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CONTENTS

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Review

Anesthetic Considerations in a Case of Fahr and Primrose Syndrome

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ABSTRACT

In this review article, brief description, concerns, anesthetic management and perioperative care patients with Fahr syndrome and Primrose syndrome has been made. There is a paucity of literature with respect to management of such cases. There are limited case reports reported in the literature. The literature search has been made by using Google scholar, PubMed, Medline, Medscape and other search-related search engines with the following keywords.

Keywords

Fahr syndrome; Primrose syndrome; Anesthesia; Calcium.

Abbreviations

ALP: Alkaline Phosphatase; CSF: Cerebrospinal Fluid; MELAS: Mitochondrial Myopathy, Encephalopathy, Lactic Acidosis, and Stroke; ECG: Electrocardiogram; NK: Natural killer; GP: Globus Pallidus; PTH: Parathyroid Hormone; cAMP: Cyclic Adenosine Monophosphate; TIVA: Total Intravenous Anesthesia.

INTRODUCTION

Fahr Syndrome

Fahr syndrome or Fahr disease is a rare inherited or sporadic neurological disorder. The prevalence of such disorder is <1/1, 000,000 and is characterized by basal ganglia calcification. It was originally described by Karl Theodor Fahr and is characterized by abnormal deposits of calcium in brain areas that control the movement of the body. Involved areas of the brain include basal ganglia, thalamus, dentate nucleus, cerebral cortex, cerebellum, hippocampus and subcortical white matter. Initially, patients present with extra-pyramidal symptoms, cerebellar dysfunction, speech dysfunction, and dementia and later on with neuropsychiatric symptoms. It is most commonly transmitted as an autosomal dominant trait but can also be transmitted as autosomal recessive or sporadically. It involves adult population in the 3rd to 5th decade and locus at 14q (*IBGC1* gene) has been suggested to be commonly involved.[1]

Diagnostic criteria for Fahr's syndrome derived from Moskowitz et al and modified by Manyam et al in 2005 include (Table 1).

Table 1. *Diagnostic Criteria of Fahr Syndrome*

1. Bilateral calcification of basal ganglia as visualized by neuroimaging, although other parts of brain may also be involved
2. Progressive neurological dysfunction, characterized by movement disorder and neuropsychiatric manifestations. Age of onset is 4th and 5th decade, although may also manifest in childhood as well.
3. Biochemical abnormalities are absent and somatic features are suggestive of mitochondrial or metabolic or other systemic disorder
4. There is absence of infectious, toxic or traumatic cause
5. Family history is consistent with autosomal dominant inheritance.

Res Pract Anesthesiol Open J. 2018; 3(1): 1-6. doi: 10.17140/RPAOJ-3-116

Differential diagnosis

- Symmetrical basal ganglia calcification can also be seen in variety of other familial and non-familial conditions, which should be taken into account of differentials.
- Usually congenital or early onset along with impairment of intelligence should be worked up for other alternative possibilities or diagnosis.
- Basal ganglia calcification associated with ophthalmological manifestation of a child should be investigated for infections.
- If there is presence of latent tetany or myopathy changes associated with changes in visual or somatosensory responses, parathyroid dysfunction, mitochondrial diseases should be ruled out.
- It is differentiated from calcified angiomas, infections, Addison's disease and encephalitis based on severity and characteristic distribution.

Primrose Syndrome

Primrose syndrome was originally described in the year 1982 and very few cases are reported in the literature. Clinical features are characterized by calcification of pinna, large head, autism, intellectual disability, brain calcification, diabetes, and sparse hair, muscle wasting, movement disorders, Parkinsonism, hypothyroidism, distorted facial features and behavioral abnormalities. Most of the cases are sporadic and are caused by a mutation in *ZBTB20* gene. These cases a have similar presentation as that of Fahr syndrome, except for associated distorted facial features and endocrine disorders in them.[2,3]

DIAGNOSTIC METHODS

CT Scan: It is performed to localize the extent of brain calcification. Most commonly involved areas include lenticular nucleus, mostly globus pallidus (GP), cerebellar gyri, brain stem and subcortical grey matter.

MRI: It is used to assess areas of calcification in basal ganglia using T2 image which gives a low-intensity signal. T1 weighted plane either gives a low or high-intensity signals.

Plain X-Ray: Calcified deposits can be seen as clusters symmetrically over sella turcica as punctate densities, while subcortical and cerebellar calcifications appear wavy.

Cerebrospinal fluid analysis: It should be undertaken to rule out infectious etiology and auto-immune disorders. If no other primary cause for brain calcification is found, molecular testing should be undertaken if family history is suggestive of autosomal dominant inheritance. In genetic analysis, sequencing of *SLC20A2* should be undertaken.

Serum concentration: Serum concentration of calcium, magnesium, phosphorus, alkaline phosphatase, parathormone, and calcitonin should be done. Levels of urinary cAMP, serum creatinine, vitamin D3 lactate, osteocalcin, alkaline phosphatase (ALP) should be evaluated at rest followed by after exercise. Natural killer (NK) cells should also be assessed in all suspected cases of Fahr syndrome. Blood sugar, HbA1c, and thyroid function tests should be sought as Primrose syndrome has associated endocrine disorders.

PATHOGENESIS

Fahr syndrome is characterized by pathological fractures. Calcification is known to affect the vessel wall, perivascular spaces, neuroglia and neurons. Progressive basal ganglia calcification compress the lumen of vessels, leading to impairment of blood flow, tissue injury and mineral deposition. It secondarily occurs around a nidus of mucopolysaccharides and other substances due to defective iron transport and production of free radicals ultimately leading to tissue damage.[4]

ETIOLOGY

Etiopathogenesis in Primrose syndrome is characterized by abnormal high amount of calcitonin, a hormone secreted by the thyroid glands to stabilize blood calcium levels, suggesting that thyroid gland releases an abnormal amount of calcitonin resulting in disruption of calcium level homeostasis (Table 2).

CLINICAL FEATURES

Fahr syndrome is associated with various neurological manifestations such as loss of consciousness and seizure, etc. It can be associated with tetany, occasional myoclonus, spasticity, gait disorder, speech impairment, dementia, parkinsonism like symptoms, chorea, athetosis, coma, dystonia, and so on. It has also been reported to be associated with papilledema and pleocytosis on cerebrospinal fluid (CSF) examination. Fahr syndrome is also known to be associated with movement disorders which include unsteady gait, slurred speech, dysarthria, dysphagia, muscle cramps, involuntary

Table 2. *The Various Etiologies of Fahr Syndrome Other Than being Idiopathic Include*

1. Endocrine disorders-Idiopathic hypoparathyroidism, pseudo-hypoparathyroidism, pseudo-hypoparathyroidism, secondary hypoparathyroidism, hyperparathyroidism, hypothyroidism, hypogonadotropic hypogonadism
2. Systemic diseases-Systemic lupus erythematosus (SLE), scleroderma
3. Neurodegenerative conditions-brain iron accumulation disease, ferritinoneuropathy, polycystic lipomembraneous osteodysplasia, primitive or secondary calcified brain tumors
4. Infectious diseases-Cockyane syndrome Type I and II, intrauterine and perinatal infections, neuro-cysticercosis, HIV, German measles, neuro-brucellosis, small pox encephalitis
5. Early Onset syndrome-Tuberous sclerosis, brucellosis, Coat's Disease.
6. Heavy metal poisoning, hemochromatosis, CO poisoning, treatment with methotrexate or radiotherapy

Res Pract Anesthesiol Open J. 2018; 3(1): 1-6. doi: 10.17140/RPAOJ-3-116

movement disorders and easy fatigability. There is no association between extensive calcifications and the higher proportion of neurological impairment, rather it has been seen that disease may be more progressive in those with limited calcification. Neuropsychiatric spectrum ranging from impaired intelligence. Dementia, psychosis, depression, schizophrenia may be seen.

Management of Fahr and Primrose Syndrome

Management of these patients is based on symptomatology.

- Management is based on treating anxiety, depression, psychotic behavior, etc.
- Anti-epileptics are given to manage seizure and oxybutynin are prescribed for associated urinary incontinence.
- Early management of hypoparathyroidism can even reverse the disease process, as reported from a 3-year child, by starting treatment of hypoparathyroidism, mental retardation was reversed.
- Correction of calcium, vitamin D3, phosphorus, magnesium levels have been shown to reverse neurological impairment and seizure and movement disorders associated with hypoparathyroidism.
- Atypical antipsychotics and clonazepam have an added advantage in the management of psychosis in Fahr syndrome. It has been suggested that use of carbamazepine and barbiturates can exacerbate gait disorders in these patients, so should be cautiously used.
- Management of hypothyroidism and diabetes is done with Eltroxin and oral hypoglycemic and insulin respectively.

ANESTHETIC MANAGEMENT

Pre-Operative Evaluation

The pre-operative evaluation in patients with Fahr syndrome is based on the functional status of the individual, symptoms of the seizure, gait disorder, myoclonus, speech disorder, dementia, mood disorders, dystonia, parkinsonism, etc. If Fahr syndrome is associated with hypoparathyroidism, it is characterized by cataract, tetany, seizures, dysarthria, soft tissue calcification, pernicious anemia, dry hair, alopecia, increased intracranial pressure, and dental caries. Fahr syndrome is also known to occur in patients with Kearn Sayre syndrome, and consists of triad of external opthalmoplegia, retinal degeneration and increase in cerebrospinal fluid protein. Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke (MELAS) syndrome, a type of mitochondrial disorder is also associated with Fahr syndrome and is characterized by myopathy, encephalopathy, lactic acidosis and stroke like syndrome. Tuberous sclerosis is characterized by hypermelanotic macules, facial angiofibromas, plaques, intellectual disability, sub ependymal nodules, seizure, angiomyolipoma in kidney, rhabdomyomass in heart and cerebral hemartomas which may be calcified. Patients may be on multiple medications including anti-epileptics, anti-psychotics, anti-parkinsonism, calcium, multi-vitamins, mood elevators, etc., same should be enquired about. Usually these patients may not respond to levodopa for Parkinsonism symptoms, but respond to risperidone, which is known to diminish psychotic symptoms. Calcium, vitamin D and parathyroid hormone are given to normalize calcium if associated with hypoparathyroidism. In physical examination, general physical examination and systemic examination is done thoroughly. Speech, balance, gait disorders may be present in systemic examination and the same should be noted. Airway examination should also be done thoroughly. Cataract may also be associated. They may have brady/tachyarrhythmia. Chvostek sign and Trousseau sign should be done to rule out hypocalcemia. Control of blood sugars should also be taken in account.

Pre-Operative Investigations

In addition to detailed history and examination, following investigations are required (Table 3).

MONITORING DURING ANESTHESIA

- Routine standard monitoring includes electrocardiogram (ECG), non-invasive blood pressure, end tidal carbon dioxide, and peripheral oxygen saturation.
- Temperature monitoring, and urine output monitoring are frequently required.
- Invasive blood pressure monitoring may be required in cases where there is a risk of major fluid shifts or blood loss.

Table 3. *Pre-Operative Investigations*

Complete Blood Count Blood urea and serum electrolytes-including sodium, potassium, calcium, magnesium, and phosphate	Laboratory investigations usually reveal normal calcium, phosphorus, parathormone, and vitamin D levels. In some patients, there may be severe hypocalcemia, hyperphosphatemia, elevated parathormone levels, normal renal function, and vitamin D levels, which require looking for hypoparathyroidism.
	Diagnosis of primary hypoparathyroidism is confirmed by low parathyroid hormone (PTH) and calcium levels. Secondary hypoparathyroidism is characterized by low PTH and high calcium levels. Pseudo-hypoparathyroidism is a condition of bone and kidneys characterized by the unresponsiveness of receptors to parathyroid hormone, and there are high PTH and low calcium. Thyroid function tests and urinary cyclic adenosine monophosphate (Camp) levels are also asked in limited cases.
X-ray findings	X-ray findings are suggestive of generalized increase bone density, thickened lamina dura and sacroiliac, femoral head and acetabulum soft tissue abnormalities (characterized by intracranial calcification, calcification of spinal and other ligaments, subcutaneous calcifications, ectopic bone formation, ossification of muscle insertion.

- Calcium levels are also frequently monitored during the intra-operative period.
- In patients with compromised cardiovascular or renal functions, additional monitoring such as invasive blood pressure, neuromuscular monitoring and measuring the depth of anesthesia *via* bispectral index may be required and may vary from case to case. Arterial blood gas analysis is also required in specific case scenario.

ANESTHESIA CONSIDERATIONS

Both regional and general anesthesia has been described by authors, although the reported cases are very few. Goals of anesthesia management revolve around managing metabolic disturbances associated with calcium metabolism. These patients are at risk of malignant hyperthermia, therefore dantrolene should be made available.[4]

Clinical Manifestations of Hypocalcemia Include

Neuropsychiatric symptoms such as seizure, anxiety, dementia, mental retardation, emotional symptoms such as anxiety and depression, extrapyramidal symptoms. Irritability as characterized by positive chvostek sign and trousseau sign, paresthesia, circum-oral numbness, myalgia and muscle spasms. Cardiovascular manifestation include hypotension, congestive heart failure, prolonged QT interval, bradycardia, impaired contractility, arrhythmia, QT, ST elevation and T inversion. Respiratory symptoms include laryngospasm, bronchospasm. Muscle weakness may also develop leading to respiratory failure. Other symptoms include diaphoresis, bronchospasm, biliary colic, cataract, steatorrhea, dry coarse skin, dermatitis, gastric achlorhydria.

Other causes of hypocalcemia should also be ruled out which include acute and chronic renal failure, vitamin D deficiency, magnesium deficiency, pancreatitis, sepsis, massive blood transfusion, radiographic contrast, etc.[5]

The decreased serum calcium associated with hypoparathyroidism produces hyper-excitability of nerves and muscle cells by lowering the threshold potential of excitable membranes. Symptoms may vary from mild characterized by muscle spasms, and severe characterized by hypocalcemia tetany, perioral paresthesia, numbness in toes and feet. Life-threatening hypocalcemia manifestation include laryngeal muscle spasm, producing stridor, labored respiration and asphyxia.[5] Signs of hypocalcemia include:

Chvostek Sign

Characterized by contracture or twitching of ipsilateral facial muscles produced when facial nerve is tapped at the angle.

Trousseau Sign

Is elicited by inflation of blood pressure cuff slightly above systolic blood pressure for few minutes, the resultant ischemia enhances muscle irritability leading to flexion of wrist and thumb, and extension of fingers known as carpopedal spasm.

Management of Hypocalcemia Include

- They should have ionized calcium levels done to confirm the diagnosis.
- Mild hypocalcemia ie ionized calcium >0.8 mmol/L are asymptomatic and seldom require any treatment.
- In more severe cases of hypocalcemia replacement therapy is essential. In patients in whom ionized calcium is less than 0.5 mmol/L may be associated with life-threatening complications and require intravenous calcium replacement therapy.
- Administration of calcium bolus 100-200 mg of elemental calcium over 10 minutes followed by maintenance infusion of 1-2 mg/kg/h is done. Serum calcium returns within 6-12 hours. Thereafter maintenance infusion is reduced to 0.3-0.5 mg/kg/h. intravenous
- Calcium should ideally be given slowly with ECG monitoring and through a central line as it is irritant to the veins.
- One must also be cautious in giving calcium to a patient who is also receiving digitalis as it may cause digitalis-induced arrhythmia and heart block.
- Once the calcium levels have reached normal, 1-4 g of elemental calcium is given *via* enteral route. Optimal therapy requires frequent monitoring of calcium, magnesium, vitamin D, potassium, and creatinine.
- Patients are supplemented with intravenous and oral calcium and vitamin therapy if serum ionized calcium levels are low. Hyperventilation should be avoided as alkalosis is associated with further hypocalcemia resulting in the seizure which may be masked due to the use of muscle relaxants and become evident at the time of recovery.

GENERAL ANESTHESIA IN FAHR AND PRIMROSE SYNDROME

During anesthesia, there is interplay of several factors which include nutritional status of the patient, disease progression, calcium levels, drugs used in peri-operative period, transfusion of citrated blood, etc. Anesthesiologist should aim to prevent changes in plasma calcium concentration and its effects on various organs. Control of blood sugars and thyroid should be taken into account. Morning blood sugar and electrolyte should be done. Anesthesia management revolves around all the above-mentioned factors. Choice of anesthesia is dictated by patient's general condition, comorbidities, type and duration of surgery, etc. Post-operative bed ventilator should be arranged depending on the associated factors.[4]

PREMEDICATION

Benzodiazepines are preferred sedative and amnesic agents, but one should be careful to use in patients who have altered sensorium, or in respiratory distress. Use of anticholinergic agent such as atropine 0.01-0.02 mg/kg or glycopyrrolate 0.01 mg/kg may be given in patients with low heart rate. Glycopyrrolate may also be reserved in patients with excessive secretions.

INTRAVENOUS DRUGS

Intravenous induction agents are associated with changes in cardiovascular function. It is crucial to avoid hypotension and arrhythmias. A combination of opioid fentanyl 2-3 mg/kg and benzodiazepine midazolam or diazepam 0.25 μg/kg is safe but should be weighed against hemodynamic stability.[4,5]

Acidosis should be avoided at all times since it is known to increase the fraction of ionized calcium by decreasing the binding of calcium to albumin whereas alkalosis decreases the same, careful attention of pH should, therefore, be maintained at all times. Metabolic acidosis should be corrected with intravenous fluids or bicarbonate. Respiratory acidosis should be prevented and treated with adequate ventilator parameters. Respiratory alkalosis may occur with hyperventilation and may lower the ionized calcium. Hepatomegaly should limit the use of inhalational agents such as halothane. Anticonvulsants may induce the liver enzymes, therefore dosage of drugs metabolized by the same should be taken into consideration. The dosage of neuromuscular blocking agents should be adjusted accordingly. Succinylcholine may be avoided in patients who presents with spastic paraplegia.[5]

In a case report, in which 58-year-old patient a known case of Fahr syndrome was posted for hernia repair, patient was anesthetized with propofol 2 mg/kg, lignocaine 1 mg/kg, fentanyl 2 μg/kg, and rocuronium 0.6 mg/kg, and maintained with 50% O_2 and N_2O in 2% sevoflurane. Twenty milli letter of calcium gluconate was given by titrating with arterial blood analysis and assessing calcium levels. The patient had spontaneous recovery after 4 minutes of stopping inhalational anesthesia. Reversal agents were not required and the patient was extubated uneventfully.[4]

MALIGNANT HYPERTHERMIA

Risk of malignant hyperthermia is found to be increased in Fahr syndrome, as suggested by various case reports.[3,4,6] It is seen that calcium homeostasis is abnormal in susceptible individuals so that various agents can increase free ionized intracellular calcium concentration. Primary abnormality is related to abnormally sensitive calcium release mechanism. Considering the possibility of malignant hyperthermia, administration of trigger agents must be stopped immediately, and anesthesia is maintained with opioids, sedatives and non-depolarizing muscle relaxants. Vaporizer should be removed from the anesthesia workstation, and patient is hyperventilated with 100% oxygen, other management include administration of dantrolene 2 mg/kg, repeated every 5 minutes until cardio-respiratory stabilization occurs. Dantrolene acts as a specific ryanodine receptor antagonist and inhibits sarcoplasmic reticulum of calcium. Side effects of dantrolene include prolonged breathing difficulty, tissue necrosis, nausea, vomiting, headache, dizziness, etc. One vial of dantrolene contains 20 mg to be dissolved in 60 ml distilled water. Volume resuscitation and vasopressors may be required to maintain hemodynamics. Monitoring of arterial blood gases, serum electrolytes, creatine phosphokinase, myoglobin, lactate levels are required to determine the success of therapy. Forced diuresis and cooling is required to prevent acute renal failure and hyperthermia respectively. The patient should be transferred to intensive care unit (ICU) for further monitoring. Total intravenous anesthesia (TIVA) can be preferred in such patients as volatile agents increase the susceptibility of malignant hyperthermia.[7] There is a relative paucity of literature with respect to the incidence of malignant hyperthermia in cases of Fahr and Primrose syndrome, but one must be cautious in predicting the same and managing accordingly. As far as possible, triggering agents should be avoided in them.

LOCAL ANESTHETICS

There have been reports which have suggested that cardiotoxicity of local anesthetic-bupivacaine may be increased in the presence of hypocalcemia. The mechanism of bupivacaine-induced cardiotoxicity is mediated *via* changes in calcium concentration and is mediated *via* inhibition of calcium current through l type calcium channels. It has also been suggested that presence of cardiotoxicity is potentiated in the presence of calcium antagonists. Loco-regional anesthesia is avoided in cases of thrombocytopenia, coagulopathy and bleeding diathesis.

SPINAL ANESTHESIA

There has been a single case report in which patient was given spinal anesthesia for repair of varicocele for non-obstructive azoospermia in a patient with Fahr syndrome. The patient maintained hemodynamic stability and was shifted uneventfully in the recovery room. The patient also voided after 6 hours and motor blockade effect was not prolonged. However, note should be made of an associated thrombocytopenia or coagulopathy in which spinal anesthesia is relatively contraindicated. Spinal anesthesia is also relatively contraindicated in patients with epilepsy, behavioral disorders, with altered sensorium, etc.[6]

Massive Blood Transfusion

When blood is transfused at the rate of 30 ml/kg/h maintaining the hemodynamic stability, compensatory mechanisms ensure that serum calcium is maintained in normal arrange. When the rate of transfusion of blood is rapid, it temporarily decreases the calcium concentration and recovers after the infusion is decreased. But it has been seen that clearance of citrate from the blood may be slowed in the presence of hypothermia. Therefore, rapid transfusion of cold citrate containing blood products results in lowering of serum calcium concentrations. Sudden decrease in calcium concentration results in hypotension that responds transiently to calcium injection. Reduction in blood pressure may be profound in patients with underlying cardiac disease and severely impaired liver and kidney functions. Clearance of citrate from the blood is done by maintaining adequate urine output, maintaining normothermia, and increasing systemic and hepatic blood flow.[5]

RECOVERY

Periodic post-operative monitoring of ionized calcium is recommended. For patients with renal compromise, fluid administration should be based on urine output. For patients with cardiovascular compromise, monitoring should be continued in recovery.

CONCLUSION

For early diagnosis of malignant hyperthermia due to volatile anesthetics and cardiac effect, careful monitoring, invasive blood pressure follow-up and blood gas investigation should be carried out. As personality changes and impairment in mental functions is marked in these syndromes and the etiology of intracerebral calcification cannot be identified, general anesthesia is safer. In these patients, preparations should be made for difficult intubation and care should be taken for the risk of the development of malignant hyperthermia in association with inhaled anesthetics. Metabolic disturbances, most of which are associated with calcium metabolism, are known. In addition, the probability of difficult intubation owing to calcium metabolism disturbance, should be borne in mind.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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Original Research

Effect of the Irrigation Fluid Temperature on Core Temperature in Transurethral Resection of Prostate Patients Under Spinal *Versus* General Anaesthesia

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ABSTRACT

Study Design

Prospective, randomized control trial.

Objectives

To evaluate and compare the effect of warm and unwarmed irrigation fluid and anaesthetic technique on core temperature in patients undergoing Transurethral resection of prostate.

Summary of Background Data

Material and Methods: The present study was conducted in 80 patients belonging to age group18-75 yrs of posted for TURP under general anaesthesia or spinal anaesthesia.

Group A: General Anaesthesia with irrigation fluid at room temperature.

Group B: GeneralAnaesthesia with irrigation fluid at 37 °C.

Group C: Spinal Anaesthesia with irrigation fluid at room temperature.

Group D: Spinal Anaesthesia with irrigation fluid at at 37 °C.

Results

Amongst the four Groups, all the subjects showed consistently reduced core temperature which was statistically significant ($p<0.05$) at all time intervals. Core temperatures were lower in the group receiving unwarmed irrigation fluid compared with the prewarmed irrigation fluid group at the end of surgery. The mean decrease in core temperature at the end of surgery 4.2105 °F in Group A 1.1105 °F. in Group B, 4.2700 °F. in Group C, 1.4250 °F in Group D. The difference in mean core temperature was not statistically significant in Groups receiving unwarmed fluid. Statistically significant difference in mean core temperature was seen in Group B and Group D.

Conclusion

Use of prewarm irrigation fluid resulted in lesser drop in core temperature as compared than that receiving unwarmed irrigation fluid. The drop was relatively least in patients under general anaesthesia.

Keywords

Transurethral prostate resection; Core temperature; Hypothermia; Prewarmed; Irrigation fluid.

Abbreviations

TURP: Transurethral prostate resection; ETT: Endotracheal tube; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MBP: Mean Blood Pressure; ECG: Electrocardiography; NIBP: Non-Invasive Blood Pressure.

INTRODUCTION

Preventing unintentional hypothermia for all surgical patients has been an important challenge for anaesthesiologist.[1] Despite body temperature been a vital sign, hypothermia during Transurethral prostate resection (TURP) has received relatively little importance in the urology literature.[2] Irrigation fluid as a cause of hypothermia during TURP was first reported by Rabke et al.[3] The consequences of unplanned hypothermia are significant and is well documented in the existing literature.[4] The type of anaesthetic technique and the temperature of irrigation fluid best for TURP is still debatable. Spinal anaesthesia is a preferred for TURP[5] however general anesthesia is indicated when blockade is counterindicated, fails or is refused by the patient. The type of anaesthetic used also influence the irrigation fluid absorption and also impairs the thermoregulatory mechanisms which contributes to the development of hypothermia.[6] Most patients undergoing TURP are elderly which is an important independent risk factor for developing hypothermia which increases susceptibility to intraoperative as well as post-operative complications and delays patient recovery from anaesthesia[6] hence increasing the financial burden on the patient. Therefore it is critical to understand the importance of maintaining normothermia in patients specially elderly undergoing surgery. Various stratigies can be used to prevent heat loss and to lower the risk of inadvertent hypothermia associated with administering anaesthesia. Warming of irrigation fluid seems appealing to achieve normothermia,[7] however studies comparing the effect of pre warmed and unwarmed irrigation fluid under different anaesthetic technique to prevent unintended hypothermia have shown conflicting results. The aim of the present study was to determine the effectiveness of warm irrigation fluid in maintaining core body temperature in patients undergoing TURP under spinal versus general anaesthesia in a limited resource setup.

MATERIAL AND METHODS

After approval from Institutional Ethical Committee and written informed consent from the patients, 80 patients scheduled for elective TURP were selected. The patients were in the age group of 60-85 years, American Society of Anaesthesiologist I and II. Patients with preexisting major cardiovascular, respiratory or endocrinal diseases, preoperative anaemia, severe electrolyte abnormality, on anticoagulant therapy or existing coagulopathy were excluded. Other exclusion criteria were patients on nitrates, angiotensin-converting enzyme (ACE) inhibitors or calcium channel blockers, as these medications might interfere with normal thermal regulation mechanisms. A thorough preoperative evaluation was done for all patients. The patients were kept nil per oral for 6 hours before surgery and received tablet diazepam 10 mg night before and on morning of surgery with a sip of water.

In the operation theater after securing intravenous access all patients were preloaded with 500 ml of Ringer lactate. Preoperative baseline vitals such as Electrocardiography (ECG), non invasive blood pressure (NIBP) and SPO_2 were noted. The temperature of operation theater was noted and kept constant at 23 °C. The patients were then randomly allocated into any of the four groups. Randomization was done with sealed envelope technique.

Group A: General Anaesthesia with irrigation fluid at room temperature
Group B: GeneralAnaesthesia with irrigation fluid at 37 °C
Group C: Spinal anaesthesia with irrigation fluid at room temperature
Group D: Spinal anaesthesia with irrigation fluid at at 37 °C

The patients in the group A & B were induced by Inj. fentanyl (2 µgm/kg) followed by injection (inj.) Thiopentone (4-7 mg/kg). Ventilation was checked by gentle mask ventilation and neuromuscular blockade achieved by utilising Injection. vecuronium bromide in dose of 0.1 mg/kg the patients were ventilated with 66% N_2O in O_2 and sevoflurane ≤1.5% for 3 minutes. A cuffed Endotracheal tube (ETT) of appropriate size was introduced into the trachea. Anaesthesia was maintained with 66% nitrous oxide in oxygen, sevoflurane and intermittent boluses of injection vecuroniun bromide 0.08 mg/kg and inj fentanyl 1-2 mcg/kg. At the end of surgery neuromuscular blockade was reversed with inj neostigmine and inj glycopyrolate in usual doses.

The patients in Group C and D were administered subarachnoid block in the sitting position using 25 G spinal needle by midline approach and 12.5 mg of hyperbaric bupivacaine was administered. The patient was turned to supine position. Level of the block was checked by pinprick method. Patients were covered with theater linen at room temperature during the procedure and were not actively heated. Monopolar resection was performed using cautery with cutting and coagulation setting of 100 and 60 W respectively A well-lubricated resectoscope (Olympus winter and IbeGmbH, Kuchnstr 61, 22045 Hamburg, Germany) and the telescope was used for resection of the prostate. The perfusion pressure was 60 cm of water in all cases. The temperature of the distilled water as irrigating fluid in Group A and Group C was similar to room temperature while in Group B and Group D irrigation fluid was warmed by using incubator (YARCO B.O.D) Yarco sales Pvt. Ltd., New Delhi, India. Before use irrigation fluid was put into irrigation fluid reservoir (sew water bath, scientific equipment works, New Delhi, India) which was also prewarmed up to 37 °C. The temperature of the irrigation fluid was measured with a mercury thermometer put inside the reservoir.

The core body temperature was monitored by nasopharyngeal probe introduced after explaining the procedure and well lubricating the probe and nasal passage. Nasopharyngeal temperature, NIBP, Heart rate, Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), ECG was continuously monitored at preinduction, induction at thereafter every 15 minutes throughout the procedure. The total duration of surgery, amount of irrigation fluid used and patient satisfaction were noted. Considering a statistical power (β) of 80%, and α error of 5% and clinically significant of temperature difference of 1 °F, a total 16 samples was found in each group. In order to allow for potential data loss, it was planned to recruit 20 patients to each group.

Statistical Analysis

Data were represented in the form of mean±standard deviation and analysis was performed utilize SPSS-version 22 (SPSS, Software, IBM Corporation, Amrok, Newyork). $p<0.05$ was considered to be statistically significant. Nasopharyngeal temperature were recorded over the study period, comparisions were performed with analysis of variance (ANOVA) with Post-hoc comparision adjusted by Tukeys test.

RESULTS

Eighty patients were initially enrolled in each group, and none of the patient was excluded from the analysis. There was no statistically significant differences in the groups concerning base line parameters such as age, height, weight, ASA grade, duration of surgery, amount of irrigation fluid used, and ambient temperature in the operating room (Table 1). (Table 2) Illustrates observed changes in core temperature during the perioperative period. Patients in all the groups who received unwarmed and warmed irrigating fluid demonstrated a significant decrease of core body temperature. In each group temperature changes were highly significant ($p<0.05$) .The drop in nasopharyngeal temperature from baseline to the end of surgery was Group A 98.7 ^{0}F to 93.70 ^{0}F, in Group B 98.7 ^{0}F to 96.7 ^{0}F, in Group C 98.7 ^{0}F to 94.0 ^{0} F and in Group D from 98.6^0 F to 96.7 ^{0}F.

Considering a statistical power (β) of 80%, and α error of 5% and clinically significant of temperature difference of 1 °F, a total 16 samples was found in each group. In order to allow for potential data loss, it was planned to recruit 20 patients to each group.

Hypothesis is to determine the effectiveness of warm irrigation fluid to 37 °C as compared to irrigation fluid at 23 °C (which is O.T temperature) in maintaining core body temperature in patients undergoing TURP under spinal versus general anaesthesia in a limited resource setup.

As a institutional protocol the temperature of operation theater is kept constant at 23 °C. Irrigation fluid at room temperature *verusus* prewarmed fluid to 37 °C using incubator is used in TURP surgeries .

The patients were randomly allocated into any of the four groups. Randomization was done with sealed envelope technique. The anaesthetist recording the intraoperative temperature and haemodynamic parameters was unaware about the irrigation fluid temperature used in TURP (Chart 1).

DISCUSSION

We found that the magnitude of hypothermia is not affected by mode of anaesthetic technique with unwarmed irrigant fluid. Although prewarming fluid to 37 °C did not completely abolish intraoperative hypothermia but definitely reduce its severity in elderly patients undergoing TURP. The incidence of hypothermia was least under general anaesthesia.

Our study is unique in the way that we studied the effect of prewarmed and unwarmed irrigation fluid on core body temperature under regional as well as general anaesthesia in a single setting that none of the published trials have reported previously.

Causes of intraoperative unintentional hypothermia are multifactorial.[8] Several methods of patient warming have been re-

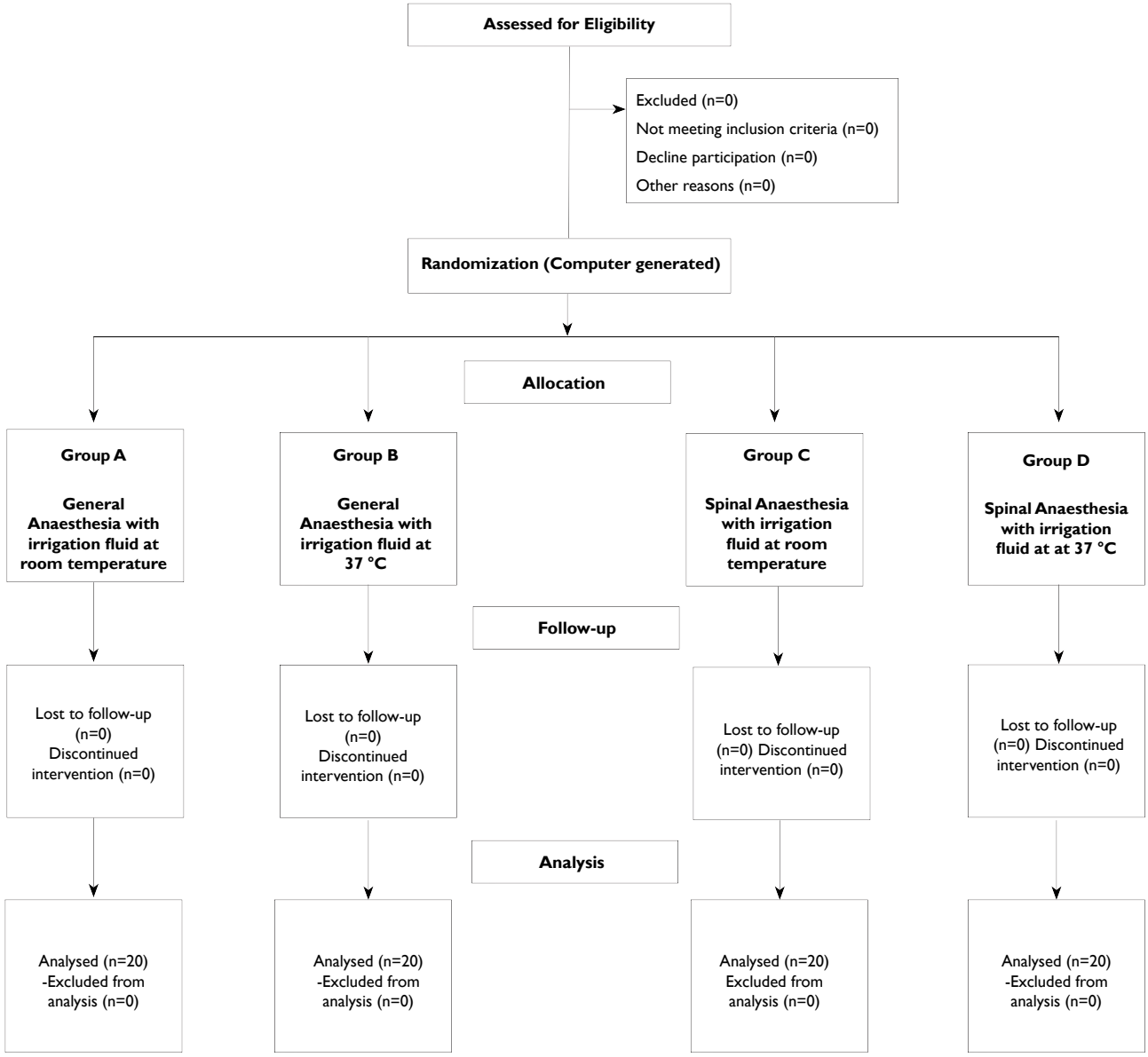
Table 1. *Demographic Profile and the Operative Details of the Patients*

	Group A	Group B	Group C	Group D	*p* value
Total number	20	20	20	20	
Age±SD (years)	64.4±9.04	68.1± 9.07	66.4 ±9.02	65.6 ±9.90	$p>0.05$
Weight±SD (Kg)	60.24±4.02	59.45±9.36	59.02±2.06	57.0±6.80	$p>0.05$
Height±SD (cm)	159.4±4.24	160.2±7.52	160.4 ±2.06	160.0±7.20	$p>0.05$
ASA(II/III)	18/2±	17/3	16/4±	15/5	$p>0.05$
Duration of surgery (min)	56.20±2.42	53.40 ±7.75	54.01±6.o4	52.75±5.45	$p>0.05$
Amount of irrigation fluid (litres)	7.60±4.10	7.70±3.10	7.82 ± 2.14	7.61±3.14	$p>0.05$
Ambient Temperture	21 °C	21 °C	21 °C	21 °C	

Table 2. *Temperature Changes (°F) Mean±S.D.*

Groups	Pre induction	Induction / Injection	Intubation /Time of effect	Start of surgery	15 minutes	30 minutes	45 minutes	60 minutes	End of surgery	*p* value
A	98.46±0.18	98.33±0.19	97.70±0.38	97.8±0.1	96.8±0.8	96.6±0.2	96.2±0.9	95.8±0.1	94.2±0.2	$p<0.05$
B	98.55±0.12	98±0.14	98±0.15	98.6±0.8	97.5±0.6	97.9±0.6	97.1±0.9	97.8±0.6	97.4±0.8	$p<0.05$
C	98.56±0.09	98.53±0.10	98.23±0.10	97.6±0.5	96.5±07	96.8±0.6	95.6±0.5	94.7±0.2	94.6±0.5	$p<0.o5$
D	98.56±0.06	98.55±0.06	98.39±0.10	98.8±0.1	98±0.3	97.6±0.4	97.4±0.7	97.2±0.8	97.3±0.6	$p<0.05$

Chart 1. *Consort Chart*



ported in clinical studies to lower the chances of inadvertent hypothermia associated with anaesthesia and surgery.[9]

Use of irrigation fluid at room temperature as a cause of hypothermia was postulated by Winter et al.[10] Similar results were observed by a study conducted in our department.[11] Hahn et al and Carpenter et al revealed the benefits of using warmed irrigation fluid for endoscopic procedures.[12] The recently published National Institute for Health and Clinical Excellence (NICE) guidelines and Cochrane review on prevention of peri-operative hypothermia recommends that blood products and fluids administered to patients under anaesthesia should be warmed to 37.0 °C.[13,14] Conversely, other authors did not confirm this result.[15] Our study and that of Dyer and Heathcote[16] provide evidence that although the temperature fall was less with prewarmed irrigant it still dropped at average of 10 °C. The reason for the observation could be the heat loss as the the prewarmed fluid is flushed into the urinary bladder which can be prevented by using continuously warming irrigation system.[17] On the other hand, Jaffe et al found no correlation between irrigation fluid temperatures and fall in core temperature in a TURP procedure.[18]

In none of our patients the core temperature fell below 93.7 °F. This may be attributed to two factors namely shorter duration of surgery (mean duration between 52.75±5.75 to 57.50±9.67 minutes) and lesser usage of irrigation fluid (Mean volume of irrigation fluid used 6.10±2.63 L to 7.61±3.14 L).

Hahn et al reported that limiting surgical time to one hour may prevent hypothermia due to lesser absorption of fluid

irrespective of fluid temperature.[19] We used prewarmed irrigation fluid in Group B and Group D. It is worth mentioning that the drop in on core temperature was less in Group B which could be explained by the work of Gehring and Colleagues, who reported that spontaneously breathing patients under regional anaesthesia absorb more irrigation fluid as compared to the patients receiving general anaesthesia with positive pressure ventilation hence exhibiting much drop in core temperature.[20] However few studies that have observed a similar incidence and magnitude of hypothermia.[21,22]

The positive relationship between hypothermia and regional anaesthesia is a common experience in the clinical settings with additional factor being higher block height and advanced age of the patients.[23] In the current study the block height achieved was T10 in all the patients and comparable age of the patients in all the group.

Regardless of the type of anaesthetic technique used no statistically significant difference was found in the mean nasopharyngeal temperature of patients receiving room temperature irrigation fluid.

The mean of difference in core temperature of the patients who received warm irrigation fluid under general anaesthesia was (1.11±0.28) which was significantly less (p=0.000) as compared to other groups.

We measured core temperature by nasopharyngeal route which is recommended as a reliable method additionally, measurement of the skin temperatures on limbs and trunk in addition to core temperature, could have helped us in estimating mean body temperature and total heat body content.[24] Another limitation of our study was that when the irrigation fluid is warmed from 17 °C to 37 °C there is corresponding change in the density and dynamic fluidity of the irrigating fluid.[25] This aspect of fluid dynamic change should also be considered when it is warmed. In our study we did not look into this aspect.

CONCLUSION

We have demonstrated that intra-operative unintentional hypothermia is more common in usual practice than recorded. Both spinal as well as general anaesthesia leads to peri-operative hypothermia the incidence of which is least when prewarmed irrigation fluid is used in patients under general anaesthesia. However, this cost effective method of prewarming of irrigation fluid should be incorporated routinely in patients undergoing TURP under general or spinal anaesthesia offering decrease post operative thermal discomfort.

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This study was conducted after the approval of Himalayan Institute of Medical Sciences, Ethical committee.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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RESEARCH AND PRACTICE IN ANESTHESIOLOGY

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Letter to the Editor

Anticipated Difficult Intubation Due to Polypoidal Squamous Cell Carcinoma on Posterior One Third of Tongue

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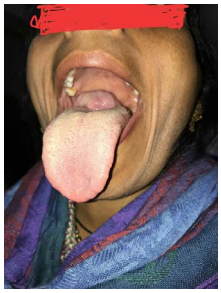
The most common type of tongue malignancy is squamous cell carcinoma (SCC) which constitutes about 36.5% of all oral malignancies.[1] It usually presents as painless swelling which is often ignored by the patient until late when it is symptomatic because of demonstrable growth in the oral cavity.[2] Airway management in carcinoma posterior one third of tongue is always a concern to the anaesthesiologist due to possibility of trauma, bleeding, dislodgement of fractured tissue, chances of aspiration, difficulty in mask ventilation following induction of anaesthesia and compromised airway consequent to difficulty during laryngoscopy and intubation.[3,4]

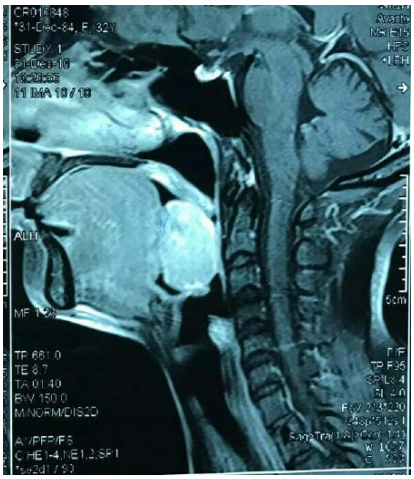
A 32-years-old, ASA grade I, female patient, regular tobacco chewer, presented with recurrent and gradually progressive intraoral polypoidal growth on right side of base of tongue. She was posted for excisional biopsy under general anaesthesia. Airway examination revealed adequate mouth opening with Mallampati grade II. The growth was obliterating the tonsillar fauces and pillars on right side but uvula and soft palate were clearly visible on phonation (Figure 1).

Figure 1. *Showing Polypoidal Growth in Oral Cavity*



Findings of swelling were confirmed by magnetic resonance imaging (MRI) and computed tomography (CT) scan neck which showed polypoidal exophytic lesion at the base of posterior part of tongue in pre epiglottic space measuring 33x23x35 mm with separation of epiglottis from the growth involving right vallecula (Figure 2).

Figure 2. *Showing CT Scan Neck Showing Polypoidal Exophytic Lesion at the Base of Posterior Part of Tongue*



Anticipating difficult intubation, written informed consent was obtained for emergency tracheostomy and patient was shifted to the operation theatre and connected to a standard multipara monitors. Awake fibreoptic intubation was not performed initially because of unavailability of it in our institute at that time.

So instead we opted for video laryngoscope which was at hand for intubation under direct visualization.

After premedication and preoxygenation for 3 minutes, she was induced with intravenous (IV) fentanyl 2 mcg.kg^{-1} and IV Propofol 2 mg.kg^{-1} and IV suxamethonium 1.5 mg.kg^{-1} was administered after confirming adequacy of ventilation by bag mask ventilation. A nasal cuffed endotracheal tube (ETT) size 7.0 mm was passed through left nostril upto oropharynx and a video laryngoscope (King Vision™) was introduced orally. Profuse bleeding started from the polypoidal mass which obscured the laryngoscopic view and hence video laryngoscopy was abandoned. Patient was immediately repositioned with a right lateral tilt and after appropriate suctioning, anaesthesia was deepened with Sevoflurane in oxygen on spontaneous respiration. Reintroduction of a conventional laryngoscope with McCoy blade and external laryngeal manipulation, helped in visualization of vocal cords and the trachea was intubated with cuffed oral ETT 6.5 mm after manipulation. Anaesthesia was maintained with Sevoflurane in oxygen and atracurium. After excision of polypoidal mass, residual neuromuscular blockade was reversed and trachea was extubated after patient was awake.

Difficult airway is the most common cause of morbidity and mortality during surgery of oral cavity malignancies. Flexible fibreoptic bronchoscopy with awake intubation is the gold standard in such anticipated difficult intubations, however friable growths may lead to profuse bleeding and difficulty in visualizing the larynx and subsequent intubation.[4,5]

Tracheal intubation in lateral position is difficult more so in right lateral as compared to left lateral position. Deterioration of the laryngeal view due to limited space between the laryngoscope handle and the table top in right lateral position contributes to difficult intubation with the conventional laryngoscope when the tracheal tube is inserted from the right corner of the mouth. In this case laryngoscopy with McCoy blade and intubation in right lateral instead of left lateral position was preferred as the bleeding mass was encroaching on right oropharynx.[6] Secondly, laryngeal view is more hampered with the King Vision™ video laryngoscope as per our personal experience since introduction of the blade of video laryngoscope is more difficult in lateral position and the camera view is further compromised by fogging or pharyngeal blood. The width and angulation of the blade occupies more oropharyngeal space further reducing the laryngeal view. Though, the video laryngoscope with C-Mac blade has higher success rate of intubation in lateral position it is not available in our institute.[7]

So if advanced intubating aids are not available in case of anticipated difficult airway, we should manage such situations with airway equipments with which we are more familiar. Maintaining oxygenation throughout the procedure should always be ensured.

CONSENT

A written informed consent was obtained from the patient.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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RESEARCH AND PRACTICE IN ANESTHESIOLOGY

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Case Series

SuperNOVA Nasal Mask Ventilation Maintains Oxygenation during Deep Sedation in High-Risk Patients: A Case Series

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ABSTRACT

With the convergence of two major medical trends, increasing obesity and the expansion of minimally invasive procedures come new challenges for airway management. In this case series we describe the use of a nasal ventilation mask, SuperNO$_2$VA™, in 10 patients at high-risk for sedation-induced airway obstruction and hypoxemia that required procedural sedation. This well tolerated device produced nasal oxygenation and positive airway pressure (PAP) that maintained oxygen saturation (SpO$_2$) > 97.0% throughout the cases. These encouraging outcomes suggest the utility of pressurized nasal ventilation masks, such as the SuperNO$_2$VA™, in patients at risk for airway obstruction requiring procedural sedation.

Keywords

SuperNOVA nasal mask ventilation; Hypoxemia; Oxygenating devices.

Abbreviations

OSA: Obstructive Sleep Apnea; HTN: Hypertension; FiO$_2$: Fraction of inspired oxygen; CPAP: Continuous Positive Airway Pressure; HLD: Hyperlipidemia; CAD: Coronary Artery Disease; MI: Myocardial Infarction; SVT: Supraventricular Tachycardia; ESRD: End-Stage Renal Disease; AV: Arteriovenous; HFpEF: Heart Failure with preserved Ejection Fraction; PVD: Peripheral Vascular Disease; AF: Atrial Fibrillation; IDDM: Insulin Dependent Diabetes Mellitus; NIDMM: Non-Insulin Dependent Diabetes Mellitus; BMI: Body Mass Index; PACU: Post-Anesthesia Care Unit; ICU: Intensive Care Unit; TEE: Transesophageal Echocardiography; PMH: Past Medical History; SpO$_2$: Blood Oxygen Saturation; UAO: Upper Airway Obstruction; RCT: Randomized Controlled Trial; NC: Nasal Cannula; CRNA: Certified Registered Nurse Anesthetist; MAC: Monitored Anesthetic Care

INTRODUCTION

With the recent trend of obesity, strategies for implementing a nasal ventilation mask, as standard therapy for deep sedation are becoming increasingly important. The prevalence of obesity has doubled since 1980, and the Centers for Disease Control and Prevention report that more than two-thirds of U.S. adults older than 20-years of age are overweight and 35.7% are obese (BMI 30-40).[1] Obese patients are at a further increased risk for hypoxemia during deep sedation due to a reduced functional residual capacity, increased oxygen consumption, and excess fat deposition within the lateral pharyngeal walls that results in a smaller than normal pharyngeal volume.[2] The prevalence of obstructive sleep apnea (OSA) is estimated to be approximately 25%, and as high as 45% in obese patients, and the prevalence of OSA and its consequences are likely to increase in light of the current obesity epidemic.[3]

Res Pract Anesthesiol Open J. 2018; 3(1): 15-19. doi: 10.17140/RPAOJ-3-119

With increasing utilization of outpatient and minimally invasive procedures, moderate to deep sedation is becoming a more commonly used method of anesthesia.[4] The ASA Committee of Standards and Practice Parameters recommends providing every patient with a continuous course of passive supplemental oxygen and continuously monitoring oxygenation and ventilation during moderate or deep sedation procedures.[5] Unfortunately, recent prospective randomized controlled trials (RCTs) reported up to 54% of all patients experience severe hypoxemia secondary to sedation-related upper airway obstruction (UAO) and respiratory depression.[1] The incidence is exacerbated by obesity and obstructive sleep apnea as independent risk factors with odds ratios 2-9 times that of normal weight patients.[6-7]

Although passive oxygenating devices have the ability to provide higher concentrations of oxygen, they are incapable of generating positive pressure, which is required in order to maintain airway patency and provide ventilatory support in the event of UAO and respiratory depression respectively.[8] Pulse oximetry is a reliable indicator of oxygenation, but has limitations due to the averaging of values causing a delay in registering fluctuations as well as its inability to measure the patient's ventilation status. Therefore, ventilation is best monitored using continuous waveform end-tidal CO_2. Generally it reveals sedation-induced respiratory depression prior to desaturation on pulse oximetry.[2] Thus, one can argue that end-tidal CO_2 ($ETCO_2$) is of greater importance in the setting of moderate and deep sedation. Although many passive oxygenating devices are equipped with CO_2 monitoring, recent prospective RCTs have not shown an improvement in the incidence of severe hypoxemia despite the continuous monitoring $ETCO_2$.[8-9] Recently, high-flow nasal cannula (HFNC) has been used during moderate and deep sedation to improve oxygenation, however, $ETCO_2$ can not be monitored with HFNC due the high flow of O_2 causing dilution.[10] Mitigating the risk for apnea and hypoxia with pharmacologic sedation while avoiding airway instrumentation requires a noninvasive device that provides adequate oxygenation and ventilatory support, protects airway patency, and allows for accurate $ETCO_2$ monitoring.

A sealed nasal ventilation mask, the SuperNO$_2$VA™ (Vyaire Medical, Mettawa, IL, USA), meets these criteria by providing supplemental oxygen, and when connected to either an anesthesia circuit or hyperinflation bag generates positive pressure while allowing for $ETCO_2$ sampling. The device maintains upper airway patency and ventilatory support, while delivering a high FiO_2 at titratable positive pressures. Its ability to generate positive pressures to overcome UAO and airway collapse can reduce the need for endotracheal intubation and its associated complications. Furthermore, the ability to monitor $ETCO_2$ provides timely detection of apnea, even at high-flow rates, due to it being a nearly closed system. We present this nasal ventilation mask as a new option for airway management because of its ability to maintain airway patency and provide sufficient oxygenation during procedural deep sedation in high-risk patients.

Description

Ten (10) patients (5 men and 5 women; mean age 52) undergoing deep sedation procedures with propofol using the SuperNO$_2$VA™ nasal ventilation mask were reported from four different institutions. Nine of the 10 patients were obese with a BMI≥34.4, and all patients were at high-risk for or diagnosed with Obstructive sleep apnea (OSA). Patient history and basic demographic data were collected and their averages were calculated (Table 1). Standard ASA monitors were reported to be used on all patients. Standard practice for the use of the SuperNO$_2$VA™ device at these institutions is to secure it to the patient's nose (Figure 1), connect it to either a hyperinflation bag or anesthesia circuit, set the oxygen fresh gas flow to 10 liters per minute, completely close the adjustable pressure limiting (APL) valve on the hyperinflation or set the anesthesia machine's APL valve to 10 cm H_2O and place the patient's head in neutral position with their mouth closed. All patients received deep sedation by an anesthesia care team. Sedation-related complications that were reviewed and analyzed included hypoxemia (SpO_2<90% for greater than 15 seconds), number of procedure interruptions or early procedure termination, and the use of a nasal airway (Table 2).

Table 1. *Demographics and Observations*[17-20]

Case	n	Age	Gender	BMI or Weight	PMHx	Procedure	Lowest SpO_2 during the case
1	1	50	M	47.2	Morbid obesity, OSA, HTN, HLD, HFpEF, asthma	TEE for Electrocardioversion	99.0%
2-7	6	28-69 (40)	3 M, 3F	104-180 (138) kg	*Obesity, OSA(4 of the 6)*	EGD	99.8%
8	1	56	F	21.6	*Crohn's disease, HTN, asthma*	SVT Ablation	100.0%
9	1	46	F	34.4	*Obesity, IDDM, PVD, CAD s/p MI, HTN, AF, ESRD*	AV Fistula Revision	98.0%
10	1	69	M	36.1	*Morbid obesity, OSA, CAD s/p MI, PVD, NIDDM, Hypothyroidism*	AV Fistula Formation	98.0%

Figure 1: *Nasal CPAP Mask SuperNO2VA™ in Use with $ETCO_2$ Attached During Sedation*

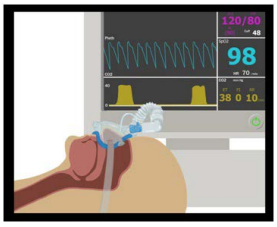


Table 2. *Observed Complications During the Cases*

Complications	n=10 (avg)
Lowest SpO2	98.0-100% (99.0%)
Incidence of hypoxemia	0/10 (0%)
Procedure interruption/termination	0/10 (0%)
Tracheal intubation	0/10 (0%)

Res Pract Anesthesiol Open J. 2018; 3(1): 15-19. doi: 10.17140/RPAOJ-3-119

Case 1

Patient is a 50 year-old morbidly obese (BMI 47.2) male with multiple comorbidities (Table 1) who presented for transesophageal echocardiography (TEE) and electrical cardioversion for persistent atrial fibrillation (AF). The patient was oxygenated with nasal cannula (NC) and sedated with titrated boluses of propofol. Five minutes into the TEE, the patient experienced upper airway obstruction (UAO) and desaturation to <85%. An OPA was inserted and the patient was ventilated with a bag-valve-mask. Secure placement of the SuperNO_2VA™ led to immediate mitigation of the airway obstruction and returned the oxygen saturation to 99%. Despite a successful TEE, cardioversion to normal sinus rhythm failed. The SuperNO_2VA™ was used when the patient returned for a second attempt cardioversion the next day. The patient was successfully cardioverted with no hypoxemic events.

Case 2-7

Six consecutive morbidly obese patients (3 male, 3 female) underwent upper endoscopic gastroduodenoscopy for pre-bariatric screening with deep sedation using the SuperNO_2VA™. The average age and weight of the patients was 40 years and 138 kg respectively. Four of the patients had documented OSA with home-CPAP use. An anesthesiologist or certified registered nurse anesthetist (CRNA) managed the deep sedation with an appropriately dosed sedative. No hypoxemic events occurred and the average lowest SpO_2 was 99.8%.

Case 8

Patient is a 56-year-old female who presented for repeat ablation for recurrent supraventricular tachycardia (SVT). After her first ablation attempt, she required an overnight CPAP. Due to her high risk for UAO with sedation, the SuperNO_2VA™ was incorporated into the anesthetic plan. The SuperNO_2VA™ was lightly secured to the patient's face and oxygen flow was set to 10 L/min. Airway obstruction occurred upon initiation of a propofol infusion. By tightening the mask and creating a seal, the positive pressure generated immediately relieved the obstruction. No other adverse events occurred and oxygen saturation remained at 100% thereafter.

Case 9

A 46-year-old obese (BMI 34.4) female patient with multiple comorbidities (Table 1) presented for an AV fistula revision for dialysis graft. UAO occurred two months prior during AV fistula surgery with monitored anesthesia care (MAC), and an oral and nasopharyngeal airway was placed. One year prior, a tracheostomy was placed for prolonged mechanical ventilation. Due to her history of airway management, the pre-anesthetic plan included placement of the SuperNO_2VA™ prior to sedation with propofol. Oxygen saturation was maintained at 98-100% with positive capnography throughout the procedure and UAO did not occur.

Case 10

Patient is a 69-year-old morbidly obese male (BMI 36.1) with multiple comorbidities (Table 1) who presented for AV fistula formation for dialysis. The SuperNO_2VA™ was placed on the patient prior to procedural sedation. Deep sedation was maintained for 3-4 hours with titrated doses of propofol. Positive $ETCO_2$ was monitored and oxygen saturation was maintained at 98-100% without incidence of UAO and hypoxemia.

DISCUSSION

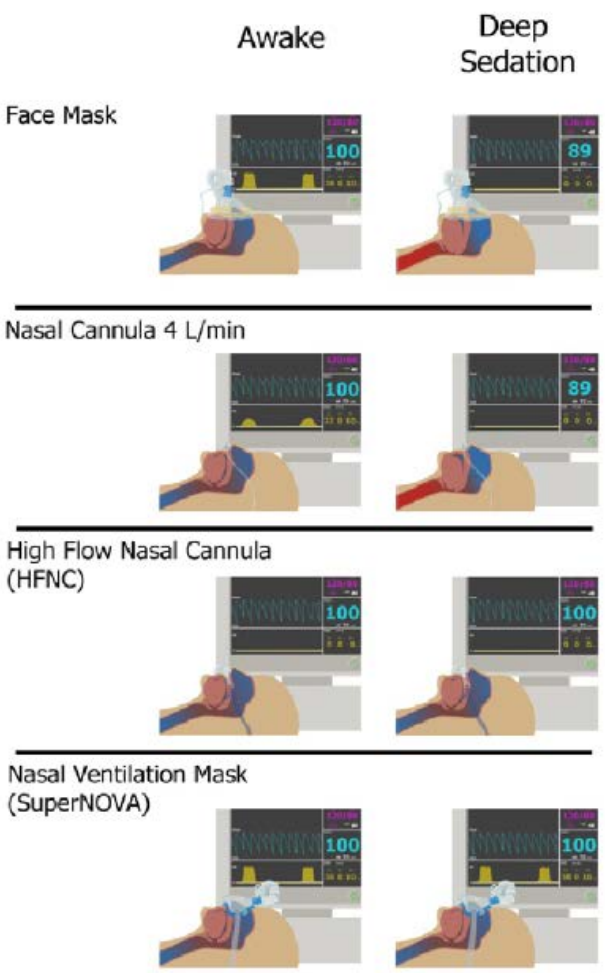
This case series demonstrates the use of the SuperNO_2VA™ nasal ventilation mask connected to either an anesthesia circuit or hyperinflation bag as a noninvasive technique to maintain patient oxygenation and ventilation during deep sedation. All 10 patients underwent procedures requiring deep sedation with propofol, and each patient was at high-risk for severe hypoxemia secondary to sedation-related UAO and respiratory depression. Nine of the 10 patients were obese with a BMI≥34.4 (Table 1), and all patients were at risk for or diagnosed with OSA. With the SuperNO_2VA™ securely placed, 0/10 patients experienced UAO and the lowest oxygen saturation was 98.0%. Airway patency was maintained in all 10 patients and the procedures were performed without interruptions. Table 2 summarizes the total number of complications. The results from this case series indicate that the use of a nasal ventilation mask connected to either an anesthesia circuit or hyperinflation bag is a safe and effective noninvasive ventilation technique to maintain airway patency and ventilation in patients at risk for airway obstruction and respiratory depression during deep sedation.

In today's practice, anesthesiologists and nurse anesthetists depend on passive oxygenating devices to provide adequate oxygenation and $ETCO_2$ monitoring to ensure ventilation in patients under moderate and deep sedation. However, these devices are incapable of establishing a patent airway in the event of UAO, occurring in up to 54% of all sedated patients.[3] HFNC has been supported in literature for relieving airway obstruction, though its utility is limited by a lack of $ETCO_2$ monitoring.[11] The direct measurement of exhaled CO_2 is essential for the early detection of airway obstruction, and its absence should not be considered inconsequential. For this reason, the interest for advanced respiratory monitoring during deep sedation, particularly capnography, is emerging. A nasal ventilation mask that creates a seal, generates continuous positive pressure when connected to either an anesthesia circuit or hyperinflation bag, and monitors $ETCO_2$ presents as a novel, noninvasive approach for ensuring adequate oxygenation and ventilation in any patient at risk for airway obstruction and respiratory depression. For a conceptual comparison of the clinical use and limitations of these devices see Figure 2.

Non-invasive ventilation has grown in popularity in recent decades and has become well-established in the management of acute respiratory failure. Non-invasive techniques avoid complications associated with tracheal intubation in mechanically ventilated patients.[12] The replacement of invasive ventilation in conditions where a non-invasive approach is more appropriate has decreased rates of airway trauma, aspiration, intubation, and overall mortality.[13] The safety and efficacy of noninvasive ventilation during procedural deep sedation is not well known and further studies are needed to clarify its impact on intubation and mortality rates.[14]

Res Pract Anesthesiol Open J. 2018; 3(1): 15-19. doi: 10.17140/RPAOJ-3-119

Figure 2: *Comparison of Face Mask, Nasal Cannula, High Flow Nasal Cannula and Nasal CPAP mask SuperNO2VATM as Used in Patients when Awake and Undergoing Procedural Sedation. Note the Differences in Upper Airway Support and Ability to Capture ETCO2 Monitoring*



Therefore if airway obstruction occurs in this setting, tracheal intubation is seen as an appropriate option, especially since the non-invasive devices available aren't designed to rescue an airway. The results from this case series may suggest that implementation of a nasal ventilation mask, such as the SuperNO$_2$VA™, in patients requiring deep sedation has the potential to prevent unnecessary tracheal intubation and its related complications.

To further report on the significance of the SuperNO$_2$VA™, we must discuss why nasal ventilation may be superior to nasal-oral ventilation. First, a nasal ventilation mask allows unobstructed access to the oral cavity for intraoral procedures in contrast to a traditional full face mask. Second, the solid and immobile structures surrounding the nasal cavity permit a better seal for generating positive pressures, when compared to the soft tissue and mobile structures surrounding the oral cavity. Furthermore, understanding the anatomy involved in airway obstruction will support the favorability of nasal ventilation. Studies have shown that the source for airway obstruction in most patients during deep sedation is the tongue falling against the soft palate which falls against the retropharyngeal wall.[15] Applying positive pressure to the oral cavity via a traditional face mask will force the tongue back into the airway, contributing to the obstruction. In contrast, the positive pressure generated from a nasal ventilation mask will force the tongue and soft palate forward off the retropharyngeal wall, aiding to alleviate the obstruction. A previous study using MRI demonstrated that a nasal CPAP can double pharyngeal volume and serve as a pneumatic splint to alleviate airway obstruction.[16] These are some of the reasons why a nasal ventilation mask is preferred.

This case series suggests a role for nasal ventilation mask in the setting of procedural deep sedation during the procedures discussed. However, the nasal ventilation mask may be applicable to other clinical settings. The advantages illustrated by the cases discussed suggest that nasal continuous positive airway pressure (CPAP) may be efficacious in the operating room, post-anesthesia care unit (PACU), intensive care unit (ICU), or emergency room. Studies that demonstrate the use of the SuperNO$_2$VA™ in the operating room during the process of securing a difficult airway, or attaching the SuperNO$_2$VA™ to a hyperinflation bag for transport to the PACU have already been reported.[21] The observations of this case series are encouraging, and suggest that a pressurized nasal ventilation mask may be a preferable alternative to improve oxygenation and ventilation in high-risk patients during deep sedation. These observations are promising, yet randomized clinical trials are

needed to demonstrate the superiority of a nasal ventilation mask in preventing hypoxia during moderate and deep procedural sedation.

CONSENT FOR PUBLICATION

Consent for publication was obtained from all the patients described in this case series.

FINANCIAL DISCLOSURES

Drs. Foley and Feinleib both report that they are on the medical advisory board of Vyaire Inc. for which they receive compensation.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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Brief Research Report

Post intubation Pharyngolaryngeal Pain in Otorhinolaryngology Surgery: Efficiency of Intra cuff and Extra cuff Lidocaine

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ABSTRACT

Introduction

Post-operative sore throat (POST) represents a real discomfort for patients. In short duration surgeries, sore throat complain can replace the post-operative pain. Many studies intended to reduce its incidence using multiples medications.

Objective

Assess the efficiency of extra cuff lidocaine jelly 2% associated with intra cuff liquid lidocaine 2% on the post extubation syndrome.

Materials and method

Prospective study lead during 3 months in Otorhinolaryngology operating rooms. Inclusion criteria: Every intubation (naso or orotracheal) performed during this period. Exclusion criteria: upper airways surgery, tonsillectomy and patient's refusal. Patients were randomized in 3 groups: First (G1): Control group (inflated cuff with air), Second (G2): liquid lidocaine 2% injected intra cuff, Third (G3): Lidocaine 2% jelly applied on the external surface of the cuff associated with liquid lidocaine intra cuff. Patients were assessed for post-operative sore throat, cough, and hoarseness at 1, 6, and 24 hours after surgery.

Results

Ninety-nine patients were randomized (G1 n=30, G2 n=34, G3 n=35). The association of liquid and jelly lidocaine reduced POST at H1, H6, and H24 after patient's discharge (p respectively at 0.0001; 0.002; 0.003 and 0.004). There was no significant difference in blunting coughing (p=0.053) and post-operative nausea and vomiting (p=0.198)

Conclusion

The association of liquid and jelly lidocaine was efficient in reducing the POST. This result needs to be supported by a larger study including an important number of patients.

INTRODUCTION

Post intubation pharyngolaryngeal pain is a real concern for anesthesiologists. In fact, it represents one of the most reported complains in post-operative care unit (POCU). Many factors were discussed: duration of intubation and intratracheal cuff's pressure. Therefore many studies have tried using lidocaine associated or not with other medications (like betamethasone or alkalinized solutions) in order to reduce this pain. In our study we wanted to assess the efficiency of liquid lidocaine 2% used to inflate the cuff and as a gel on the cuff's external surface on post-operative sore throat (POST).

MATERIALS AND METHODS

It's a prospective study realized during three months in the otorhinolaryngology operative rooms in the 20 August hospital in Casablanca, Morocco.

After a full explanation of the procedure to the patients and obtaining their consent, we randomized them in three groups: control group with no lidocaine (Group 1), use of liquid lidocaine in the cuff (Group 2), use of both lidocaine gel around the cuff and liquid in the cuff (Group 3).

Inclusion criteria were: every orotracheal or nasotracheal intubation realized in our operative rooms.

Exclusion criteria were: non cooperative patient, surgery concerning upper airways or tonsillectomy and sore throat before surgery. Patients with an age less than 18-years-old were excluded.

Cuff's pressure was standardized for all patients to prevent air leak during ventilation. Collected data concerned: demographics, type of surgery with the duration of intubation, number of attempts in intubation with the use or not of other airway device for difficult intubation, coughing after extubation with reintubation. Pain was assessed with visual analog scale (VAS) at H1, H6, H24 and before patient's discharge from the hospital. A physician applied the protocol during anesthesia and the VAS assessment was determined with a help of another anesthesiologist without knowing which protocol was used.

Extracted data was analyzed using SPSS software (IBM New York, United States), Chi-square test was used to assess the relation between sore throat and the protocol. A significance threshold of 0.05 was adopted for all statistical analyses.

The protocol of anesthesia was standardized for all patients. Induction was performed using: Fentanyl 2,5 µg/Kg, propofol 3 mg/Kg and rocuronium at 0,6 mg/Kg to facilitate intubation after a proper ventilation and preoxygenation. Intubation was performed using a single use cuffed PVC tracheal tube. Cuff's pressure was adjusted to 25 cm H_2O. In Group1: the cuff was inflated with air, in the second group with liquid Lidocaine 2%; for the third group, the cuff was inflated with liquid lidocaine 2% and lidocaine 2% gel was applied on the external surface of the cuff.

RESULTS

During the period of the study we included 99 patients. They were randomized into 3 groups:

Group 1: 30 patients,

Group 2: 34 and

Group 3: 35 patients.

3 cases of difficult intubation were noted.

Table 1. *Demographic Data*

Demographic Data	Group 1	Group 2	Group 3
Mean Age (years)	35	43	38
Sex ratio	0.60	0.38	0.49
Mean BMI (kg/m2)	23,81	23,25	23,28
Smokers (n)	4	7	2
Diabetes (n)	1	1	1
Cardiopathy (n)	0	0	0
Hypertension (n)	0	7	3
Dyslipidemia (n)	0	0	0
Orotracheal/nasotracheal (n)	26/4	32/2	25/10

Table 2. *Type of Surgery between the 3 Groups. (Chi Square Test p=0,003)*

		Protocol			Total
		1	2	3	
Surgery	Ear Surgery	15	15	11	41
	Esthetic Surgery	3	8	11	22
	Mandible Surgery	3	3	4	10
	Orbit Surgery	1	0	5	6
	Parotid Surgery	3	2	0	5
	Thyroid Surgery	5	6	4	15
Total		30	34	35	99

Table 3. *Result Comparison between the Groups (Chi Square Test)*

		Group 1	Group 2	Group 3	*p*
Sex	*M*	18	13	17	0.221
	F	12	21	18	
Smoking	*Yes*	4	7	2	0.188
	No	26	27	33	
Difficult intubation		0	2	1	0.390
Number of attempts for intubation					
=1		16	24	22	0.556
=2		12	8	12	
=3		1	2	1	
=4		1	0	0	
VAS (H1) = 0		8	21	26	0.02
=1		0	6	6	
=2		14	7	3	
=3		7	0	0	
=4		1	0	0	
VAS (H6) = 0		17	30	29	0.003
=1		6	2	0	
=2		2	1	4	
=3		4	0	2	
=4		1	1	0	
VAS (H24) = 0		23	33	32	0.004
=1		5	0	0	
=2		0	0	3	
=3		2	1	0	
=4		0	0	0	
VAS at patient's discharge					
=0		23	33	35	
=1		6	0	0	
=2		1	0	0	
=3		0	1	0	
=4		0	0	0	
Coughing		19	14	12	0.053
PONV		4	11	28	0.198

*PONV: Post-operative nausea and vomiting.

DISCUSSION

This POST can represent a discomfort and even a painful experience. It is represented by a syndrome called: Post Extubation Syndrome (PES).[1]

The present study revealed that lidocaine used as liquid in the cuff and as jelly on the external surface reduced the incidence and the intensity of the POST. Although this finding, emergence coughing and the incidence of PONV did not decrease.

The specificity of our study is to relate the PES in short surgeries and in day hospital interventions conducted under general anesthesia. Therefore, intensity of POST can be more important than the post-operative pain.

The incidence of POST is influenced by many factors such as intubation procedure, endotracheal tube (ETT) cuff's pressure, ETT mobilization during procedure, coughing and aspirations before extubation.[2,3,4] After mucosae irritation with the ETT, lidocaine, with its analgesic and anti-inflammatory effects seems to be the first choice for POST topic therapy. Therefore, therapies using lidocaine were applied in order to lower its incidence and severity.[5]

Protocols using lidocaine associated with alkalinized solution or with betamethasone were also evaluated.[6,7] They found that the use of betamethasone and lidocaine did not decrease the incidence of hoarseness, but it increased sore throats incidence. We can hypothesize that the anesthetic effect can decrease the incidence of sore throat but associated lidocaine jelly with its spray increased its side effects.

Post extubation cough can increase the incidence of several complications: bleeding, bronchospasm, higher intra ocular, intra cranial pressure, and wound dehiscence. Therefore, IV lidocaine was efficient in extubation and previous investigation demonstrated that lidocaine jelly applied on the ETT with barrel-shaped cuff prevents cough at immediate post-operative period.[6] Whereas, our study did not find a significant difference in emerging cough.

We found multiple limitations. The first one concerned the subjectivity of the POST. The second one concerned the small number of included patients. The third one is that we included a young population with a maximum mean age at 43-years-old; therefore, results cannot be generalized to elderly people.

It would have been interesting to study smokers' population. With underlying airway irritability, lidocaine can be evaluated in reducing the PES.

CONCLUSION

The present study demonstrated that lidocaine applied on both sides of the cuff reduced efficiently the incidence and the intensity of POST without reducing coughing or PONV. There is a need in conducting larger studies to support this result.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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