Role of preemptive use of mannitol in reducing airway edema following maxillofacial and radical neck surgeries

RM Reyad1*, EG Saleh1, KA Abdel Kader2, RR El Baiely3, AA Ghanem2

Abstract

Introduction

Major head and neck surgeries especially in difficult airway patients have a great hazard for post-operative laryngo-pharyngeal oedema and airway obstruction. In this prospective study, mannitol was administrated intra-operatively in an attempt to reduce airway oedema and hence post-extubation airway collapse and obstruction.

Materials and methods

Two hundred patients undergoing maxillofacial and radical neck surgeries were randomly allocated into the following two equal groups: (1) Group M: in which 0.25 gm /kg mannitol was given after intubation and 30 minutes before the end of surgery. (2) Group C: in which similar volume of the infused mannitol but lactated Ringer was given in the same time points. Cuff-air leak test, flexible fiberoptic laryngoscopic assessment of the upper airway before extubation, post-extubation clinical evaluation of upper airway obstruction and incidence of post-extubation stridor have been conducted to evaluate airway oedema.

Results

The total mean cuff-leak volume was significantly higher in Group M than in the Group C. The incidence of moderate upper airway lesion was statistically significant lower in mannitol group than in control group. The incidence of post-extubation stridor (after failed cuff-leak test was 4/17 (24%) in the mannitol group and 6/26 (23%) in the control group after passed cuff-leak test it was 2/83 (0.02%) in the mannitol group and 4/74 (0.5%) in the control group).

Conclusion

Pre-emptive use of mannitol in maxillo-facial and radical neck surgeries is effective and nearly side effect free to reduce airway oedema and post-extubation airway obstruction.

Introduction

Maxillofacial and orthognathic surgeries, drainage surgeries for severe odontogenic infections and major neck surgeries, all have a great hazard for post-operative laryngo-pharyngeal oedema and airway obstruction1. This condition usually develops either immediately or slowly over several hours and its start is mostly unpredictable.

Management of the difficult airway does not end with patient intubation; in many cases, extubation could be more challenging for the difficult airway, which is defined by the ASA.

Task Force as, ‘it is the clinical situation in which a conventionally trained anaesthesia practioner experiences difficulty with mask ventilation, difficulty with tracheal intubation or both’2.

Multiple pre-disposing risk factors may account for the development of post-operative airway oedema in this category of surgeries and could be either surgery related, anaesthesia related or other factors linked3.

Surgical factors implicated are obstruction or injury of great neck vessels or lymphatics, injury of nerve-supply of the airway, haematoma, massive tongue swelling, e.g. after cervical spine surgery4, direct airway trauma, e.g., laryngeal contusion during sub-mental liposuction5 and jaw wiring6. Anaesthetic factors are prolonged intubation and repeated intubation attempts3, residual anaesthetic, sedative or narcotic effects, inadequate reversal of muscle relaxants or mismanagement of fluid balance with development of interstitial oedema. Angloedema and anaphylaxis7 are immune-mediated mechanisms that may be responsible for acute post-operative upper airway obstruction.

Finally, post-operative airway obstruction may follow surgeries in patients with originally difficult airway, e.g., sleep apnoea syndrome, ankylosis surgery, drainage of massive odontogenic infection8 and Pierre Robin’s sequence9.

Fiberoptic laryngoscopic assessment of the airway revealed oedema of the soft palate and tongue base following uvulo-palatoplasty and this oedema extends to the pharyngeal wall if tonsillectomy is combined10. If maxillomandibular advancement (MMA) has been done, lateral pharyngeal wall oedema occurs and may be associated with hypopharyngeal oedema of the pyriform sinus, areyepiglottic fold, arytenoid and false vocal cords which partially could obstruct the airway11. Glottic oedema on the other hand may be supra-glottic, retro-arytenoidal and sub-glottic. This pattern of airway oedema is of a great importance as it influences the time and degree of post-operative airway obstruction12.

Mannitol, an osmotic agent, is a naturally occurring sugar alcohol that can be used orally or intravenously. Oral mannitol is used for bowel preparation. Intravenous (IV) mannitol is used to induce osmotic diuresis in many clinical situations such as cerebral oedema, traumatic brain injury, raised intra-ocular pressure, as well as assessment of the renal functions13.

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Attributions contributed to conception and design, manuscript preparation, read and approved the final manuscript.
Mannitol can reduce interstitial oedema by two mechanisms, transient reduction of viscosity and a more potent osmotic diuresis. Its usual dosage is 0.25–1 gm/kg IV in divided doses provided that serum osmolality is kept under 320. Mannitol should be avoided in renal failure, serum osmolality > 330, more than 3 days usage, hypotension, cardiac patients and systemic hypertension. Mannitol has a theoretical risk of enlarging intra-cranial haematoma and tearing of bridging subdural veins especially in the elderly. Other beneficial outcomes were linked with use of mannitol include, free radical scavenging and its ability to minimise the effects of mannitol and hence reducing the hazards of steroids.

In this prospective multicentre study, mannitol was used prophylactically in an empiric manner in patients undergoing orthognathic, maxillofacial and radical neck surgeries. Mannitol was administrated intra-operatively in two doses in an attempt to reduce airway oedema and hence post-extubation airway collapse and obstruction.

### Materials and methods

In accordance with ethical Guidelines for Research in Humans, this study was designed as a prospective, multicentre, randomised, controlled clinical study from March 2010 to February 2013, in the National Cancer Institute, Cairo University, together with Cairo University Dental Hospital, Maxillofacial Unit Ain Shams University. The study protocol was approved by the ethical committee and signed informed consent was obtained from all patients allocated in the study. Two hundred patients were involved in the study in these multiple centres, randomly selected and allocated for elective surgeries.

They met the following:

<table>
<thead>
<tr>
<th>Type</th>
<th>Endoscopic aspect</th>
<th>Possible evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early non-specific</td>
<td>Hyperemia</td>
<td>Remission</td>
</tr>
<tr>
<td></td>
<td>Oedema</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Erosion</td>
<td></td>
</tr>
<tr>
<td>Oedema</td>
<td>Protrusion of ventricular mucosa</td>
<td>Remission</td>
</tr>
<tr>
<td></td>
<td>Vocal cord oedema</td>
<td>Reinke’s oedema</td>
</tr>
<tr>
<td>Granulation tissue</td>
<td>Subglottic oedema</td>
<td>Subglottic oedema</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Tongues from vocal process of the arytenoid cartilages</td>
<td>Remission, granuloma, fibrous nodules</td>
</tr>
<tr>
<td></td>
<td>Ulcerating depressions</td>
<td>Scar tissue furrows</td>
</tr>
<tr>
<td></td>
<td>Annular ulcerations in posterior glottis</td>
<td>Synechia of the posterior glottis</td>
</tr>
<tr>
<td></td>
<td>Subglottic ulcerations with cricoid involvement</td>
<td>Subglottic stenosis</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Bleeding, lacerations, dislocated arytenoid cartilage,</td>
<td>Scars, hematoma, infection or abscess, fistula,</td>
</tr>
<tr>
<td></td>
<td>perforation, cricoid ulcerations</td>
<td>cricoarytenoid cartilage fixation</td>
</tr>
</tbody>
</table>

### Research study

The selected patients were randomly allocated into two groups each containing 100 patients: (1) Mannitol group (Group M): in which mannitol is given in doses of 0.25 gm/kg after intubating the patient and before skin incision (first dose) and a similar dose was infused 30 minutes before the end of the surgery (second dose). (2) Control group (Group C) in which similar volume of the infused mannitol but of lactated Ringer was given in the same time points.

### Anaesthetic technique

For all Patients, atropine sulphate 0.015 mg/kg intramuscular (IM) as anti-sialagogue together with dexamethasone 8 mg IV. Hydrocortisone 100 mg and ranitidine 50 mg, were all given as pre-medications 15–30 minutes before induction of anaesthesia meticulous assessment of the airway was done again by the anaesthesiologist. Then, the patient was transferred to the operating theatre where ASA-basic monitors were applied to the patient (pulse–oxymetry, non-invasive blood pressure, ECG 3-Leads and capnography). Insertion of urinary
The difficult intubation trolley was always ready including different types and sizes of airway oral and nasopharyngeal tubes, laryngoscopes, intubating aids, ventilating bougies, paediatric exchange catheter and fibro-optic laryngoscope. Intubation had been carried out using a blind nasal intubation technique by experienced physicians in that manoeuvre if available or the fibro-optic technique with lidocaine spray 10% ‘spray where you go’ to abolish pressor response. After checking the endo-tracheal position of ETT by capnography and chest auscultation, the ETT had been secured carefully. Thereafter, fentanyl 2.5 µg/kg IV and atracurium besylate 0.1 mg/kg every 100% O2 + 1% carbon dioxide at 12 breaths/minute. While the ETT cuff inflated, the mechanical exhaled volume was observed and recorded. Then, the ETT balloon cuff was deflated and the expiratory VT was recorded over the six subsequent respiratory cycles and the average of the lowest three values was taken for analyses. The cuff-leak-volume (CLV) was measured as the difference in the actual VT before and after cuff deflation.

### Table 2: Parameters assessed by means of upper airway obstruction score.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inspiratory sounds</strong></td>
<td>Normal</td>
<td>Snoring</td>
<td>Slow</td>
</tr>
<tr>
<td><strong>Wheezing</strong></td>
<td>Absent</td>
<td>Inspiratory</td>
<td>Inspiratory and expiratory</td>
</tr>
<tr>
<td><strong>Coughing</strong></td>
<td>Absent</td>
<td>Hoarse</td>
<td>Barking</td>
</tr>
<tr>
<td><strong>Retraction and MNA</strong></td>
<td>Absent</td>
<td>MNA and supra sternal retraction</td>
<td>MNA, sub-costal, inter-costal and supra-sternal retraction</td>
</tr>
<tr>
<td><strong>Cyanosis</strong></td>
<td>Absent</td>
<td>Room air</td>
<td>FIO2 &gt; 40%</td>
</tr>
</tbody>
</table>

Anesthesia was maintained using 100% O2 + 1–1.5 MAC isoflurane + atracurium besylate 0.1 mg/kg every 30 minutes. The ratio of the ETT size to laryngeal size was determined using the regression equation developed by Higenbottam and Payne for estimating laryngeal anterior–posterior (A–P) diameter: A–P diameter (mm) = (33.9 × height [cm]) − 33.7. Each patient’s height was recorded, and the A–P diameter was deduced with that regression equation. The ratio was then established by comparing the outer diameter of the ETT to the determined A–P diameter of the larynx.

Analgésia was provided using with Ketolac 30 mg IV drip and paracetamol 1 g IV drip. For mannitol group (group M), 0.25 mg/kg (nearly 100 ml of 20% solution) of mannitol was given at two points: (a) after intubation and before skin incision, (b) 30 minutes before end of surgery. For the control group (Group C), equal volume of lactated Ringer was given at the same time points.

At the end of the surgery, the volatile agent was discontinued, residual muscle relaxant effect was reversed using (pro-stigmine 0.04 mg/kg plus atropine sulphate 0.15 mg/kg) after making sure that respiratory attempts were regained.

When extubation criteria were met with haemodynamic stability, good O2 saturation, adequate respiratory drive with haemodynamic stability, good O2 saturation, adequate respiratory drive VT, RR, Ve inspiratory force of 15-25 cm H2O northermometer and of most importance a fully conscious, alert, oriented patient who can obey demands. Lidocaine 1–1.5 mg/kg IV was given prior to airway assessment in order to ameliorate pressor response and reduce the incidence of laryngeospasm following extubation.

### Evaluation of airway oedema

Several methods and scores have been conducted to evaluate airway oedema. Of which the following:

**Cuff-air leak test**

This test is non-invasive, easy to perform and gives an idea about upper air way patency. The principle of this test is simple and based on the fact that air leakage around cuffed ETT (after deflation) is inversely related to the degree of largengeal oedema. The higher the leakage, the lower the incidence of post-extubation oedema.

In our study, the patients were mechanically ventilated in the volume-assisted control mode with a VT 10 ml/kg of the ideal body weight and RR of 10–12 breaths/minute. While the ETT cuff inflated, the mechanical exhaled volume was observed and recorded. Then, the ETT balloon cuff was deflated and the expiratory VT was recoded over the six subsequent respiratory cycles and the average of the lowest three values was taken for analyses. The cuff-leak-volume (CLV) was measured as the difference in the actual VT before and after cuff deflation.

### Flexible fibre optic laryngoscopic assessment

The assessment of the upper air way was done immediately prior to extubation for all patients by the same physician. Endoscopic findings were classified according to the scale made by Benjamin, who defined endoscopic aspects and prognosis associated with supra-glottic, glottic and sub-glottic oedema.

Based on this classification, we put the following definitions:

- **Minor lesions:** include oedema, hyperaemia and erosions. They usually have favourable outcomes.
- **Moderate lesions:** include subglottic oedema, oedema of the vocal folds, ulceration, granulation tissue, laceration, haematoma and dislocated arytenoids. They probably develop sequelae.
- **Three severe lesions:** stenosis, synechia, paresis or paralysis of the...
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Post-extubation clinical evaluation of upper airway obstruction

Score of Downes and Raphaelly is shown in table 2 (ref. 20). The score is applied by two different experienced observers for all patients. If there is a conflict between the observers in terms of values of each variable and the total score, the opinion of the most experienced observer is accepted. The score is recorded 30 minutes after extubation clinical evaluation.

Upper airway respiratory distress is graded as:

- Absent→score (0)
- Mild→score (1–3)
- Moderate→score (4–6)
- Severe→score (≥7)

Incidence of post-extubation stridor and its severity

In our study, we recorded stridor as either absent or present.

Exubation technique

Direct assessment of the airway using routine laryngoscope and flexible fibre-optic laryngoscope was done to remove the throat pack usually used in oro-maxillofacial surgery and also to remove any debris or foreign bodies and to perform meticulous suctioning of the airway under direct vision to lessen airway trauma. In addition, we assessed both the degree and pattern of airway oedema that may end in post-extubation airway obstruction. Different patterns of airway oedema may be encountered.

Then, after meticulous evaluation of the airway, extubation done with all facilities for re-intubation are in vicinity including the task of surgical airway (retrograde intubation, cricothyrotomy and tracheostomy) which should be available in every case. Those cases with extreme airway difficulty or major airway anatomical changes because of the surgical techniques used were extubated over a paediatric tube exchanger of suitable length and diameter. Patients were transferred to intensive care unit or high dependency post-anesthesia care unit accordingly and subjected to close monitoring over the subsequent hours.

Statistical analysis

Demographic data and type of surgeries performed were collected and tabulated (Table 3 and Table 4). Data were analysed with commercially available software (SPSS for Windows, version 10.0, SPSS, Chicago, Illinois). All continuous variables are reported as mean±SD. Frequencies are used to describe categorical data. The unpaired t-test was used to compare differences between patients for continuous variables with the Bonferroni test for non-parametric variables and the chi-square test was used for a categorical variable.

Results

In the mannitol group, five patients (from six who developed post-extubation stridor [PES]) responded to medical treatment and only one patient needed re-intubation, while seven patients (from 10 who developed post PES) responded to medical treatment and only three patients (from 10 who developed PES) responded to medical treatment and only one patient needed re-intubation (Table 5, 6, 7, and 8).

Discussion

Due to ongoing increased prevalence of both trauma and cancer victims, more and more radical, plastic and reconstructive procedures are done during head and neck surgeries. These vocal cords. They follow prolonged intubation and have marked sequelae19.

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surgeries are now getting lengthier, complex, advanced and staged with more complicated surgical techniques. Making extubations of these patients’ category is extremely challenging.

To re-establish the airway in these patients can be also extremely hazardous and often result in considerable morbidity and mortality. Indeed, adverse events had represented the main cause of injury in the ASA closed claim study (34%), with mortality or brain injury occurring in (85%) of these cases.

In this work, we used several methods to evaluate and predict upper airway oedema and utilised mannitol empirically aiming to reduce the incidence of such hazards.

This study revealed a statistically significant increase in the total mean CLV in the mannitol group than in the control group, and this means a decrease in the incidence of airway oedema with mannitol use.

The incidence of moderate upper airway lesion was statistically significant lower in the mannitol group than in the control group, while there was no statistically significant difference in regards to mild and sever lesions in both groups, also, the incidence of PES was insignificantly lower in the mannitol group than in the control group. This could be explained as mild lesions are not expected to lead to upper airway obstruction while in severe lesions in the upper airway obstruction are mostly due to other factors either surgical or patient related, hence, mannitol has no obvious role in these situations.

It was noticed that the incidence of PES after failed cuff-leak test was 4/17 (24%) in the mannitol group and 6/26(23%) in the control group while the incidence of PES after passed cuff-leak test was 2/83 (0.02%) in the mannitol group and 4/74(0.05%) in the control group. This means that failed cuff-leak test is a good screening test for PES occurrence but passed cuff-leak test does not exclude the possibility of PES and hence there is a need for other methods to assess the upper airway oedema.

In our study, we described cuff-air leak test, direct laryngoscopic and flexible fibre-optic laryngoscopic assessment prior to extubation. These selected manoeuvres were both clinically applicable and their results could be immediately evaluated allowing a more or less clear and sharp decision about the extubation scenario.

Other methods had been described to assess facial and airway oedema including laryngeal ultrasound monitoring and several topographic scales to quantify facial volumes such as photographic techniques, ultrasound, CT and magnetic resonance imaging. However, these techniques have shown variable accuracy and sensitivity and require special circumstances.

Recently a 3-dimensional optical scanner was described for that purpose and proved to be accurate but time consuming (evaluation may extend to about 6-month period). Miller and Cole were the first physicians who tried to make cuff-leak test quantitative by measuring the leak volume and correlating it to the likelihood of developing laryngeal oedema and PES. The cut-off value of the leak volume with highest sensitivity and specificity was calculated as ≥110 ml or ≥12–24% of the delivered VT.

It was suggested to be of low sensitivity (56%) and specificity (92%) in detecting post-extubation laryngeal oedema. It is of limited value in cases such as pharyngeal pathology, because the naso-tracheal tube acts as a stent that keeps the airway patent until the moment of extubation.

So, a routine direct laryngoscopic or even better flexible fibre-optic laryngoscopic assessment of the airway down the glottis were done to evaluate the airway patency and effect of any evolving haematoma.

Flexible fibro-laryngoscope had been used to examine the airway and introduced either orally or nasally. It can assess the airway oedema down to the hidden regions of the airway, e.g. sub-glottic oedema without undue stress on the surgical techniques. It had been used routinely prior to extubation especially if cuff-leak test had revealed unfavourable results.

### Table 5: Endotrachial cuff-leak test values.

<table>
<thead>
<tr>
<th>p Value</th>
<th>Control group (N = 100)</th>
<th>Mannitol group (N = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.43</td>
<td>N = 26</td>
<td>N = 17</td>
</tr>
<tr>
<td>0.51</td>
<td>N = 74</td>
<td>N = 83</td>
</tr>
<tr>
<td>0.001</td>
<td>168 ± 122</td>
<td>284 ± 142</td>
</tr>
<tr>
<td></td>
<td>Failed cuff-leak test (volume &lt; 110 ml)</td>
<td>Passed cuff-leak test (volume &gt; 110 ml)</td>
</tr>
</tbody>
</table>

*p Value ≤ 0.05 is significant.*

### Table 6: Incidence of post-extubation stridor in relation to cuff-leak test.

<table>
<thead>
<tr>
<th>p Value</th>
<th>Control group (N = 100)</th>
<th>Mannitol group (N = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.07</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>0.89</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>0.64</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Total number of PES</td>
<td>Number of PES after failed cuff-leak test</td>
</tr>
</tbody>
</table>

*p Value ≤ 0.05 is significant.*
The sizes of ETT 6.5 mm 7.0 mm and 7.5 mm were selected in this work according to regression equation developed by Higenbottom and Rayne for estimating laryngeal (AP) diameter which consider the ETT outer diameter in relation to laryngeal size and thus we exclude the laryngeal size-ETT diameter disproportion as a misleading factor in evaluation of CLV.

Mannitol is used basically and currently in managing elevated ICP 'Intra-cranial hypertension' (ICH) or cerebral oedema. This medical emergency can happen post-operatively due to haematoma, cerebral oedema, vasodilatation and CSF obstruction. The efficacy of mannitol in treating critically head-injured patients is well settled without the need for randomised controlled trials. About 83% of all USA centres use osmotic diuretics in over 50% of patients with severe head injuries. In another study in the UK, nearly all neurological centres use mannitol in treating ICH.

Mannitol is most metabolised and excreted by glomerular filtration within 30–60 minutes without significant tubular re-absorption or secretion. Mannitol exerts its osmotic diuresis in the proximal tubule and descending limb of Henle's loop. It may oppose the ADH action in the collecting tubules. It thus interferes with normal absorption of water by a countervailing osmotic force. So, urine volume increases and results in water diuresis greater than natriuresis with overall excess water loss plus hypernaemia.

In our study, we used mannitol prophylactically pre-emptive in an attempt to minimise and prevent both cellular and interstitial oedema, which reflect clinically as brain, airway oedema. We relied upon the osmotic diuretic effect of mannitol besides its supposed antioxidant and free radical scavenging property that may interfere with the cascade reaction which ends in cellular and interstitial oedema. Other beneficial effects of routine use of mannitol in our opinion is its marvellous action as a cerebral dehydrating measure to prevent both cellular and interstitial oedema, which reflect clinically as brain, airway oedema. We relied upon the prophylactic, routine, pre-emptive use of mannitol twice (just after intubation and 30 minutes before the end of surgery) as a simple, effective and nearly side effect free manoeuvre to reduce the emergence of airway oedema with its lethal outcome of post-extubation airway obstruction.

**Conclusion**

In conclusion, regarding maxillofacial, orthognathic and radical neck surgeries, drainage of severe odontogenic infections and other operations in difficult airway patients, we recommend the prophylactic, routine, pre-emptive use of mannitol twice (just after intubation and 30 minutes before the end of surgery) as a simple, effective and nearly side effect free manoeuvre to reduce the emergence of airway oedema with its lethal outcome of post-extubation airway obstruction.

**References**