronary blood flow to make desirable endocardium in the natural and being blocked heart. Davis and his colleagues (1986), confirm these observations with their findings of the changes in myocardial oxygen supply/ ratio demand in addition to reducing of hemodynamics and correlations of myocardial oxygen consumption. In patients with severe CAD and unstable angina, high TEA relieves chest pain and has a favorable impact on the key factors of determining myocardial oxygen consumption by reducing the systolic arterial blood pressure and heart beating and also pulmonary artery and pulmonary capillary pressure, and does not cause significant change in coronary blocking pressure. These results have been confirmed in a recent randomized controlled trial which in it, the block with 5-10 ml of 3% ropivacaine, increases myocardial

oxygen level prior to the re-formation of blood vessels without damaging hemodynamic perturbations.

As a whole, TEA without compromising the coronary venous pressure in myocardial areas with local anemia, will improve oxygen supply and demand ratio. Furthermore, cordial selective epidural blocks may increase luminal diameter of pieces with stenosis of the lumen of the epicardial coronary arteries, by no affecting on diameter of the without stenosis pieces and by no influence on coronary resistance vessels.

5. Effect of topical anti-anemia of TEA

It has been shown that TEA reduces the adverse cardiac events before surgery. Better pain relief with a continuous decrease in blood pressure response after surgery and systemic sympathetic activity may contribute in this effect.

Regional sympathetic block includes cardiac sympathetic nerves not only reduces the pain of localized anemia, but also improves coronary artery pressure during the measuring of the cold blood pressure. This effect is most obvious in stenotic vessels. These data confirm findings about influence of localized anti-anemia before TEA surgery in cardiac surgery. Also TEA improves the diastolic function in patients with coronary artery disease that incurs the formation of new blood vessels. The function of diastolic condition has reported as an early sign of localized anemia in heart. In this study, any influence has not registered on the systolic function. But a study has shown improve of systolic function and mural motion in patients with coronary artery. Troponin release, the long- term survival after coronary artery bypass, has shown potential for cardiac support. TEA in the localized anemia of experimental myocardial reduces the infarct size. Clinical data are not conclusive on the myocardial localized anemia and mortality. TEA in a randomized experiment, 30-day complication rate did not decline after the cardiac surgery. TEA study in most patients has used just for 24 hours. While after coronary bypass grafting, applied TEA reduced arrhythmias for 72 hours and has improved postoperative pain control and recovery. The next great experiment on the effects of TEA output does not show improvement in survival after surgery. Although this experiment is reduced to show the average effect of TEA, and thus the interpretation of the results may be inaccurate. Some high- level analyzes show that Tea can reduce the incidence of heart disease and morality after the cardiac and mostly non-cardiac surgery. While others do not confirm this and are emphasized on reduce of incidence of diseases such as respiratory problems and cardiac arrhythmias, after the cardiac surgery.

6. TEA and severe drop blood pressure

In healthy volunteers, systolic and diastolic pressures decrease after epidural anesthesia. Severe drop blood pressure is partly due to reduction of cardiac activity and partly is also due to the swelling of the blood arteries and veins vessels. Peripheral vascular tone with adrenergic alpha and beta reporters and indirectly controls by circulating of the released catecholamines from adrenal glands and as a result, the sympathetic outflow between pieces of T5 and L1.

Range of reducing effect caused by high epidural block can be quite extensive, depending on the amount of the removal of afferent of spine column piece. In dog as a model, the roots of the upper thoracic prove lateral difference in the influence on homeostasis. For example, an increase in the blood pressure is highest when four roots of thoracic on the left side are stimulated, which in this case T1 has the largest response and after that, are T3, T2 and T4. Unlike that T5 on the left side, gives a non- significant response, while T5 response on the right size is significant. If these findings can be extrapolated in to human, the biggest pause in blood pressure should be observed while targeting of the upper piece of chest in the left side. Detained effects of tourniquet sympathetic outflow lead to the functional hypovolemia. The epidural anesthesia itself has no effect on the intravenous volume or hemoglobin concentration. Holt et al (2004), are carefully examined changes in plasma volume and venous fluid kinetics after TEA, by implementation of vasopressor or plasma expander in 12 volunteers, and has found a dramatic reduction in the hemoglobin concentration after hydroxyl ethyl searching. So vasopressors may be preferred to treat severe drop of blood pressure after TEA, and not only for patients with cardio- pulmonary diseases. Patients' undergone surgery can also benefit from this regime with water restriction. So should be prevented from the voluminal preload to neutralize the drop of blood pressure after the influence of TEA.

If the sympathetic block is not too great, the vasodilatation and the blood separation can be compensated to some extent with vasoconstriction in the remained unblocked areas. In addition, the increase of activity in the remained unblocked visceral nerve fibers can cause circulating of catecholamines and also cause their releasing from cerebrospinal system, and as a result is involved in an increase in the sympathetic activity below the blockage site.

Renin- angiotensin and vasopressin systems act as the support mechanisms for the maintenance of arterial blood pressure during the circulation problems in humans and

animals. TEA with integrity of the rennin- angiotensin system in a patient by blocking sympathetic fibers conflicts before the nervous node, but at the same time increases the concentration of vasopressin and at the time of creation of Sympatho- adrenal responses, probably it reduces the arterial blood pressure to compensate cardiac filling.

Despite the influence of hypotensive, some studies have even shown a profitable output for epidural anesthesia during the hemorrhagic shock. Shibata et al (1989) found that beginning of TEA before the severe bleeding increases the survival rates and reduces the metabolic acidosis in dogs. The survival rate, increases especially in the case of more use of TEA.

The survival advantage in using of more TEA cannot be explained just by differences in the rate of plasma catecholamines. In fact, Shibata and his colleagues have not found a clear difference in the amount of catecholamines at any point of time, for TEA treatment after severe bleeding in dogs with and without venous injection of epinephrine and norepinephrine. This shows that difference in the amount of catecholamines in the direct amount of nervous terminals or the other factors may have a greater impact on the survival rate.

7. The cardio- vascular response to hypoxemia and hypercapnia

TAE can moderate blood circulation to maintain arterial blood pressure during the hypoxemia. Two studies in the canine assess the cardio- vascular response to the hypoxemia during the epidural anesthesia.

Peter and his colleagues (1990) have reported that TEA, in conscious dogs, makes slow change in vital signs in response to the short- term hypoxemia, while improves the secretion of vasopressin and maintenance of the ventilator response. Consistent with these results, Shibata and his colleagues, concludes that the longer period during the hypoxemia ($FiO_2 = 0.09$ for 120 min) in anesthetized dogs, TEA in this case can remove the early cardio-vascular signs, but TEA reduces the needs for oxygen in myocardial, it also increases the extraction of oxygen from blood and reduces the development of acidosis metabolic.

Data are contradictory due to the effects of epidural blocks on the effects of hypercapnia. The thoracic and thoracic- lumbar epidural anesthesia in dogs, during the cardiac output, distributes the hypercapnia and the middle arterial blood pressure. Of course physiological increase in the amount of circulating catecholamine will just disappear in the group of the thoracic- lumbar epidural. However, previous studies in aroused humans were not found

significant changes in the heart beating and the blood pressure, after blockade of thoracic epidural of uterus cervical, in response to CO₂, and no ventilation and no response was received for ventilation. Further studies are needed to understand the physiological mechanisms.

8. TEA in the coronary artery bypass

Patients undergoing coronary artery bypass graft (CABG) have an increased risk of cardiac postoperative complications, and therefore, strategies for reducing of the postoperative risk of affection have focused on various studies and experiments. Liem and colleagues (1992), studied the effects of TEA in 30 patients who undergone the coronary artery bypass graft. TEA with 0.375% of bupivacaine and 5 µg/mL of sufentanil was applied in combination of the general anesthesia with ration of N₂O/ midazolam. The epidural block was spread to the part T1 from T10. Hemodynamic results, the postoperative results and adrenergic response were compared with the sufentanil IV receiving group and midazolam. Hemodynamic stability and low heart beating, lead to reduced using of nitroglycerin for treatment of myocardial ischemia in TEA.

After surgery, patients who received TEA during and after coronary artery surgery, conscious earlier and also the chip is removed earlier. The TEA effect was described first by Joachimson and colleagues (1989), which is able to improve patients at least 2 hour after coronary artery bypass surgery. These patients in contrast with the IV anesthesia were less sedated and the improvement of pain was better. The better function of cardiac- pulmonary variables was improved. In investigation of changes in stress hormones in 20 patients, Liem and colleagues (1992) found that less increase in norepinephrine and less diversity in the concentration of epinephrine during the anesthesia with TEA combined during the coronary artery bypass grafting. Cortisol release during the bypass was higher in the general anesthesia/ TEA group than general anesthesia. During the first day and second day after surgery, plasma epinephrine and cortisol levels were lower in TEA.

Recent studies have confirmed the results of Liem and colleagues (1992). Stenseth and colleagues (1994) compared TEA effects as an aid for small or large dose of fentanyl against large dose of fentanyl in 30 patients undergoing coronary artery bypass (CABG). TEA contains 10 ml of 5% bupivacaine followed by 4 ml per hour. Although the researchers given to the strong sedatives are not able to test the extension of block, according to the “TEA

experience” they assumed the spread of obstruction from T1 to T12. Hemodynamic stability was again better in both of TEA groups, by need to reduce propranolol and nitroglycerin in the both of TEA groups. Better hemodynamic stability and early extubation in patients who have been received small doses of fentanyl, in relation to bupivacaine for TEA in contrast with high dose of fentanyl were studied again by Stenseth and colleagues (1994). They also confirmed that postoperative function of pulmonary is better, and in the TEA group the extubation was done faster ($P < 0.05$). Achieve to adequate occlusion but too long and lack of using of smaller dose of localized anesthesia seems to be preferred in this case.

Trying to avoid endocrine and/ or metabolic response to the surgery and reduce of the postoperative complications has been the focus of a number of studies and experiments. The neuroendocrine response to surgery, trauma, and myocardial infarction lead to increase of plasma concentration of free fatty acids, which resulting in increase of oxygen consumption of myocardial, which can help to myocardial ischemia and apoplexy in patients with reduce of coronary reserves. Hotvedt and colleagues (1984) has shown the reduction of concentration of free fatty acids in plasma, during TEA. Reducing of myocardial oxygen consumption may have beneficial effects on the ischemic conditions.

9. Dangers of TEA

Patient safety issues are a dominant aspect in the clinical use and understanding of patient from TEA. However, the risk of injury as a result of TEA is less than the other postoperative treatment strategies.

For example, study of the balance of treatment of the blocker-b after surgery in one patient of 98 patients who were undergoing for treatment causes death or neurological deficit. This risk is much higher than TEA, but can say that its sign are far clearer. And usually is not related clearly to the treatment intervention, which leads to caution in the use of TEA in critically ill patients, despite the potential benefits (Devereux and colleagues, 2008).

9.1. Epidural hemorrhage after TEA

Up to date, the risk of bleeding complications after epidural anesthesia and specifically after TEA are not known. However, there is evidence that suggest the total number of vertebral canal hematoma after epidural block may be misleading in clinical decision making. The overall incidence of bleeding in the spinal canal in decade1990 was 01:18 000 in Sweden. These numbers, however, included patients with epidural in childbirth who are at the low risk

of hemorrhage of spinal column after epidural puncture have been in past analysis and in the most recent providence of audit project 3 (NAP3) in the UK. The patient's postoperative epidural bleeding risk was higher in pervious study and the risk for surgical patient is 1:10 200, which is based on data from prospective NAP3. 5747(pessimistic estimate) and 1:12 195 (optimistic estimate) in the postoperative patients: in this study, the estimation risk of vertebral canal hematoma finds expression in range between 1: 27 000 and 1: 4761 in a recent analysis of central database. (Moen and colleagues, 2004; Cook and colleagues, 2009).

These numbers, however, are including TEA and lumbar epidural. In the Swedish study, hematoma occurred after eight TEAs and 17 epidural puncture in lumbar areas. However, it is not clear that how often the related procedure was performed, and the estimated risk of TEA is not possible. In NAP3, five cases of eight bleeding complications occurred after TEA, but are not available the number of fundamental lumbar epidural and TEA. It seems that there is a higher risk of bleeding complications with TEA compared with lumbar epidural block. This is supported by the past analysis with 8100 person, in which occurs three hematoma pieces of spine column after TEA, but none of them occur after the epidural lumbar puncture. The total numbers of relevant procedures have not been provided. In contrast, no epidural bleeding has been reported in 10 000 cases of TEA, but three cases of them occurred after the lumbar epidural anesthesia and as a result the risk of affliction has occurred in 1: 832. Age and sex of patients appears to have major influence on spine column hematoma after the TEA (Moen and colleagues, 2004).

Existing information have appropriate estimation from the overall risk of epidural anesthesia, but have not good conclusion for incidence of bleeding complications with TEA. TEA should be done with caution in patients who receive anti -platelet, anti -coagulant, and/ or fibrinolytic drug. Sudden increase in bleeding with low molecular weight heparin (LMWH) daily twice has led to the first national guidelines on the use of block neuraxial in anti-coagulation patients. In 2010, the European direction was update and now covers the introduced anti-platelet and anti- coagulant drugs. Gogarten and colleague, (2010) recommended that see the patients with normal drug excretion. In patients with impaired organ function (unknown), for example, kidney failure, carful patient selection and the evaluation of adaptation are essential. The glomerular filtration can evaluated from creatinine serum, by a simple valid equation in modification of diet in renal disease (MDRD) tests. The risk of bleeding after epidural anesthesia in older women is emphasized in studies.

For example, even mildly impaired of renal function, LMWH increases the effective time of consumption of anti- coagulation drugs from 6.6 to 9.9 hour. LMWH takes 15 hours in the chronic kidney disease. In these patients, a 50% reduction in dose of LMWH is required. Many cases of elective surgery in hospital are not for more than 1 day before the surgery; as a result, the consumption of anti- coagulation and prevention drugs can be started in the night after the surgery. This guarantees TEA maximum safety even in older patients with impaired renal function.

Withdrawal of anti- platelet drugs can lead to effects with increased rate of thromboembolic events. This effect of reaction escalates by thrombotic and inflammatory response after surgery.

Stopping consumption of the anti-platelet drugs within 3 weeks after stenting will result in 30- 86% of mortality. Late stent thrombosis after stopping the consumption of anti-platelet drugs can occur more than 1 year after stenting. As a result, is achieved a consensus to continue the anti-platelet drug in almost all cases with emergency surgery including the spine column, intracranial, and intraocular surgeries in which hemorrhage is potentially catastrophic, and bridging with tirofiban and heparin are recommended (Chassot and colleagues, 2007). In patients who are taking acetylsalicylic acid, the instructions of United States and Europe allow that neuraxial blocks in time and dose, unlimitedly (Gogarten, and colleagues, 2010). In all instructions are emphasized greater risk concomitant use acetylsalicylic acid and the other anti- coagulant. While acetyl acid is considered as a safe anti-platelet treatment, thienopyridine derivatives such as clopidogrels are not recommended 5- 7 days before TEA. Such a warning in incidence of bleeding is about thienopyridines surgery and two cases of hematoma vertebral column after blocked neuraxial by clopidogrel drug. Recently, 309 cases of vessels surgery were published treated with lumbar epidural anesthesia. Of these, 217 cases were for dual inhabitation of platelet aggregation with acetyl acid. Any of the patients did not show the sign of bleeding in spine column and/ or epidural. There are two cases of removal of epidural catheter after initiation of dual anti-platelet treatment due to the postoperative myocardial infarction. Of course, this process is described without complication after spinal anesthesia during the treatment of dual anti-platelet. In contrast, some of the reported have been shown serious concerns in cases of spontaneous hematoma of spine column during the dual anti-platelet treatment without anesthesia.

Moreover, the spontaneous spinal hematoma is described with clopidogrel and acetyl acid. Thus, these cases should not lead to a safe assumption (Gogarten, and colleagues, 2010).

9.2. Complications of infection

TEA is an invasive analgesic technique and inevitably associated with the risk of complications due to infections. Consequence of infected pathogen and haematogenous infection from entrance and/ or epidural catheter are the potential causes of infection in the spinal canal. The estimation of incidence is widely various. Recent data from Germany report an incidence of an abscess in 10000 cases that treated with TEA. In the UK, there is the incidence of 000 1: 24 of epidural abscess after postoperative neuraxial block with 10 cases of 13 patients in the study period relates to the epidural anesthesia (Cook and colleagues, 2009). For treatment of children with postoperative pain, epidural abscess and infections are rare. The epidural abscess with spinal and the root compression are dominant compression that after TEA and usually are caused by the staphylococcus aureus. Also meningitis have been reported, but with lower incidence. This means that meningitis is usually caused by streptococcus. Infectious complications may occur on the second day, but usually incidence is in the fourth day. They may be accompanied by signs of wound infection in the entrance site, but they are usually associates with nonspecific symptoms. Often they asserts in diagnosis of the results and necessity of clinical observations and high level of suspicion. The complications obtained by infection are better that epidural bleeding (Cook and colleagues, 2009).

SUMMARY AND CONCLUSIONS

The thoracic epidural anti-analgesia has significant influence on the cario- vascular system. Given to the electrical activity of the heart in the animal models, a TEA was found with repolarzation and more resistant period in ventricle and in atrium. Also, AV transformation and resistance have become too long. Human studies have recorded a partial impaired in the reflex sensitivity of sensor, but small amount were respond for sympathy with different stressors agents if TEA is limited to the first five thoracic vertebrae. Although it may reduce the overall risk of postoperative dysrhythmias, TEA did not reduce the incidence of postoperative atrial fibrillation. Animal studies have produced conflicting results regarding the effect of TEA on ventricular function. TEA in healthy people seems for the changing of contraction of the left ventricle and reduces of cardiac output, while it maintains well the

motion of the general and regional of the left ventricular wall in patients who have heart surgery.

TEA is shown in canine models for the improve of regional blood flow of heart in favor of endocardium, and in human patient is shown for reduction of the major causes of cardiac oxygen consumption and even for increase of stenosis of lumen diameter of the coronary artery without compromising coronary perfusion pressure.

Therefore, TEA can reduce the severity of acute cardiac ischemic injury and can facilitate recovery after a short ischemic in the experimental models. In patients, changes in troponin T and national polish are not compatible, but it is clear that TEA reduces the natriuretic peptide levels of brain and as a result the total incidence of myocardial infarction. Moreover, it interferes with integration of the rennin- angiotension system, but gradually increases the vasopressin concentration in plasma. Despite its reducing effect, TEA has shown therapeutic benefit during the hemorrhagic shock. Response to hypoxemia but not to hypercapnia was provided by TEA. TEA produces applied hypovolemia by inhibiting the vasoconstrictor output.

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