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### ANESTHESIA OF A CHILD FOR A SURGICAL ABDOMINOPLASTY OF A PHEOCHROMOCYTOMA IN THE CHILDREN'S UNIVERSITY HOSPITAL LITERATURE REVIEW AND CASE REPORT

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#### ABSTRACT

**Background and Objective**: Pheochromocytoma is a rare neoplasm usually arising from the chromaffin cells of the adrenal medulla or from other chromaffin tissues outside the adrenal gland, which results in releasing of huge amounts of catecholamines causes a hypertensive crisis that may occur during pheochromocytoma resection. Controlling these seizures is the goal of this research. **Research materials and methods:** Remifentanil, Sodium Nitroprusside, Sevoflurane, and Dexmedetomidine were used as pharmacological adjuncts to achieve good hemodynamic stability in a 5 years old boy who went under adrenal gland resection. Intraoperative pressure attacks were managed by raising sevoflurane values to 6% and increasing the dose of sodium nitroprusside from 1-2-4 mcg/kg/min. During the period between tumor intervention and adrenalectomy we increased the dose of remifentanil infusion within the safe range to 1.3 mcg/kg/min and increased the dose of Dexmedetomidine "which is the strongest synergistic of sevoflurane" to 0.7 mg/kg/h to ensure stabilization of pressure and pulse and to control pressure attacks. **Results**: Using these elements allowed us to maintain hemodynamic stability during pheochromocytoma resection and prevent a life-threatening crisis. **Conclusion:** This combination appears to be a successful way to suppress the release of catecholamines and reduce circulatory fluctuations.

KEYWORDS: Pheochromocytoma, Dexmedetomidine, Remifentanil, Sevoflurane, Sodium Nitroprusside.

#### INTRODUCTION

Pheochromocytoma, which can also be spelled as Phaeochromycytoma, is a benign, non-cancerous tumor that rarely spreads to other parts of the body, only in 10% of cases. The tumor arises at the expense of chromaffin cells in the adrenal medulla. 80-85% of pheochromocytomas grow in the inner layer of the adrenal gland and from other chromaffin tissue outside the adrenal gland, 15-20% grow outside this area and are called paraganglioma.<sup>[1]</sup> Adrenal gland tumors usually occur in adults over 25 years old, therefore pheochromocytoma in children is considered rare, less than 20% of diagnosed cases, and the child often has a genetic factor with an autosomal dominant pattern, and this disease often affects males more than females. The most common are bi-sided tumors.<sup>[2]</sup> The incidence rate of the tumor is 2 to 8 cases per million annually. In patients with hypertension the prevalence rate is 0.2-0 .6%<sup>[3]</sup>, and the prevalence rate at the United State is

1:6500-1:2500.<sup>[4]</sup> The prevalence of pheochromocytoma and paraganglioma has increased relatively (32-41%) due to mutations in the lineage of ten known susceptible genes. This rate is particularly true when mutations appear as part of family syndromes or when they are malignant.<sup>[5]</sup> Three known family syndromes associated pheochromocytoma and with paraganglioma: neurofibromatosis type 1, von Hippel-Lindau syndrome, and multiple endocrine neoplasia type2 syndrome.<sup>[1]</sup> It is with also associated angioreticuloma, hemangioblastoma, neuroendocrine tumors in pancreas and renal cell carcinoma 40-60%.<sup>[4]</sup> Common clinical symptoms are high blood pressure, headaches, sweating, palpitations, arrhythmia, anxiety and panic attacks. Hypertension episodes are usually paroxysmal and acute and can lead to significant morbidity and life-threatening emergencies, such as myocardial infarction, infarction or cerebral bleeding.<sup>[6]</sup>

Pheochromocytoma and paraganglioma can produce and release different groups of catecholamines, most commonly norepinephrine and epinephrine. In one of the studies norepinephrine was excreted by 32% of tumors, while the combination of norepinephrine and epinephrine was excreted by 27% of tumors.<sup>[7]</sup> Only 5.7% of tumors were non-secretory. 20% of paraganglioma in the head and neck are secretory.<sup>[8]</sup>

#### **Patient Preparation**

Most patients, after careful drug preparation before surgery, have had their tumor removed without serious problems, but the reviews is filled with serious conditions like: trauma, cardiomyopathy, orthostatic hypotension and even cardiovascular failure.<sup>[9,8]</sup>

At present, there are various techniques and multiple recommended anesthetic management to adjust hemodynamic stability (especially during intervention on the tumor), where they receive adequate preoperative preparation from  $\alpha$  -blockers, this strategy has been suggested to reduce preoperative complications to less than 3%.<sup>[13-11]</sup> However, preoperative antihypertensive therapy has not shown to be beneficial in patients undergoing pheochromocytoma resection with normal pressures.<sup>[13,12,11,10]</sup> The effectiveness, strength and speed of antihypertensive and antihypotensive drugs with anesthetic drugs have reduced mortality ratios to almost zero<sup>[14]</sup>, and decreased in other studies to 0-2.9%.<sup>[15,7]</sup>

The effectiveness of treatment is judged by reducing symptoms, stabilizing blood pressure and heart rate relatively to age and height<sup>[2]</sup>, and preventing wide fluctuations in hemodynamic.

Phenoxybenzamine was the most commonly used drug for preoperative control of high blood pressure, but currently it is not considered as the best medication for this purpose. Phenoxybenzamine is a  $\alpha 1$  and  $\alpha 2$  receptors antagonist, with a half-life of 24 hours. Significant hypotension and reflex arrhythmia results due to the blockade of  $\alpha 2$  receptors. This drug has been suggested for a long time to contribute lowering blood pressure after the tumor is removed.<sup>[14,10]</sup> Selective al blockers such as terazosin and prazosin have a shorter duration of action, and therefore can induce minimal hypotension, which follows a decrease in catecholamine levels.<sup>[14,11,10]</sup> We should never start with  $\beta$  blockers without blocking  $\alpha$ receptors because the loss of  $\beta$  adrenergic vasodilation in a patient with catecholamine-induced vasoconstriction can lead to serious hypertension on one hand and to prevent reflexive arrhythmias on the other hand.<sup>[17,16]</sup> Preparation with phenoxybenzamine compared to preparation with selective al blockers, there was no difference in the final result, but the group of required more phenylephrine phenoxybenzamine (pressure lifter) during the operation, and the group of selective al blockers recorded higher blood pressure.<sup>[18]</sup> A variety of calcium channel blockers "that prevent the release of calcium caused by catecholamine into smooth

vascular muscle cells")<sup>[14,10]</sup> clonidine, labetalol, and magnesium sulfate were also suggested to prepare patients for surgery.<sup>[19]</sup>

Laboratory analysis: It is important for anesthesiologists to obtain detailed information about 24-hour urinary catecholamine and metanephrine levels, to identify and prepare patients high risk of intraoperative and postoperative hemodynamic instability. Preoperative laboratory analysis should include complete blood count, basic metabolic profile and compensation of nutrients and rare minerals.<sup>[7]</sup> The current recommendations fractioned emphasize that metanephrine and normetanephrine in plasma and urine must be tested, instead of testing catecholamines levels, or both if available. The test sensitivity is almost 100%. Compared to only 64% sensitivity of urinary mandelic valproic acid examinations in adults.<sup>[4]</sup>

Therefore, measurements of free plasmatic metanephrines and normetanephrines are the most reliable biochemical test available for diagnosis.<sup>[2]</sup> The most important factor for protecting patients is the adequate preoperative blockade against the effects of catecholamine. Many supports preoperative  $\beta$ - and  $\alpha$ blockade of adrenal and extra-adrenal tumor resection even with normal measured levels of catecholamines.<sup>[4]</sup> Electrocardiography is mandatory in all patients to evaluate ischemic deficiencies, arrhythmias, conductivity disorders, ST-segment/T wave changes, and left ventricular hypertrophy. ECHO is performed to evaluate ventricular function, and to look for congestive heart failure and cardiomyopathy. It is also useful to gain an insights to volume statues and to prepare for perioperative fluid administration.<sup>[7]</sup>

The goals of preoperative medical measures are to adjust blood pressure, heart rate, and restore intravascular volume. The duration of preoperative preparation in most centers is between 2 to 6 weeks.<sup>[20]</sup> Most centers use the Roizen criteria for adequate blockade of alpha receptors before surgery:<sup>[21]</sup>

- 1. No blood pressure > 160/90 mmHg should be evident for 24 hours before surgery.
- Systolic blood pressure decreased at least 15% on going from supine to standing, but was > 80/45 mmHg while standing.
- 3. No ST-segment or T-wave changes is present in electrocardiogram for at least two weeks.
- 4. No more than five PVC per minute.

**Hypertension during surgery and irregular heartbeat**: The instability of hemodynamic circulation during the operation arises from two different physiological mechanisms<sup>[22][26]</sup>:

**First**: is to enhance the interaction of the sympathetic nervous system. In these patients, the response of the sympathetic nervous system increases due to several mechanisms:

- 1- Increasing neurovesicle load of catecholamine.
- 2- Increasing the frequency of neural impulse.
- 3- Selective desensitization of presynaptic  $\alpha$ -2 receptors.<sup>[23]</sup>

Any stimulus to the SNS may lead to a hypertensive crisis and irregular heartbeat in these patients. Perioperative anxiety, direct anesthetic, endotracheal intubation, hypoxia, and surgical incision, leads to exacerbate the sympathetic response. The best prevention is to get an easy and deep anesthesia before stimulation and induction.

**Second**: The other cause of unstable circulation in these patients is the direct release of catecholamines from the tumor:

- Either through pneumoperitoneum during intervention on the tumor –which is an abnormal presence of air or other gases in the peritoneal cavity, a potential void within the abdominal cavity.
- Direct maneuvering on the tumor.

The hemodynamic consequences may be a severe lifethreatening hypertensive crisis due to norepinephrine, or cardiac arrhythmias due to the release of epinephrine.<sup>[24]</sup>

The first most important intervention to manage the crises is timely communication with the surgeon to either remove pneumoperitoneal, or stop direct maneuvering on the tumor until hemodynamic control is achieved by infusion of rapid-acting antihypertensive drugs and vasodilators.

A life-threatening hypertensive episode/crisis during anesthesia: An episode threatens the occurrence of cerebral hemorrhage, vascular explosion, cardiac failure, and even kidney failure. Systolic pressure values is 90% greater than its direct values, and values greater than 190 mmHg are considered life-threatening values in children. The occurrence of retinal hemorrhage in the eye is evidence of high pressure to critical values that are almost life threatening.

Our success in controlling a hypertensive episode is evaluated by:

- 1) Measuring the highest value of systolic pressure and pulse.
- 2) The length of time during which the pressure and pulse remain elevated until the episode is controlled.
- 3) The occurrence or absence of any arrhythmia.

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**High risk factors**: a history of coronary artery disease, female gender, episodes of intraoperative hypertension with systolic blood pressure of 200 mmHg and mean arterial pressure greater than 60 mmHg.<sup>[25]</sup> Several other factors associated with an increased risk of hemodynamic instability during surgery were described, including tumor size greater than 4 cm.<sup>[26]</sup> For clinical variables identified to predict prolonged hypotension

after lumpectomy are tumor size greater than 60 mm and high preoperative levels of norepinephrine.<sup>[27]</sup>

**Sodium nitroprusside**: is a strong arterial vasodilator that works through the nitric oxide pathway and prevents the release of intracellular calcium into smooth muscle cells. The effect occurs within a few minutes and it is easily titrated. Sodium nitroprusside dose is 1 - 2 - 4 mcg/kg/min, its effect occurs in 30 -60 seconds, half-life of the drug is 2-3 minutes, dosage effect remains 3-5 minutes.<sup>[24,23]</sup> It has been commonly used as a first-line treatment of hypertension during surgery in patients undergoing resection of pheochromocytoma.<sup>[28,11]</sup> On the other hand, nitroprusside may cause complications such as, methemoglobinemia, cyanide toxicity. This limits its usage, especially in high doses and prolonged periods.<sup>[32]</sup>

Remifentanil: is a µ-opioid agonist, which has low molecular size and high lipid solubility. It has a low pKa, and therefore the percentage of molecular displacement is low in physiological PH 7.4, which allows a rapid equilibrium on both sides of the cell membrane, including the blood-brain barrier. This results in rapid response to the direct anesthesia. Its effect occurs in 1-2 minutes, and the dosage effect remains 5-10 minutes, the safe range is up to 1.3 mcg/kg/min. It affects the cardiovascular system by slowing the heart rate, inhibiting the sympathetic activity of the heart, and lowering blood pressure by vasodilation the arteries and veins, especially veins without causing any arrhythmia with the applied doses and concentrations.<sup>[30,29]</sup> It has a very short action that can be used to control the acute response represented by hypertension during anesthesia.<sup>[30]</sup> However, when used in a patient taking  $\alpha$ 1- and  $\alpha$ 2-blockers as preoperative preparation, slowing of the heart rate and significant hypotension requiring administering of ephedrine occur.<sup>[31]</sup> This does not occur with a preparation with selective  $\alpha$ 1-blockers, so it should be used with caution in all circumstances.<sup>[18]</sup>

**Dexmedetomidine**: is a highly selective  $\alpha$ 2-agonist. It is in the same class of clonidine but differs from clonidine in that its binding to  $\alpha 2$  adrenergic receptors compared to  $\alpha$ 1 adrenergic receptors is eight times greater.<sup>[32]</sup> Its biological half -life is two hours, with a protein binding rate of 94%, and the redistribution time is at least 6 minutes. It has the following effects: at a dose of 0.3mg/kg/h it activates the G protein and inhibits the secretion of norepinephrine, at higher doses, peripheral norepinephrine secretion levels were reduced by more than 90%, reduces our needs for Propofol by 30%, decreases concentrations of inhaled drugs (Sevoflurane concentrations) and synergizes its effects and reduce anesthesia requirements. Alpha-2 are found within the central nervous system, and their activation leads to anesthesia<sup>[33]</sup> A 60-80% decrease in levels of activated sympathetic outflow and catecholamines with it as well.<sup>[34]</sup> Dexmedetomidine reduces heart rate in a dosedependent manner in children<sup>[35,28]</sup> useful for the hemodynamics stabilization during pheochromocytoma

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surgery.<sup>[36]</sup> Theoretically the use of Dexmedetomidine has unique properties, we assume that its reduction and decrease of catecholamine levels can help reduce sudden fluctuating changes in hemodynamics after intubation.<sup>[37]</sup>

-In the treatment of hypertension crisis that may occur during pheochromocytoma resection<sup>[29,37,38]</sup> although it is not enough alone to deal with the seizure during the manipulating with the tumor.<sup>[31]</sup> But increasing his dose increases his support for sevoflurane (sephoflurane is the basis in the speed of seizure control). The synergistic sephophlorane with dexmidetomidine is sure to be efficient in managing a high-pressure attack.<sup>[39,30,28,11]</sup>

Sevoflurane: It has a low solubility in blood and fat, i.e. it is a psychedelic drug through which the level of anesthesia can be easily changed<sup>[30,38]</sup> does not affect the sensitivity of the heart muscle to cathicolamines, which is one of the preferred inhalatory drug agents in pheochromocytoma surgery. It is has a very fast impact with a Mac value of  $1.71 \pm -0.07$  in more specific way, the Mac values change according to age and to the use of Nitrous Oxide first. Mac values for children from 3 to 12 years without nitrus are 2.5% which gives an idea of how quickly this anesthetic gas works. The actual impact speed during the operation depends on the gas evaporator (manual or electric) the flow rate of the gases and the ventilation system, practically within less than 20 seconds as a maximum, the effect of sevoflurane on the cardiovascular system has become effective. At the high concentrations that used here, sevoflurane affects cardiac activity, lowering blood presseure, and causing bradycardia. It also does not induce any effectivity that causes high concentration in children, especially in the absence of any accompanying organic cardiac disease.<sup>[38]</sup>

#### CASE REPORT

A 5-year-old child who weighs 12.5kg and is 1 meter long who underwent a pheochromocytoma excision (total adrenalectomy) in 2023.The child was nominated for surgical consultation after completing the diagnostic study, examinations, chemical investigations, computed tomography (CT scan), magnetic resonance imaging (MRI), and MIBG which was also focused on. The recommendations according to the surgical consultation were to prepare the child for total adrenalectomy.

A glandular consultation was conducted to prepare the child and the recommendations were to prepare from four to six weeks with alpha-blockers and two weeks with beta-blockers while adjusting the diastolic pressure values by age from 75-120 mmHg and heart rate ranges from 60 to 95 beats per minute between sleep and wakefulness, this is due to the return of the volume inside the vessels to the normal values. The child's nutrition was taken care of and the multivitamins, minerals and trace elements were replaced since the hormonal disorders of the pheochromocytoma causes significantly malnutrition for that we rely on the consultation of a specialist in nutrition with children.

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After preparing the child and scheduling the surgical work, We have secured units of red cells with units of plasma, making sure to secure the necessary medications. In addition to secure a bed in the intensive care unit (ICU) with a respirator for the postoperative period. The morning of the surgery and the evening before, a cleansing enema was placed in the colons. A peripheral intravenous was placed to replace fluids, maintain volume and replace the fasting need for energy (dextrose) and fluids. All patients must have adequate fasting before surgery more than 8 hours while allowing drinking water up to 2 hours of general anaesthetic.<sup>[40]</sup>

Anesthesia administration: In normal conditions, direct anesthesia and endotracheal intubation always carries the risk of a hypertensive crisis, and its probability increases with age, gender, cardiovascular diseases, hormonal and metabolic diseases as well. Therefore, the first controlling test for the patient begins with direct anesthesia and endotracheal intubation. The child was administered intravenous anesthesia due to the presence of a peripheral venous line and the fact that IV medications would be continued. At the Beginning we prepared the child during the waiting period an hour before starting anesthesia in the recovery room with midazolam 0.05mg/kg as a single dose. As we continue, when preparing the child on the operating table, we started placing non-invasive monitoring devices: the ECG monitor, the NIBP monitor, and the SO2 oxygen saturation monitor, and ensured that the pressure and pulse values are within the agreed limits, and the oxygen saturation values without oxygen are 97% and without any cardiac arrhythmia on the ECG. We started with intravenous administration of lidocaine 0.01 mg/kg as a prevention of hypertensive attacks caused by endotracheal intubation as it reduces laryngeal reaction to intubation. A Propofol (2.5-3.5) mg/kg was infused over 20 to 30 seconds, Then we infused Remifentanil, Nambix, and dexmedetomidine, using pumps. Nambix (Cisatracurium) 0.15 mg/kg infused over 5 to 10 seconds as a direct dose followed by a continuous intravenous infusion at 3 mcg/kg/min, Remifentanil 0.25 mcg/kg/min and continue on it as long as pressure values allows also we can reduce or increase it during surgical work within the field of safety [0.05 - 1.3 mcg/kg/min], and we can also give the child a supplemental dose of 1 mcg/kg within 30 to 60 seconds to manage any pressure emergency, then we started to infuse dexmedetomidine at 1 mg/kg over 10 minutes as a start, followed by a continuous infusion at 0.5 mg/kg/h. All this with application of a face mask with 100% oxygen. Then the endotracheal intubation is done with the appropriate endotracheal tube after the lubricated local anesthetic was placed. After that the child is placed on a ventilator, in children the forced and directed pressure regimens are preferred, for example IPPV (Intermittent Positive-Pressure Ventilation). The day of surgery : The child is five years old and weighs 16.5 kg, so the following values were set: respirations rate was (20 to 22) per minute, the maximum pressure applied to the alveoli

PMX (14 to 19) with PEEP from (1 to 3) to protect the alveoli because the surgery time is about 4 hours, the ratio I:E 1:2 and the ratio of oxygen in the gaseous mixture with compressed air ranged from 60% to 80%, where these values were modified during surgery according to the values of SO2 (94 to 99%) and ETCO2 values from (30 to 45).

All CPR tools and medicines are ready on the recovery table that is located next to the anesthesia table, because this way in anesthesia is sort of strong and may cause a heart attack by vague nerve stimulation, However, atropine is not indicated as prevention as long as the administration is calm and non-invasive. During the process, an increase of up to 200000 - 1.000.000 pg/ml (normal catecholamine levels under stressful events: 200-2.000 pg/ml) should be expected. and avoided)<sup>[41]</sup> Using this method of intubation, no life-threatening high-pressure attack occurred as the high values in pressure or pulse did not exceed 20% to direct values.

The second stage: Preparing the child and continuity of anesthesia: After the child is stabilized from the stage of direct anesthesia and endotracheal intubation, the second stage begins, which is the continuation of anesthesia using Sevoflurane 1 Mac, and it is raised to 1.5 Mac after 5 to 10 minutes of initiation of anesthesia in which propofol is used. Preparing the child for surgery and placing invasive anesthesia monitors (IBP) "direct monitoring of arterial pressure" by placing a venous catheter in the radial artery. Thus, real-time monitoring of pressure and pulse values is achieved with the possibility of direct withdrawal of arterial blood gases. With monitoring of SO2 and ETCO2 monitoring was recorded every 5 minutes Routine and with high pressure in the seizure, values were recorded every 5 to 10 to 20 seconds for the study and to draw charts that show how the seizure was managed and the drug response to lowering pressure. Value 10-12 cm of water, as it is necessary to maintain the intravascular volume during the surgery. Values from 5 to 12 are considered normal in children. The volume is increased using fluids (Ranger lactate) and given that the child takes the daily and fasting need naturally and continuously from 1ml of fluids /kg/min The surgical needs remain at 1-1.5 ml/kg/min.

#### C.V.C triple-people catheter

- 1- Nitroprusside-Na sodium nitroproside is placed with a special division because it is rapidly destroyed by light needing special syringes and special infusion links 1mcg/kg/min.
- 2- A special fluid infusion division (Ringer lactated Ringer, Volvin Voluven) with remifentanil remifentanil and with Nimbex (Cisatracurium) and Dexmedetomidine.
- 3- Special division for blood and plasma infusion with which a spare vein line is placed for dopamine or noradrenaline infusion if necessary.

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Nitrous oxide is not used in this type of surgery for fear of increasing the size of cavities. Because it is likely to cause bulging of the bowel<sup>[42]</sup> increases the risk of peritoneal palpation and of nausea and vomiting after surgery.<sup>[43]</sup> An EtCO2 End-tidal CO2 measurement is placed to monitor carbon dioxide changes in circuit air and adjust the values to approximately 35 cm Hg by a ventilator.A urinary catheter was inserted to monitor the urine flow, which is supposed to be 1 ml/kg/hour. We used 1 mg/kg Furosemide as a diuretic, which is usually sufficient especially with normal blood volume and C.V.P values of 10 to 12 CmH2.With the course of surgery the mean pressure values are adjusted within the limits values (direct values  $\pm$  20%). The carbon dioxide change monitor is placed in the circuit air of EtCO2 Endtidal CO2 and adjusts the values approximating 35 cm Hg by ventilator. The installation of a urinary catheter to monitor the urinary pour is supposed to be 1 ml/kg/hour. We use orbits such as Furosemid at a dose of 1mg/kg that is mostly sufficient, especially with natural size and C.V.P values of 10 to 12 centimeters of water. As surgical work proceeds, median pressure values are adjusted within limits (direct values  $\pm 20\%$ ).

## During surgical work there are two phases that caused a high-pressure attack

**Phase 1:** manipulation with the adrenal gland and the adrenal tumor that leads to release a huge amounts of catecholamine into the bloodstream, at the 70th minute the systolic pressure is 178 mmHg and the pulse is  $155^{[44]}$ 

**Phase II:** The phase of ligation of the vessels and excision of the tumor also causes the release of a huge amount of catecholamines until the adrenal glands are removed from the body, per minute 130 the systolic pressure is 170 mmHg and the pulse is 149

# And in both cases, the hypertensive episodes were managed as follows:

**First:** increasing the values of sevoflurane to 6% which is equivalent to 2 MAC, while nitroprusside and remifentanil are used, then reduce it to 4% which is equivalent to 1.5 MAC. We may have to raise the concentration to 8% if we are surprised by a dangerous rise in pressure within a monitoring period of less than 5 seconds (a dangerous crisis) and then reduce it.

**Second:** increasing the dose of sodium nitroprusside to 1-2-4 mcg/kg/min. The speed of the drug's effect is 30-60 seconds. The half-life time of the drug is 2-3 minutes. The effect of the dose remains 3-5 minutes. As we mentioned, it affects the blood vessels, especially the arteries.

We decided to start by raising the sevoflurane concentration even if we already had a steady nitroprusside infusion in order to benefit from the prevention of the possible side effects. the intraoperative high blood pressure that occurred during the surgical intervention on the tumor, was controlled by adjusting the concentration of sevoflurane and increasing the depth of anesthesia. With this technique, i.e. using sevoflurane, which affects the heart, and sodium nitroprusside, which affects the vessels. The rise of catecholamines is controlled very well

**Third:** During the period between tumor intervention and adrenalectomy, we can increase the dose of remifentanil infusion within the safe range to 1.3 mcg/kg/min. We can also give a Supplemental dose of remifentanil 1 mcg/kg over 30 to 60 seconds, to control any serious emergency (a life-threatening crisis).

**Fourth:** increasing the dose of Dexmedetomidine -which is the strongest synergist of Sevoflurane- to 0.7 mg/kg/h. We did not rely on Dexmedetomidine as an antihypertensive drug during the episode its said specifications but increasing its dose to increase its support for sevoflurane, which is the basis for its speed controlling of the seizure.

After adrenalectomy: The need for antihypertensive drugs, especially sodium nitroprusside, remains until the effect of the released catecholamines during the surgical procedure disappears. the time varies according to the size of the tumor and the age of the child. In our case the need for sodium nitroprusside infusion at the mentioned doses has no longer been required within half an hour of lumpectomy, but the low infusion was maintained at a dose of 0.2 - 0.4 - 0.5 mcg/kg/min, because the complete (demise) of the effect of catecholamines is related to specific surgical and anesthetic measures to each operation separately. Therefore, stopping it completely remained as a decision to be taken in the intensive care unit. The Remifentanil dose was reduced to 0.25 mcg/kg/min, as was sevoflurane 1 Mac and dexmedetomidine to 0.3 mg/kg/h.

Taking into account if there is a hypotensive tube caused by overdose, dopamine infusion with intravenous fluids for a sufficient period to control the decline and deal with this condition and then stop it leaks as needed 5-10-15 mcg/kg/min. Large doses can be reached if suspected of cardiac toxicity up to 50 mcg/kg/min with infusion of light. We didn't have any low pressure attack of value. Liquids were leaked, blood (red pellets) and bleeding plasma were compensated during surgical work, maintaining a central vein pressure of 10 - 12 cm water and maintaining a minimum poly yield of 1 ml/kg/hour to accelerate the rollout of catecholamine metabolism products.

Before the end of the surgical work a dose of intravenous paracetamol was infused with a dose of 15mg/kg i.e. 1.5ml/kg. After stopping the infusion of Remifentanil at the end of the surgical work and all anesthetic drugs the child was given Pethidine 0.5/mg/kg, my vein with the child's health so that we also avoid the irritation and annoying noise of the child. The child was corrected and the foam intubated. After disinfecting the child to the intensive care unit for monitoring and follow-up.

#### RESULTS

- 1- The maximum of the recorded systolic pressure has not exceeded 178 mmHg and the percentage increase from the pressure of the anaesthetic direct has not exceeded 61%. (direct pressure 110 mmHg). Scheme 1 monitors systolic pressure changes over time for the child during the study and the atoms show sudden pressure attacks resulting from the release of variable and non-static catecholamines.
- 2- The maximum value of the recorded pulse did not exceed 155 beats per minute and the increase in pulse relative to the direct pulse did not exceed 60%. Direct pulse 86 beats per minute Chart 2: Pulse monitoring appears over time for the child and the atoms show sudden pulse attacks resulting from the release of variable and non-static catecholamines.

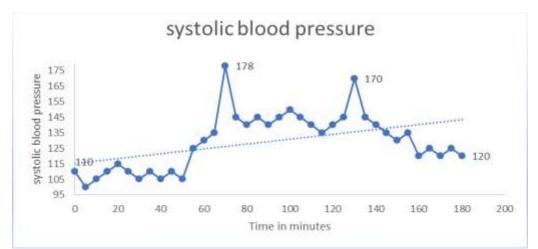


Chart 1: Systolic pressure changes appear over time (pressure in mmHg and time in minutes). It shows two peaks of systolic pressure the first systolic pressure rise in the 70th minute were 178mmHg and the second in the 130th minute was 170mmHg.

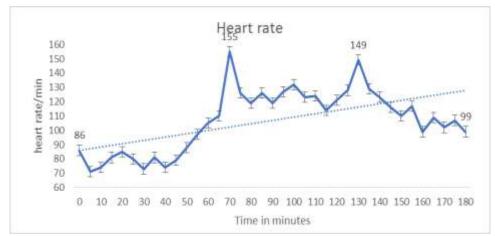


Chart 2: Heart rate changes show over time. (pulse/minute and time in minutes). Two peaks show the first pulse height in the 70th minute were 155 beats per minute and the second in the 130th minute was 149 beats per minute.

3- The time period between the start of the seizure and the control of pressure and pulse and their return to acceptable values for direct pressure did not exceed 2 minutes in the most difficult and severe seizure. Chart 3 shows the pressure response of Sevoflurane during the most serious seizure since the onset of sudden high pressure during the high pressure seizure until its return to normal values within 5 minutes. Blueprint 4 also shows pulse response to sevoflurane from the beginning of the seizure until return to natural values 4- No arrhythmia occurred during surgical work.

Pressure response to sevoflurane during the most severe attack

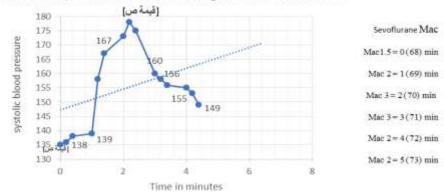


Chart 3: The pressure response to sevoflurane is shown during the most severe hypertensive attack (from the onset of the rise until it returns to normal within 5 minutes). It shows the pressure values, the MAC values of sevoflurane used per minute, and the pressure response of the applied MAC.

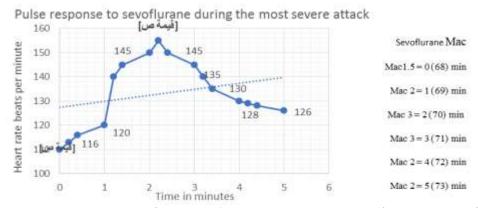


Chart 4: The heart rate response to sevoflurane during the most severe attack (from the onset of the rise in the episode until it returns to normal values within 5 minutes). It shows the pulse values, the MAC values of sevoflurane used per minute, and the heartbeat response of the applied MAC.

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#### DISCUSSION

It was reported that up to three different antihypertensive drugs were simultaneously used to treat hypertensive crisis.<sup>[45]</sup> Nitrates followed by blockers, were given most often. during surgical interference, hypertension crises can be controlled by administering Nitroprusside, nitroglycerin, Nicardipine, and Labetalol.<sup>[46,39]</sup>

 $\alpha$ -blockers before surgery, intraoperative vasodilators, and deepening anesthesia, they were the measures taken to prevent wide changes in the hemodynamic state.<sup>[30]</sup>

The response to hypertension control by increasing the depth of anesthesia can be limited with traditional overlaps..<sup>[28]</sup> Nowadays, it is known that intra- and postoperative hypotension is the result of vasodilation after tumor removal, not because of hypovolumia. Moreover, fluid administration does not change the result in patients undergoing pheochromocytoma surgery.<sup>[10]</sup> As it appears from the previous review of the published cases, there is an agreement on the broad and detailed outlines as well. Efficiency of Sevoflurane synergistic with Dexmedetomidine in managing hypertensive episodes (with studies that used Sevoflurane). The intraoperative hypertensive episodes that occurred during the maneuver of the tumor were quickly controlled by adjusting the concentration of sevoflurane and increasing the depth of anesthesia.<sup>[11,28,30,39]</sup> We were able to monitor and record an approximate time to control the episode using Sevoflurane. We were able to extubation, and restore the child's consciousness to normal before converting him or her to the ICU. This has become customary in the published studies in our hands. Although not all studies agree.

#### CONCLUSION

Sevoflurane synergistic with Dexmedetomidine in anesthesia using Remifentanil and sodium nitroprusside is highly efficient in adjusting the sudden increase in pressure and pulse resulting from the release of large quantities of catecholamines in the operation of pheochromocytoma resection in children.

We emphasize the necessity of preparing the child well before the surgery (within the previous 6 weeks) and conducting specialized endocrinal, nutritional, radiological, surgical and anesthetic consultations, and ensure that all its standards are met. This preparation is the cornerstone of the success of the surgical work.

The use of all means of invasive and non-invasive monitoring methods has achieved the desired results by controlling all the episodes that occurred with high efficiency and quality, which is the main reason for the success of the work.

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