COMPARATIVE STUDY BETWEEN PROPOFOL AND DEXMEDETOMIDINE SEDATION IN REDUCING DELIRIUM AFTER CARDIAC SURGERY IN ELDERLY PATIENTS

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ABSTRACT:

**Background:** Delirium is an acute mental disorder that involves changes in consciousness, attention, cognition, and perception. Postoperative delirium occurs frequently in patients after cardiac surgery and is associated with a prolonged hospital stay, higher costs, and increased morbidity and mortality.

**Aim of the work:** To evaluate and compare propofol vs dexmedetomidine sedation in reducing the incidence of postoperative delirium in elderly patients after cardiac surgery.

**Patients and methods:** The study was done on 150 patients to compare dexmedetomidine versus propofol in reducing delirium post-cardiac surgery in elderly patients. They were divided into 2 equal groups; 75 patients received dexmedetomidine in a dose ranging from 0.2 μg/kg/hr up to max 0.7 μg/kg/hr immediately post-operative, the other group; 75 Patients in the propofol group receiving propofol infusion in ICU from 25 to max 50 μg/kg/ min. until readiness for tracheal extubation. Assessment of delirium was performed with confusion assessment method for ICU. Primary outcome was the incidence of POD.

**Results:** The result of this study showed that there was a statistically significant decrease of incidence of delirium in dexmedetomidine group (17.3%) in comparison to Propofol group (32%) (P < 0.05), there was a statistically significant delayed onset of delirium and there was a statistically significant decrease of mean days of delirium in dexmedetomidine and propofol groups respectively. There was a statistically significant decrease in mean hours of mechanical ventilation in dexmedetomidine group in comparison to propofol group (P < 0.05). Also, our study showed that there was a statistically significant increase in ICU and hospital stay in patients with delirium in comparison to patients without delirium (P < 0.0001).

**Conclusion:** The study revealed that dexmedetomidine reduced the incidence, delayed onset, and shortened duration of delirium in elderly patients after cardiac surgery, without difference in length of stay in ICU and hospital length of stay when compared with propofol.

**Keywords:** Propofol, Dexmedetomidine, Delirium, Cardiac Surgery, Elderly Patients

INTRODUCTION:

The reported incidence of delirium for patients after cardiac surgery ranged from 11% to 46%. Delirium in the ICU is associated with an increased risk of self-extubation, removal of IV catheters, prolonged stay in the ICU, increased mortality, the hospital more days on...
mechanical ventilation and higher costs of care\(^{(1)}\).

Pain, agitation, and delirium are commonly occurring in a critically ill patient, with potential consequences that necessitate treatment with analgesic, sedative, and antipsychotic medication. Sedation is an important component of postoperative management after cardiac surgery and has an important effect on patient outcomes\(^{(2)}\).

Current guidelines suggest that sedation strategies using nonbenzodiazepine sedative (either propofol or dexmedetomidine) may be preferred over sedation with benzodiazepines to improve clinical outcomes in intensive care unit patient\(^{(3)}\).

Dexmedetomidine is a highly selective alpha-2 adrenoceptor agonist used within the ICU for its sedative and anxiolytic effects. Dexmedetomidine exerts both sedative and anxiolytic effects via a mechanism different from other sedatives such as midazolam and propofol. Use of dexmedetomidine is associated with improved patient interaction and provides sedation characterized by prompt response to stimuli with no respiratory depression, therefore it does not interfere with weaning from mechanical ventilation\(^{(4)}\). However, the use of Dexmedetomidine is accompanied by hypotension and bradycardia\(^{(5)}\).

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**THE AIM OF THE WORK:**

The aims of the work is to evaluate and compare propofol vs dexmedetomidine sedation in reducing the incidence of postoperative delirium in elderly patients after cardiac surgery.

**PATIENTS AND METHODS:**

The study was interventional randomized single-blind study. This study was conducted in the national heart institute, Cairo, Egypt, from March 2017 to May 2019.

The study was done on 150 patients to compare dexmedetomidine (Group D) versus propofol (Group P) in reducing delirium post-cardiac surgery in elderly patients.

**Inclusion criteria:** Age > 60 years and patients undergo elective cardiac surgery.

**Exclusion criteria:** Patients with liver (Childs Pugh class-C) or renal impairment. Recent myocardial infarction, heart block and heart rate < 50 beats/min. Systolic blood pressure < 90 mmHg despite continuous vasopressors infusion. Patient on sedative or antipsychotic medication preoperative. Allergy to dexmedetomidine or propofol and documented stroke within the last 6 months.

**Sample Size:** The sample size was calculated using the PASS version 11 program, setting the type-1 error (\(\alpha\)) at 0.05 and the power (1-\(\beta\)) at 0.8. Results from a previous study Maldonado et al.\(^{(6)}\), showed that the incidence of delirium was 32% among dexmedetomidine compared to 55.5% among propofol. Calculation according to these values produces a minimal sample size of 75 cases per group with a total of 150 cases\(^{(7)}\).

**Sample method:** This study was designed to be a randomized single-blind study in which the investigators was aware of the drugs given. Randomization was done using computer-generated numbers. Table of random numbers in 1: 1 ratio in an opaque and sealed envelope. The patient was allocated into two groups upon arrival to ICU postoperatively (75) patient in each group.

**Ethical Consideration:** After obtaining approval from the medical ethics committee of the faculty of medicine Ain Shams University, also from national heart institute written informed consent was obtained from every patient after explaining the procedure. The patient was allocated to the following two groups Dexamedetomidine & Propofol.
Study drugs: Dexmedetomidine (Precedex; Hospira, Precedex 200 mcg/2 ml, Hospira, Inc, Lake Forest, USA), and Propofol (Diprivan, Fresenius Kabi, 10 mg/ml, lack Zurich, USA)

Preoperative Setting: Routine preoperative investigations were done to all patients including laboratory investigations (complete blood picture, kidney function tests, liver function tests), Electrocardiogram (ECG), Echocardiography and others as needed by the patient's condition.

Study Interventions: Patients were randomly allocated into two groups, Dexmedetomidine group (D) and Propofol group (P).

Group (D): Upon arrival to ICU, patients (75 Patients) received IV dexmedetomidine infusion in a dose started with 0.2 μg/kg/hr with incremental dose 0.1 μg/kg/hr till maximum 0.7μg/kg/hr. Dexmedetomidine was diluted in 5% dextrose, given through a separate line and no bolus doses were admitted. The infusion of dexmedetomidine started in ICU and was continued for a maximum of 24 h.

Group (P): Upon arrival to ICU, patients (75 Patients) received IV propofol infusion undiluted started in ICU in a dose of 25μg/kg/ min. with incremental dose to maximal 50μg/kg/ min. until readiness for tracheal extubation.

Upon arrival to the ICU, Infusion rates of the studied drugs were titrated in order to achieve and maintain light sedation using Richmond Agitation-Sedation Scale (RASS -2 to +1) before extubation and (RASS 0) after extubation (8).

Titration of the study medication infusion included interruption (4-hourly) and reduction of dose aimed to achieve light sedation resulting in a calm and co-operative patient. Once the patient is awake and responsive, accurate sedation, pain, and delirium assessment can be obtained, as well as a spontaneous breathing trial of the ventilated patient. The sedative infusion was discontinued, in preparation for extubation. Extubation was undertaken when there was no evidence of bleeding and the patient was alert, hemodynamically stable, normothermic and with an arterial oxygen tension ≥70 mmHg on an inspired oxygen concentration ≤ 35% and had positive end-expiratory pressure < 5 cm H2O, spontaneous respiration had been established with pressure support < 10 cm H2O, a tidal volume of > 6 ml/kg and respiratory rate ≥10 breaths/min but < 20 breaths/min. Because of specific pharmacological properties of Propofol (respiratory depression) therefore, patients have weaned off propofol infusions before extubation, whereas patients receiving dexmedetomidine infusion was stopped at the time of extubation. If mechanical ventilation was required beyond the 24 hours, patients in the dexmedetomidine group were converted to propofol sedation.

Primary Outcome: Incidence of delirium in both groups.


Statistical Analysis: Results of the present study were statistically analyzed using SPSS v. 22 and MedCalc v. 18.2. Data were represented as mean, standard deviation (SD), or number and percentage. A comparison between quantitative variables was carried out by the student's t-test which was used to test the difference of means between two groups. The Chi-squared test is used to test the relationship between two classification factors. P value less than 0.05 was considered statistically significant.
RESULTS:

Table (1): Demographic data for both groups.

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>Group D (n=75)</th>
<th>Group P (n=75)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) Mean±SD</td>
<td>67.9 ± 4.2</td>
<td>68.9 ± 3.6*</td>
<td>0.116</td>
</tr>
<tr>
<td>Males N (%)</td>
<td>39 (52%)</td>
<td>38 (50.7%)*</td>
<td>0.08</td>
</tr>
<tr>
<td>Females N (%)</td>
<td>36 (48%)</td>
<td>37 (49.3%)*</td>
<td>0.09</td>
</tr>
<tr>
<td>BMI Mean±SD</td>
<td>27.8 ± 1.5</td>
<td>28.1 ± 1.4*</td>
<td>0.134</td>
</tr>
</tbody>
</table>

Data are presented as mean± standard deviation, number of patients (%). P> 0.05 is considered statistically non-significant. BMI=body mass index. • Chi-squared test, ♦ Student's t-test.

The results of the current study showed no statistically significant difference in demographic data including age, sex, body mass index between two groups of the study (P > 0.05) (Table 1).

Table (2): Type of surgery in both groups.

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Group D (N=75)</th>
<th>Group P (N=75)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG N (%)</td>
<td>42 (56%)</td>
<td>44 (58.7%)*</td>
<td>0.089</td>
</tr>
<tr>
<td>Valve surgery N (%)</td>
<td>29 (38.7%)</td>
<td>24 (32%)*</td>
<td>0.078</td>
</tr>
<tr>
<td>Replacement of ascending aorta N (%)</td>
<td>4 (5.3%)</td>
<td>7 (9.3%)*</td>
<td>0.099</td>
</tr>
<tr>
<td>Number of grafts</td>
<td>3 ± 0.75</td>
<td>2 ± 0.75*</td>
<td>0.075</td>
</tr>
<tr>
<td></td>
<td>3 (1-4)</td>
<td>2 (1-4)</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as a number of patients (%). P> 0.05 is considered statistically non-significant. • Chi-squared test,

There is statistically no significant difference in the distribution of surgery types between the two groups of the study (P > 0.05) (Table 2).

Table (3): Incidence, length of stay and side effects of drugs in all patients in both studied groups.

<table>
<thead>
<tr>
<th>Postoperative</th>
<th>Group D (N=75)</th>
<th>Group P (N=75)</th>
<th>Relative risk (RR)</th>
<th>CI 95%</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of delirium N (%)</td>
<td>13 (17.3%)</td>
<td>24 (32%)</td>
<td>0.54</td>
<td>0206-0.962</td>
<td>0.037*</td>
</tr>
<tr>
<td>ICU stay (h)</td>
<td>71.3 ± 7.83</td>
<td>71.75±7.34♦</td>
<td></td>
<td></td>
<td>0.708</td>
</tr>
<tr>
<td>Hospital stay (day)</td>
<td>8.69 ± 0.62</td>
<td>9.2 ± 0.68♦</td>
<td></td>
<td></td>
<td>0.127</td>
</tr>
<tr>
<td>Drugs side effect</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>10</td>
<td>7</td>
<td>0.669</td>
<td>1.06 - 5.51</td>
<td>0.44</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>6</td>
<td>3</td>
<td>0.479</td>
<td>0.115-1.99</td>
<td>0.302</td>
</tr>
</tbody>
</table>

Data are presented as the number of patients (%), mean± standard deviation, RR = Relative Risk, CI 95%= confidence interval 95%. *P<0.05 is considered statistically significant (student's t-test).

The result of this study showed that there is a statistically significant decrease of incidence of delirium in Dexametomidine group (17.3%) in comparison to Propofol group (32%) (P < 0.05), with relative risk 0.54 means that incidence of delirium in the group (D) is 0.54 times less than group (P). As regards ICU stay, there was no statistically significant difference between both groups (P > 0.05). As regards the hospital stay, there was no statistically significant difference between both groups (P > 0.05). Drug side effects (hypotension & bradycardia), showed there were no statistically significant differences between both groups (P > 0.05) (Table 3).
Patients with delirium in the dexmedetomidine group showed a significant delay of onset of delirium when compared with the propofol group (P < 0.001). Also, the duration of delirium was reduced in the dexmedetomidine group (P < 0.001). The duration of mechanical ventilation was reduced in the dexmedetomidine group when compared with the propofol group (P < 0.001) (figure 1).

Data are presented as the number of patients (%), mean ± standard deviation, N= number of the patient. *P < 0.05 is considered statistically significant. • Chi-squared test, * student's t-test.

This study showed that the number of patients who received haloperidol was significantly less in the dexmedetomidine group than the propofol group (9 vs 20 respectively with (P < 0.001). As regard patients with delirium, the dose of haloperidol was a statistically significant decrease of the mean dose of haloperidol in the group (D) in comparison to group (P) (P <0.05). There was a statistically significant decrease in the mean dose of morphine and fentanyl in the group (D) in comparison to the group (P) (P <0.05) (Table 4).

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Group D (N=13)</th>
<th>Group P (N=24)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need haloperidol N(%)</td>
<td>9 (69.2%)</td>
<td>20 (83.3%)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Dose of haloperidol (mg)</td>
<td>1.09 ± 0.5</td>
<td>2.11 ± 0.68</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Total morphine dose (mg)</td>
<td>5.16 ± 1.06</td>
<td>6.8 ± 1.07</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Total fentanyl dose (ug)</td>
<td>654.8 ± 18.22</td>
<td>680 ± 12.7</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Acetaminophine dose (g)</td>
<td>8 ± 0.7</td>
<td>8.2 ± 0.8</td>
<td>0.91</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation. *P<0.05 is considered statistically significant. * student's t-test.

Table (5): Comparison between Patients with and without Delirium.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Patient with delirium (37)</th>
<th>Patient without delirium (113)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>67.05± 2.45</td>
<td>66.8± 2.1*</td>
<td>0.709</td>
</tr>
<tr>
<td>Duration of mechanical ventilation (h)</td>
<td>6.01 ± 0.62</td>
<td>4.32± 0.51*</td>
<td>&lt; 0.0001*</td>
</tr>
<tr>
<td>ICU stay (h)</td>
<td>70.65 ± 4.8</td>
<td>63.2 ± 3.9*</td>
<td>&lt; 0.0001*</td>
</tr>
<tr>
<td>Hospital stay (day)</td>
<td>8.41 ± 0.55</td>
<td>6.73 ± 0.5*</td>
<td>&lt; 0.0001*</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation. *P<0.05 is considered statistically significant. • student's t-test.
This study showed that there was a statistically significant increase in the mean duration of mechanical ventilation in patients with delirium in comparison to patients without delirium (P < 0.0001). Also, our study showed that there was a statistically significant increase in ICU and hospital stay in patients with delirium in comparison to patients without delirium (P < 0.0001) (Table 5).

Regarding the onset and duration of POD, our results showed that there was significant delay of onset of delirium and significant decrease of mean days of delirium in the dexmedetomidine group in comparison to the propofol group with (p < 0.001).

The result of this study is in agreement with Shehabi et al. (11) compared to the prevalence of delirium with dexmedetomidine versus morphine-based sedation in patients undergoing cardiac surgery. The frequency of delirium was assessed daily for the first five days after surgery using the (CAM-ICU) showed a shorter duration of delirium in the dexmedetomidine group.

Li et al. (12), evaluate the use of dexmedetomidine in the incidence of postoperative delirium in elderly patients undergoing cardiac surgery. The study was done in 285 elderly cardiac surgical patients. The patients were randomized into two groups, one receiving dexmedetomidine and the other receiving saline solution and analyzed the results. Dexmedetomidine was given at the rate of 0.6μg/kg over 10 minutes, then at a rate of 0.4μg/kg/h until the end of surgery. After surgery, the study drug infusion was continued at a rate of 0.1μg/kg/h until the end of mechanical ventilation. CAM-ICU and CAM were used to assess delirium. There was no significant difference between the two groups regarding the incidence of delirium during the first 5 days after surgery. Although the time to extubation was shorter for patients in the dexmedetomidine group, there were no significant differences between the two groups regarding the incidence of delirium within 5 days after surgery, the duration of delirium, the lengths of stay in ICU and hospital after surgery.
In the current study, as regards to the duration of mechanical ventilation in delirious patients, there was a significant decrease of mean hours of MV in the dexmedetomidine group than the propofol group with (p<0.001), and there was a significant increase of mean duration of MV in patients with delirium in comparison to patients without delirium (p<0.001).

The results of this study in agreement with Curtis et al.(13), who reported in his results that dexmedetomidine based sedation resulted in the achievement of early extubation more frequently than propofol-based sedation. Mean postoperative time to extubation and average hospital length of stay (LOS) was shorter with dexmedetomidine-based sedation and met a statistical level of significance. There was no difference in ICU-LOS or in-hospital stay between the two groups.

These results go in agreement with Wanat et al.(14) there study done on 352 patients undergoing elective cardiac surgery and upon arrival to the ICU, 33 patients received initial sedation with dexmedetomidine and 319 patients received propofol, and their results showed that Sedation with dexmedetomidine resulted in a significant reduction in time on mechanical ventilation. However, no difference was seen in ICU or hospital LOS.

As regard to analgesic and rescue requirements in delirious patients, our results showed there was a significant reduction in the dose of fentanyl, morphine, and haloperidol used in the dexmedetomidine group in comparison to propofol group (p<0.001).

This goes in harmony with Priye et al. (15), in their randomized, double-blind study, sixty-four patients who underwent elective cardiac surgery divided into two groups. Group A (n = 32) received a 12 h infusion of normal saline and group B (n = 32) received a 12 h infusion of dexmedetomidine 0.4 μg/kg/h. Postoperative pain was managed with bolus intravenous fentanyl. Their result showed that dexmedetomidine treated patients had significantly less morphine and total fentanyl consumption.

Moharram and El Midany(16), in their randomized, prospective, double-blind study, investigated the effect of postoperative dexmedetomidine on the analgesic requirement in post-cardiac surgery patients. The study was conducted on 60 patients scheduled for elective coronary artery bypass graft surgery, group D (n=30) received dexmedetomidine infused at a rate of 0.1–0.2 μg/kg/h, whereas group C (n=30) received an equal volume of saline at an infusion rate of 0.1–0.2 μg/kg/h immediately from the end of surgery and postoperatively in the ICU thereafter. Postoperative analgesia was assessed using the Numeric Pain Intensity Scale. Their study showed that the addition of dexmedetomidine infusion following CABG was associated with a reduction in morphine consumption with a significant reduction in the time to extubation and the length of ICU stay.

Our results revealed that as regard ICU and hospital stay in all patients there was no statistically significant difference between dexmedetomidine and propofol group also in delirious patients there was no statistically significant difference (P > 0.05). On the contrary, there was a statistically significant increase in ICU and hospital stay in patients with delirium in comparison to patients without delirium.

This agrees with Lin et al.(2) who found that there was no significant difference in the duration of ICU stay and hospital days following cardiac surgery (p = 0.4).

Djaiani et al.(10) their study showed that the ICU and hospital stay were shortened in the dexmedetomidine group when compared with propofol-based sedation in elderly patients after cardiac surgery.

Our result showed that the incidence of bradycardia and hypotension was more in
the dexmedetomidine group when compared with the propofol group but without statistically significant differences with \( p > 0.05 \), These results go in harmony with a meta-analysis done by Liu et al.\(^{17}\).

Gong et al.\(^{18}\), in their meta-analysis, their result showed that dexmedetomidine was found to lower heart rate, lower systolic blood pressure, lower the incidence of tachycardia and arrhythmias in both adult and pediatric patients, but elevated the risk of bradycardia.

The result of the current study showed that dexmedetomidine based sedation regimen in the post-cardiac surgery operations was associated with a reduction in the incidence, onset, and duration of delirium, with a significant reduction in the duration of mechanical ventilation, with the reduction in analgesic, an anti-psychotic requirement but no significant reduction in ICU and hospital stay when compared with propofol infusion.

**Conclusion**

Comparing dexmedetomidine and propofol, sedation in reducing the incidence of postoperative delirium in elderly patients after cardiac surgery was associated with a significant reduction the incidence, onset, and duration of delirium, but no difference in length of stay in ICU and hospital length of stay between both groups. Also, there was a reduction in the postoperative duration of mechanical ventilation and the dose of analgesics and sedatives requirements in the dexmedetomidine group than and propofol group.

**REFERENCES:**


دراسة مقارنة بين عقار البروبوفول و الديكسيديميتوميدين كمهمّدة للحد من الهذيان في المرضى كبار السن بعد جراحة القلب

سامية إبراهيم شرف. سامح حنفي. شريف جورج أسعد. مروة ممدوح الفار.

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اخصائي الرعاية المركزية – معهد القلب القومي – القاهرة**

الخلفية العلمية: يُعرّف الهذيان بأنه اضطراب عقلي حاد وزيادة في تكلفة في الوعي والانتباه، يتراوح بين حالة عقلية اضطراب وفقدان القدرة على التفكير والتفكير غير متظم. وقد يعاني المريض من الهذيان من الأوراق في شاشة ولد الأفكار في المرضى كبار السن بعد جراحة القلب والذي دائما ما يكون مصاحباً مع البقاء في الخرف أو الهذيان المختلط. وتشمل هذه المشاكل وارتفاع الكشف والإداف والتغييرات في الوعي والتفاوت المنظوري في حالات الهذيان التي تبلغ عددها عند كبار السن بعد جراحة القلب، ويتراوح نسبة انتقال الهذيان في حالات الهذيان في المرضى المسنين بين 11% إلى 64%.

الهدف من البحث: تقييم ومقارنة عقار البروبوفول مقابل الديكسيديميتوميدين في حالات الهذيان في المرضى المسنين بعد جراحة القلب.

المريض وطريقة البحث: تم إجراء الدراسة على 90 مريض من أصل مصريان عقار ديكسيديميتوميدين مقابل عقار البروبوفول في الحد من الهذيان في المرضى المسنين بعد اجراء جراحة القلب. تم تقسيم المرضى إلى مجموعتين متساويتين حيث تلقى 45 مريض عقار ديكسيديميتوميدين جرعات تتراوح بين 2-0 ميكروغرام / كيلوغرام / ساعة إلى 7 ميكروغرام / كيلوغرام / ساعة على الفور بعد العملية الجراحية. المجموعة الأخرى 45 مريض في مجموعة البروبوفول الذين يتلقون حق البروبوفول في وحدة العناية المركزية من 50 إلى 55 ميكروغرام / كغ / دقيقة حتى الاستعداد لزخ الأدوية الحضرية.

نتائج البحث: أظهرت هذه الدراسة وجود زيادة ذات دلالة إحصائية في متوسط مدة الهذيان الميكانيكي لدى المرضى الذين يتلقون علاج عن الهذيان بالمقارنة مع المرضى الذين ليس لديهم هذيان (P<0.001). أيضاً، أظهرت دراسة أن هناك زيادة ذات دلالة إحصائية في وحدة العناية المركزية والبقاء في المستشفى في المرضى الذين يتلقون علاج عن الهذيان بالمقارنة مع المرضى الذين ليس لديهم هذيان.

الاستنتاج: كشفت الدراسة أن المريض بالمقارنة مع الديكسيديميتوميدين أقل في نسبة حدوث وحدة الهذيان وكذلك مدة الهذيان الميكانيكي، وأقل احتجاجاً للسكتات والمهنودات بوحدة العناية المركزية ولكن لا يوجد فرق بين المجموعتين في هذه الاقتراع بالرعاية المركزية أو المستشفى.

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