Dexmedetomidine Induced Hypotension

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INTRODUCTION

Induced or controlled hypotension

- method by which the arterial blood pressure is decreased in a predictable & deliberate manner.

The intent of deliberate hypotension is :

- to reduce bleeding (facilitate surgery)

-to decrease the amount of blood transfused.

-In other procedures, a dry field may result in a more definitive removal of a neoplasm as well as in less damage to vital structures.

-trauma and tissue infection are minimized because fewer sutures are required and less electrocoagulated, devitalized tissue remains in the wound.

DEFINITION

- Generally, it is taken that a MAP as low as 50 mmHG or a 30% drop in MAP is safe for an ASA 1 subject.

- This might not be appropriate for a chronic hypertensive patient who may not tolerate a drop of more than 25 % of the MAP.

N.B : This level might not be appropriate for a patient with cerebrovascular disease who may not tolerate any drop whatsoever in the MAP.

⇒With reference to the discussion on physiology above, it is suggested that inducing hypotension to a MAP of 30% below a patient's usual MAP, with a minimum of 50mmHg in ASA 1 patients and 80mmHg in the elderly is clinically acceptable

B) CORONARY CIRCULATION

- Coronary blood flow is dependent upon the aortic diastolic blood pressure and the coronary vascular resistance.

- Control of coronary blood flow is autoregulated predominantly by means of alteration in coronary vascular resistance that are made to meet myocardial oxygen demand.

Hypotensive anaesthesia will decrease coronary blood flow.

↓

However, it simultaneously decreases myocardial oxygen demand due to the reduction in afterload or/and preload.

↓

Furthermore, coronary autoregulation ensures adequate myocardial blood flow.

Studies have shown that during hypotensive anaesthesia there is a poor correlation between the lowest degree of hypotension achieved and the development of ischaemic ECG changes (Rollason et al, 1991-96)

BE CAREFULL!!!

- Patients with coronary artery disease may have some areas of myocardium that are entirely dependent upon pressure to supply adequate blood flow. In addition, the use of vasodilators in these patients may induce a steal phenomenon.

Hence, controlled hypotensive anaesthesia is accompanied by significant intraoperative risk of myocardial infarction.

C) RENAL CIRCULATION

- Renal blood flow is controlled in two ways : extrinsic autonomic and hormonal mechanisms and intrinsic autoregulation

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- Autoregulation of renal blood flow :

When decreased renal blood flow occurs with even moderate decreases in arterial blood pressure (systolic value of 80-90mmHg).

- <u>If arterial blood pressure drops below these values renal blood flow may decrease to a point where urine flow stops. Also, when the MAP drops below 75mmHg, GFR falls</u>

D) HEPATIC CIRCULATION

- Most of the liver blood flow (70%) is via the portal vein. The remainder of the liver blood flow is supplied from the hepatic artery. The splanhic circulation is richly innervated by the sympathetic nervous system.

***In contrast to the brain and kidney, the liver is not an autoregulated organ.

- Therefore a decrease in arterial pressure will lead to a decrease in liver blood flow.

E) RESPIRATORY SYSTEM

During controlled hypotensive anaesthesia the following occurs:

- Pulmonary blood flow gravitates to the dependent areas of the lungs. → Hence, the non dependent regions are ventilated but not adequately perfused → increasing dead space.

**This scenario is aggrevated by the head up position.

- The use of vasodilators to induce hypotension

➡ inhibits the hypoxic pulmonary vasoconstriction response ➡ increasing intra-pulmonary shunt.

➡ lead to hypercarbia, an increase in arterial-end tidal CO_2 gradient and hypoxaemia ➡ Hence, regular $PaCO_2$ measurements are necessary during controlled hypotension.

= so a higher FiO_2 may be necessary.

- CONTRAINDICATIONS : use of Hypotensive Anaesthesia

ANAESTHETIST LIMITATIONS

- Lack of understanding of the technique
- Lack of technical expertise
- Inability to monitor the patient adequately

- PATIENT LIMITATIONS

- Cardiac disease
- Diabetes mellitus
- Anaemia, haemoglobinopathies, polycythaemia
- Hepatic disease
- Ischaemic cerebrovascular disease
- Renal disease
- Respiratory insufficiency
- Severe systemic hypertension
- Intolerance to drugs available to produce hypotension

RISKS OF HYPOTENSIVE ANAESTHESIA

- By far, the commonest causes of mortality was compromise of the circulation to vital structures such as the kidney, brain and the heart.

  Other causes of mortality included reactionary haemorrhage, high spinal anaesthesia, over heparinization following arteriotomy, arterial air embolism, pulmonary infarcts and pulmonary oedema

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TECHNIQUES : of Hypotensive Anaesthesia

- MAP = CARDIAC OUTPUT X SYSTEMIC VASCULAR RESISTANCE

- Hence MAP can be manipulated by reducing either SVR or Cardiac output or both. Inducing hypotension purely by a reduction in cardiac output is not ideal because the maintenance af tissue blood flow is essential.

- SVR can be reduced by peripheral vasodilation (of the resistance vessels) whilst cardiac output can be reduced by lowering venous return, heart rate, myocardial contractility or a combination of these.

- METHODS TO REDUCE PERIPHERAL VASCULAR RESISTANCE

- 1. Blockade of alpha adrenergic receptors eg. Labetalol, phentolamine.
- 2. Relaxation of vascular smooth muscle eg. Direct acting vasodilators (nitroprusside), calcium channel blockers, inhalational agents, purines (adenosine), prostaglandin E1.

A hypotensive technique reduces the peripheral circulation. This is especially important in areas overlying weight-bearing and bony prominences.

Hence,

additional supportive pads should be placed beneath the patient with special attention paid to the occiput, scapulae, sacrum, elbows and heels. Also, pressure must be kept off the orbits (especially in the prone position) to avoid compromising retinal blood flow

Pharmacologic technique

- **Ideal agent**
  - Ease of administration
  - Predictable & dose-dependent effect
  - Rapid onset/offset
  - Quick elimination without the production of toxic metabolites
  - Minimal effects on blood flow to vital organs

Inhalational anesthetics

negative inotropic effect
vasodilation

Advantage

- Provides surgical anesthesia
- Rapid onset/offset
- Easy to titrate
- Cerebral protection

Disadvantage

- Decreases CO
- Cerebral vasodilation

Sodium nitroprusside

Direct vasodilator (nitric oxide release)

Advantage

- Rapid onset/offset
- East to titrate
- Increases CO

Disadvantage

- Cyanide/thiocyanate toxicity
- Increased ICP
- Increased pulm. shunt
- Sympathetic stimulation
- Rebound hypertension
- Coronary steal
- Tachycardia

Nitroglycerin

Direct vasodilator (nitric oxide release)

Advantage

- Rapid onset/offset
- East to titrate
- Limited increase in heart rate
- No coronary steal

Disadvantage

- Lack of efficacy- depending on anesthetic technique
- Increased ICP
- Increased pulm. shunt
- Methemoglobinemia
- Inhibition of plt. aggregation

Beta adrenergic antagonist

Beta adrenergic blockade (will decreased myocardial contractility)

Advantage

- Rapid onset/offset
- Decreased myocardial O2 consumption
- No increase in ICP
- No increase in pulm. shunt

Disadvantage

- Decreased CO
- Heart block
- Bronchospasm
- Limited efficacy when used alone

Calcium channel blocker

- vasodilation

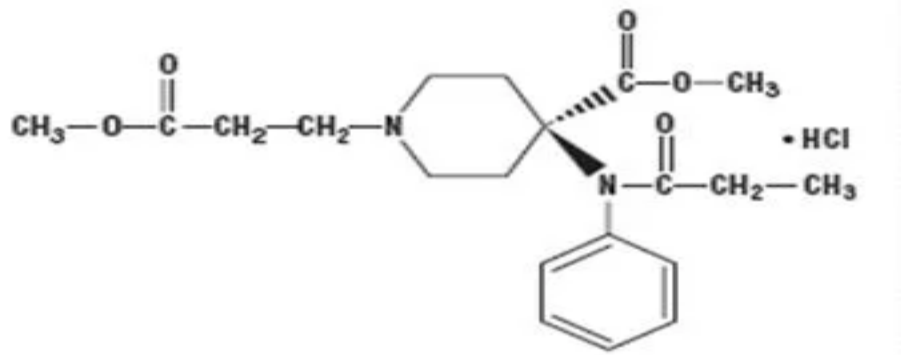
Advantage

- Rapid onset
- Limited increase in HR
- Increase CO
- No effect on airway reactivity
- Increased GFR/urine output

Disadvantage

- Prolonged duration of action
- Increased ICP
- Increased pulm. shunt

Remifentanil



- **Remifentanil is an OPIOID**
- **Pure μ agonist**
  - **little binding at κ, σ, and δ receptors**
- Rapid onset/offset
- Decreases blood pressure & heart rate
- No need for additional use of a potent hypotensive or adjunct agents

Remifentanil Key Concepts

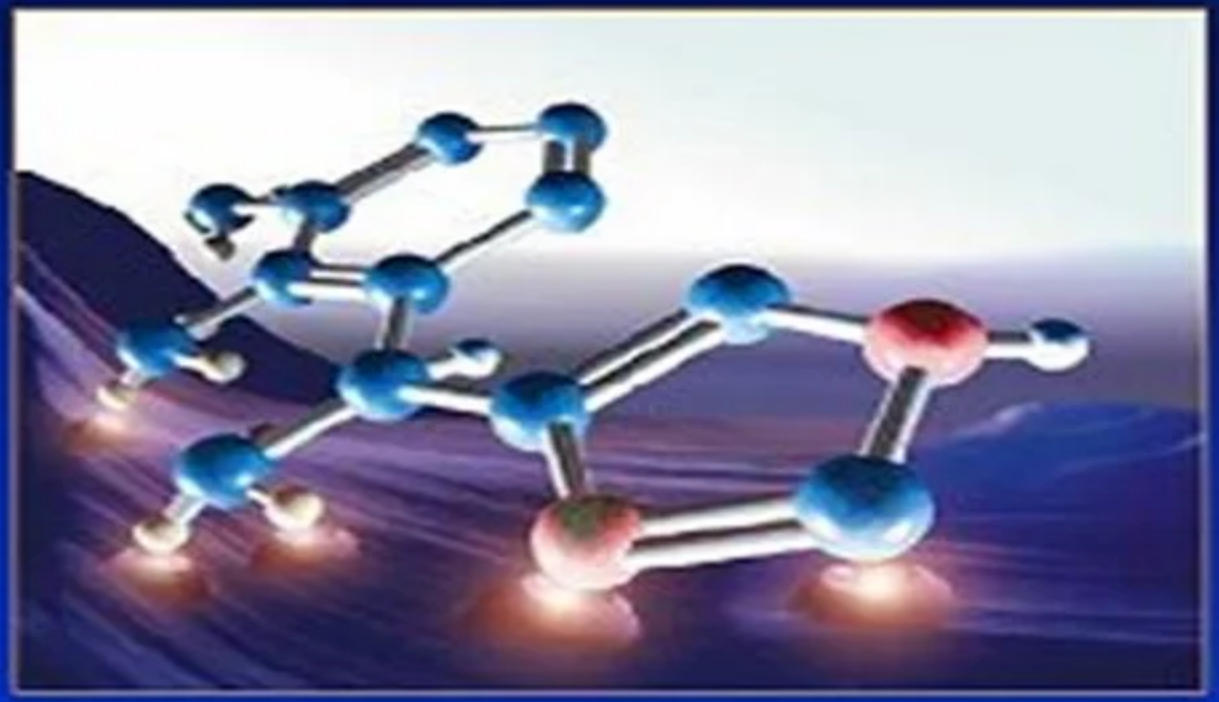
- Remifentanil is an metabolized by nonspecific esterases in blood and tissue

- Anesthesia maintained with high-dose remifentanil will be associated with rapid recovery.
  - Within 5-10 minutes of turning off an infusion there is virtually no residual remifentanil drug effect

Dexmedetomidine: alpha$_2$ adrenergic selective agonist

- Dexmedetomidine selectively acts on alpha$_2$-adrenergic receptors in the brain and CNS[1]

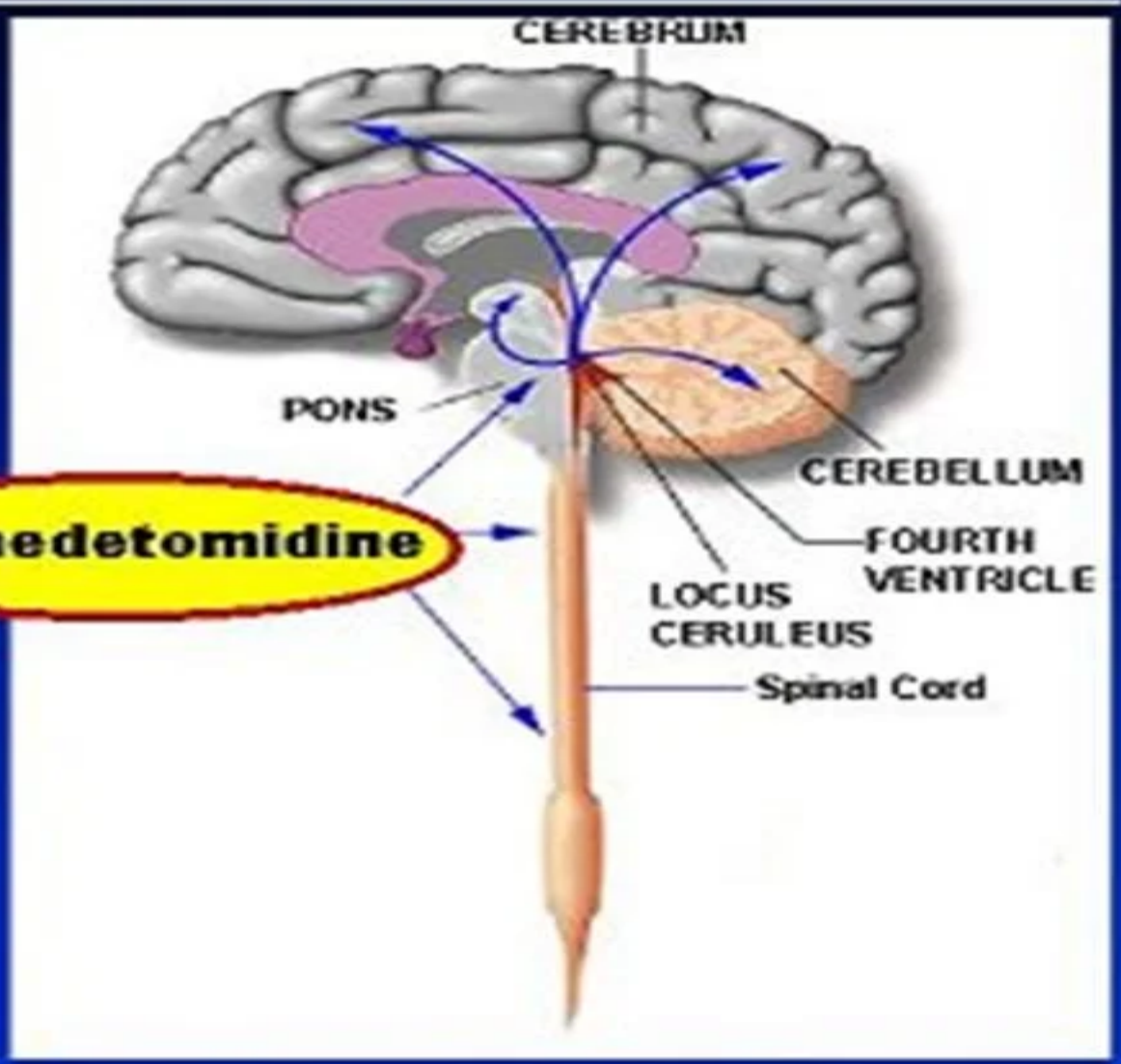
Drug	α_2/α_1 selectivity
Dexmedetomidine	1,600
Medetomidine	1,200
Clonidine	220
I-medetomidine	23



1. Dyck, Shafer. *Anaesth Pharm Review.*1993;1.

Dexmedetomidine, α_2 receptors, and the CNS

- **Sites of action**
  - Brain (locus ceruleus)
  - Spinal cord
  - Autonomic nerves
- **CNS**
  - Sedation/hypnosis
  - Anxiolysis
  - Analgesia
- **Autonomic nerves**
  - ↓ Sympathetic activity
  - ↓ BP, ↓ HR



Dosing and Administration

- Dex. should be administered using a controlled infusion device.
- Dex. dosing should be individualized and titrated to the desired clinical effect
- For adult patients Dex. is generally initiated with a infusion of 1mcg/kg over 10 minutes, followed by a maintenance infusion of 0.2 to 0.7 mcg/kg/hr
- It is not necessary to discontinue Dex. prior to extubation

Journal of Cellular & Molecular Anesthesia (JCMA

Original Article

Effect of Bupivacaine and Combination with Dexmedetomidine and Dexamethasone on Mice Neural Apoptosis

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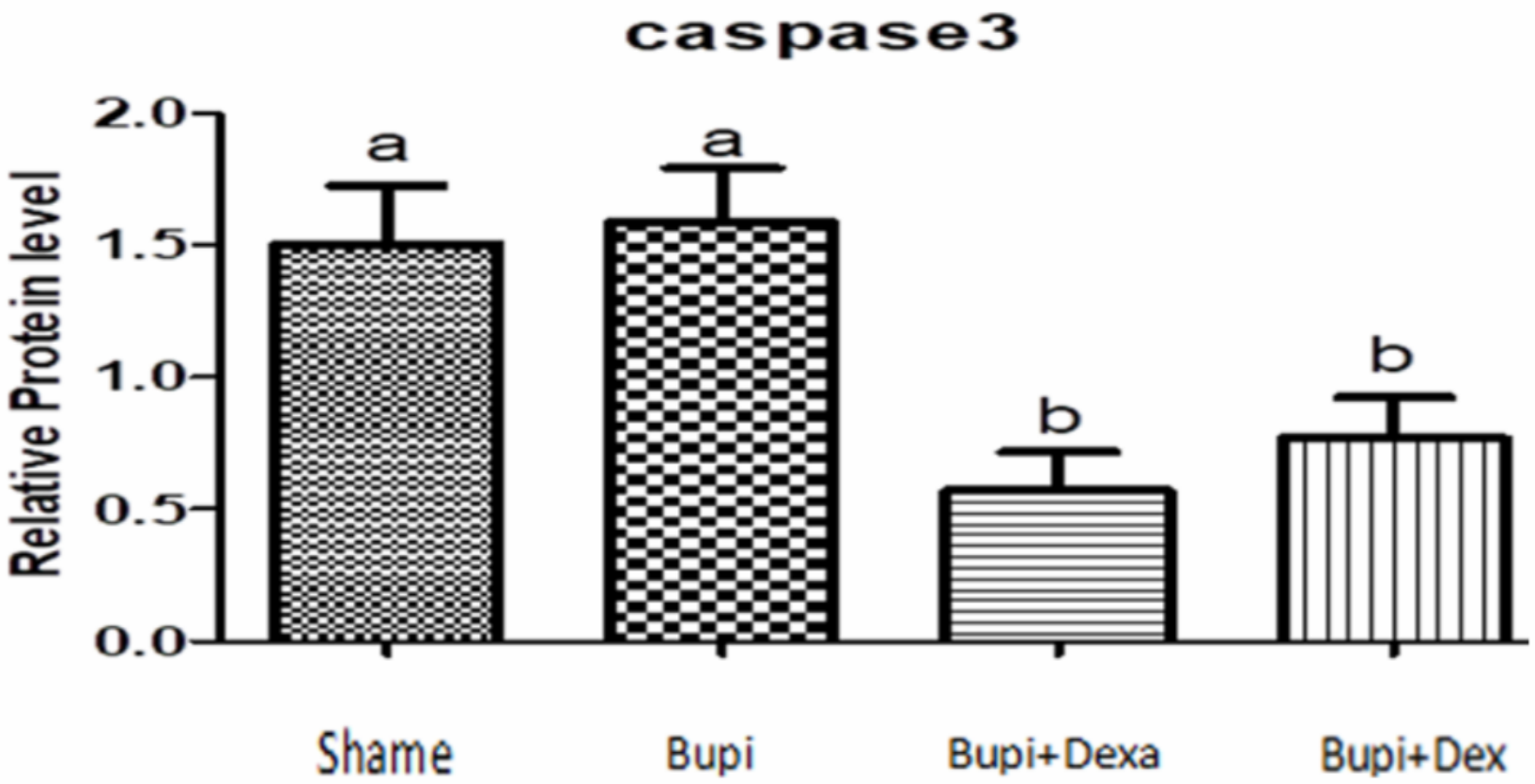

Figure 1. Diagram (P. Value) of caspase3 expression compared to GAPDH in rat femoral nerve (24 h after injection) in four groups (control, bupivacaine, bupivacaine + dexamethasone and bupivacaine + dexmedetomidine).

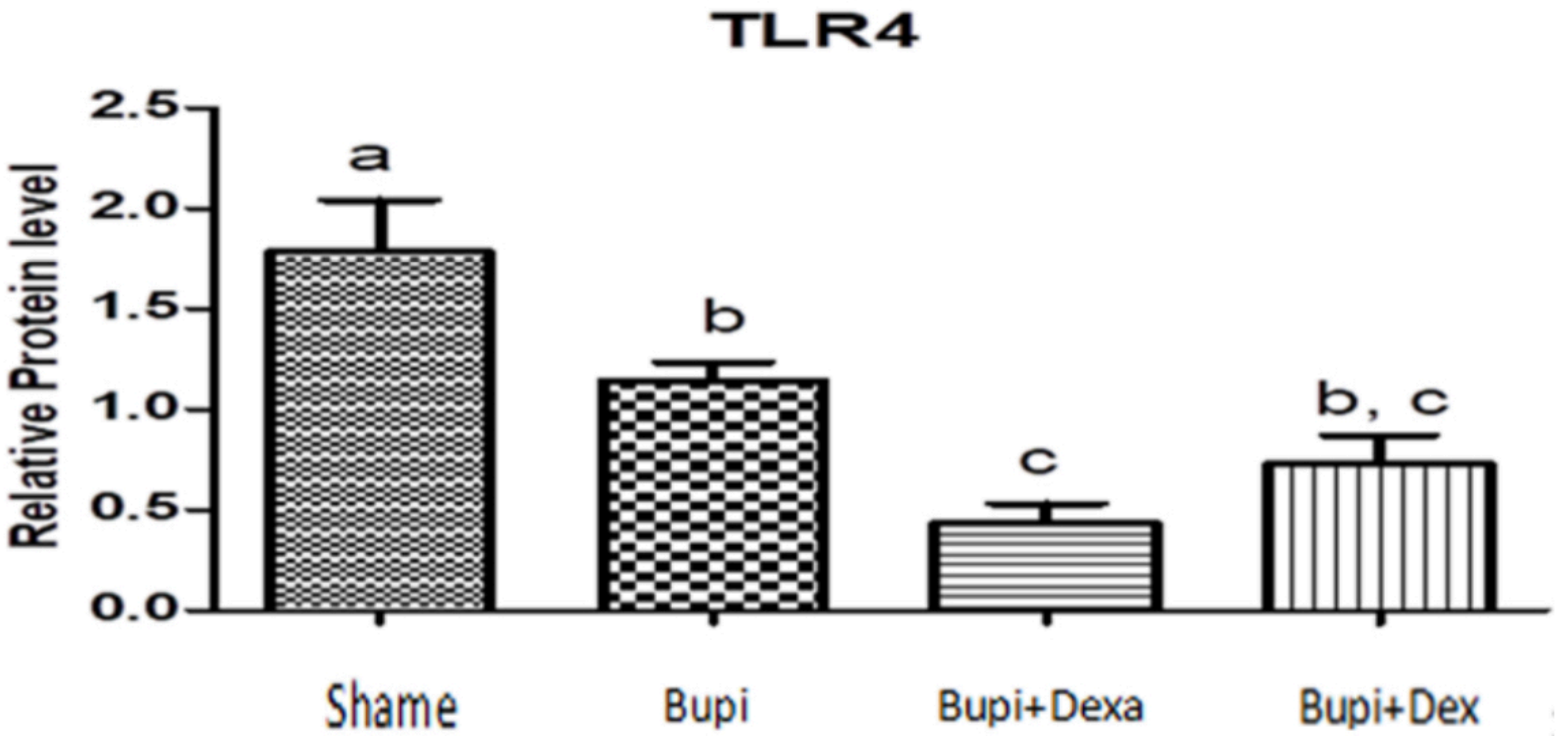

Figure 3. Diagram (P. Value) of TLR4 expression compared to GAPDH in rat femoral nerve (24 h after injection) in four groups (control, bupivacaine, bupivacaine + dexamethasone and bupivacaine + dexmedetomidine).

Results: The bupivacaine + dexamethasone group showed better outcomes in terms of cytotoxicity than bupivacaine + dexmedetomidine (p=0.568); also, bupivacaine + dexamethasone reduced neurotoxicity risk (P=0.431).

Conclusion: Bupivacaine+dexamethasone leeds to better outcomes in terms of neurotoxicity compared with bupivacaine+dexmedetomidine.

Keywords: Bupivacaine, Dexmedetomidine, Dexamethasone, Toll Like Receptor, Glyceraldehyde 3-phosphate dehydrogenase, Cysteine-aspartic acid protease