# Potential Reno-Protective Effect of Dexmedetomidine Versus N. Acetylcysteine Among Patients Undergoing Cardiac Surgery

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## Abstract

**Background:** Acute kidney injury (AKI) is one of the severe complications after cardiac surgeries, raising morbidities and mortalities.

**Objectives:** The study aimed to compare the potential reno-protective effect of continuous I.V infusion of Dexmedetomidine (DEX) and N-Acetylcysteine (NAC) among cases undergoing Cardiac surgeries.

**Patients and Methods:** This randomized, double-blind, placebo-controlled trial was done at Qena University Hospitals and Sohag Cardiac Institute in period between October 2019 to October 2021, including 90 cases listed for elective on pump open-heart surgeries.

**Results:** Regarding Urine Output(UOP), the DEX group showed a significantly higher UOP value than both NAC and placebo groups at day 1 postoperatively. Still on day 2 postoperatively, the DEX group showed a statistically significant higher UOP value than the placebo group only. Also, there were non-statistically significant differences between pre-operative and postoperative values in each group (between basal and final values). Regarding urinaryNeutrophil Gelatinase-associated Lipocalin (NGAL), there were non-statistically significant differences between groups at baseline, but the DEX group showed a significantly lower NGAL values than the placebo group at T1 and T2 postoperatively. Also, there were statistically significant differences between pre-operative and postoperative values in all groups.DEX group showed significantly lower postoperative AKI incidencethan placebo group.

**Conclusion:** DEX could have a more reno-protective effect among patients undergoing cardiac surgery than N-acetylcysteine or placebo. This was demonstrated by lower urinary NGAL level, raised UOP, and lower postoperative AKI among cases treated with DEX.

**Keywords:** Acute kidney injury, Dexmedetomidine, N-Acetylcysteine, Cardiac surgeries.

## Introduction

Acute kidney injury (AKI) is one of the severe complications after cardiac surgerieswhich raises morbidities and mortalities. The risk factors include reduced left ventricular function, diabetes mellitus, high blood pressure, generalized atherosclerosis, pre-operative kidney dysfunctions, advanced ages, and extended cardiopulmonary bypass (CPB) **(Engelman et al., 2019).**

Dexmedetomidine (DEX) is a highly selective α2-adrenoceptor agonist with substantial sympatholytic properties and ameliorating stress response **(Xue et al., 2016).** DEX also reduces the norepinephrine levels in the blood, and consequently, it persuades renal artery vasodilatation and increases renal blood flow and urine output (UOP). moreover, it reduces antidiuretic hormone secretion and elevates the release of atrial natriuretic peptidescausing natriuresis. N-Acetylcysteine (NAC) is also an alternative therapy because of its anti-inflammatory and anti-oxidant characteristics that attenuate AKI throughout cardiac surgeries explicitly through the control of systemic inflammation, free radical injuries, and ischemia **(Priyanka et al., 2021).**

This study aimed to compare the potential reno-protective effect of continuous I.V infusions of DEX and NAC among cases undergoing cardiac surgeries.

## Patients and methods

This prospective, double-blind, randomized placebo-controlled trial was conducted at Qena University Hospitals and Sohag Cardiac Institute in period between October 2019 to October 2021.

Ninety consecutive cases aged 18-60 years and listed for elective open-heart surgeries via the CPB method were selected to participate in the study. Cases were randomly (using sealed envelopes) allocated to 3 groups:

Group A, (DEX group) (PRECEDEX vial 200 mcg in 2 ml)( Hospira Inc.-USA, United group pharmaceutical),30 patients receiveda continuous I.V infusion of DEX starting 5 minutes before CPB procedure (0.5mcg/kg over 20 minutes followedby 0.4 mcg/kg/hr) diluted to a total volume of 50 cc using 0.9% NaCl solution until the end of the surgery.

Group B, (NAC group) (ROTACYSTEINE 20 %)(Egypt pharm) (vial 25 ml volume), 30 patients received a continuous I. V infusion of NAC initiated 5 minutes before CPB (100mg/kg over 20 minutes followed by 20 mg/kg/hr) diluted to a total volume of 50 cc using 5% dextrose solution until the end of the surgery.

Group C (Placebo group), 30 patients received an equal volume of saline as a bolus and infusion.

**Exclusion criteria:** Patient refusal, pregnancy, pre-operative renal damage (Serum creatinine >2.5mg/dl), prior renal or Cardiac transplantation, recognized allergy to research medications, severe heart failure (HF) (cases with ejection fractions (EF)<35%) and planned off-pump surgery.

***Perioperative management***

Upon arrival to the OR, I.V midazolam pre-medication (0.03–0.1 mg per kg) was applied 10 minutes before induction of general anesthesia.All patients were connected to baseline monitor. Under complete aseptic technique and regional anesthesia, a 20-gauge arterial cannula was introduced in the radial artery. A triple lumen central venous pressure (CVP) catheter was also inserted into the right internal jugular vein.Blood Urea (BU), Serum creatinine (S. Cr) and Creatinine Clearance (estimated Glomerular Filtration Rate) (eGFR) according to Cockcroft-gault equation) were ordered at 5 periods: baseline earlier to induction(T0), after surgery (T1), and then at 12 (T2), 24 (T3), and 72 (T4) hours postoperatively.

Anesthesia was induced via propofol 1.5-2 mg/kg and fentanyl 3-5 mcg/kg titrated according to hemodynamics. Tracheal intubations were simplified using atracurium 0.5 mg/kg, and anesthesia was maintained with isoflurane 1 MAC in 50% oxygen and air, fentanyl 3-5 mcg/kg/h, and atracurium 2 mcg/kg/min.The urinary bladder catheter and nasopharyngeal temperature probe were inserted after induction of anesthesia.

UOP was documented within the whole procedure of operation, postoperative day (POD) 1 and 2.Urinary Neutrophil Gelatinase-associated Lipocalin (NGAL) was recorded after urinary catheter insertion (T0), at 6 h and 24 h postoperatively (T1, T2).(urinary NGAL was measured via enzyme linked immunosorbent assay**(ELISA kit)** (Elabscience, Catalog No: E-EL-H0096,China).Ventilation was adjusted to maintain end-tidal $CO_2$ from 35 to 45 mmHg. Heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure (MAP) were continuously observed. The pressure transducers were zeroed versus atmospheric pressure and preserved above 60 mmHg by vasoconstrictors (Ephedrine ornorepinephrine). CVP was maintained within normal range by intravenous fluids infusions. Blood glucose levels had been kept in values between 140 to180 mg per dl. Then 5 minutes before CPB, patients received either one of the drugs in the A, B, and C groups mentioned before.

***Study endpoints***

a. **Primary endpoints:** Incidence of postoperative AKI in the 3 groups was guided by serum creatinine level, BU, creatinine clearance (Cockcroft-Gault formula), amount of UOP, and urinary NGAL.

b. **Secondary endpoints:** duration of postoperative mechanical ventilation (MV), reoperation within 24 hours, ICU period, hospitalization period,postoperative AKI, postoperative Acute Renal Failure (ARF), 30days needfor Renal Replacement Therapy (RRT) and 30days mortality.

**Sample size calculation:** The sample size was calculated to achieve a decrease in AKI from 40% in the placebo group to 15% in either (DEX or NAC) group. The calculation was performed using 2-side $X^2$ testing with a significance level at 0.05 and a power of

80%; the sample size was 30 cases for each group. Consequently, a number of 90 patients were enrolled in the current work.

***Ethical consideration***

The study protocol was approved by the Ethical Committee of Faculty of Medicine, South Valley University and written informed consent was taken from each patient.

**Statistical tests:** Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20. The qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric. The comparison between two groups with qualitative data was done by using Chi-square test and/or Fisher exact testwas used instead of Chi-square test when the expected count in any cell was found less than 5.The comparison between more than two independent groups with quantitative data and parametric distribution was done by using One Way ANOVA Test.The comparison between more than two paired groups with quantitative data and parametric distribution was done by using Repeated Measure ANOVA.

**Results**

Non-significant changes were found among the study groups regarding age, weight, body surface area, and gender **(Table 1).**

**Table 1. Patients' Characteristics and Pre-Operative Clinical Data of Studied Groups**

| Variable | DEX group (n=30) | NAC group (n=30) | Placebo group (n=30) | P value |
|---|---|---|---|---|
| **Age (year)** | 58.32 +0.45 | 56.77 +3.32 | 57.18 +1.36 | 0.065 |
| **Weight (Kg)** | 83.18+3.31 | 85.51+7.12 | 82.25+3.24 | 0.064 |
| **Body surface area ($m^2$)** | 1.93+0.21 | 1.91+0.41 | 1.95+0.62 | 0.142 |
| **Sex:**<br>**- Male**<br>**- Female** | 18 (60%)<br>12 (40%) | 14 (46.7%)<br>16 (53.3%) | 13 (43.3%)<br>17 (57.7%) | 0.093 |

There was a non-statistically significant difference between groups at baseline, T1, T2, T3, and T4 measures regarding serum creatinine, BU, and creatinine clearance. Also, there was a non-statistically significant difference between pre-operative and postoperative values in each group (Between basal and final values) **(Table 2).**

**Table 2. Comparison of creatinine, urea and creatinine clearance rate of studied groups**

| Variable | DEX group (n=30) | NAC group (n=30) | Placebo group (n=30) | P value |
|---|---|---|---|---|
| **Serum creatinine (mg/dL)** | | | | |
| **T0** | 1.57±0.35 | 1.67±0.23 | 1.55±0.22 | 0.296 |
| **T1** | 1.51±0.46 | 1.65±0.51 | 1.64±0.62 | 0.229 |
| **T2** | 1.48±0.63 | 1.63±0.38 | 1.69±0.47 | 0.157 |
| **T3** | 1.44±0.38 | 1.74±0.61 | 1.72±0.81 | 0.106 |
| **T4** | 1.43±0.42 | 1.75±0.48 | 1.76±0.55 | 0.094 |
| **PX** | 0.232 | 0.316 | 0.110 | |
| **Blood Urea (mg/dL)** | | | | |
| **T0** | 50.31±4.65 | 48.66±3.24 | 47.66±6.50 | 0.121 |
| **T1** | 48.62±6.21 | 50.38±8.46 | 48.26±2.42 | 0.373 |
| **T2** | 48.56±5.39 | 51.93±6.24 | 50.29±9.35 | 0.199 |
| **T3** | 48.13±8.26 | 51.53±7.43 | .63±7.2450 | 0.210 |
| **T4** | 48.28±5.83 | 51.26±5.32 | 52.81±10.22 | 0.082 |
| **PX** | 0.384 | 0.290 | 0.088 | |
| **Creatinine clearance (mL/min)** | | | | |
| **T0** | 84.13±13.45 | 87.15±12.34 | 85.58±14.32 | 0.484 |
| **T1** | 87.21±13.37 | 84.63±16.23 | 83.72±18.48 | 0.395 |
| **T2** | 89.71±15.33 | 86.21±15.12 | 84.11±17.10 | 0.262 |
| **T3** | 89.32±14.28 | 83.73±13.42 | 82.88±16.77 | 0.197 |
| **T4** | 88.74±16.33 | 82.94±15.21 | 81.93±17.60 | 0.188 |
| **PX** | 0.320 | 0.204 | 0.312 | |

***: Chi-square test, One Way ANOVA Test**
**PX: Comparison between basal and final values**
***P<0.05 significant comparison between the groups**
**(T0): baseline before induction; (T1): after completion of surgery; (T2); 12 hr; (T3):24 hr; (T4):72 hours postoperatively.**

As regards Urine output, there was a non-statistically significant difference between groups at baseline measures. In contrast, the DEX group showed a statistically significant higher UOP value than both NAC and placebo groups at day 1

postoperatively. On day 2 postoperatively,the DEX group showed a statistically significant higher UOP value than the placebo group. Also, there was a non-statistically significant difference between pre-operative and postoperative values in each group (between basal and final values) **(Table 3).**

**Table 3. Comparison of the Urine Output of Studied Group**

| Urine output (mL) | DEX group (n=30) | NAC group (n=30) | Placebo group (n=30) | P value |
|---|---|---|---|---|
| **Baseline** | 1271.23±241.11 | 1157.41±257.11 | 1216.72±231.57 | 0.200 |
| **Day 1** | 1418.63±513.31 | 1214.35±352.35 | 1157.37±312.43 | **0.005*** **P1= 0.049*** **P2= 0.001*** P3= 0.348 |
| **Day 2** | 1262.25±336.29 | 1083.63±361.48 | 1050.44±324.21 | **0.024*** P1= 0.071 **P2= 0.032*** P3= 0.680 |
| **PX** | 0.576 | O.324 | O.108 | |

**Chi-square test, One Way ANOVA Test.**

**PX: Comparison between basal and final values. P1: Significance between DEX group and NAC group. P2: Significance between DEX group and Placebo group. P3: Significance between NAC group and control group *P<0.05 significant comparison between the groups.**

Regarding urinary NGAL, there was a non-statistically significant difference between groups at baseline, but the DEX group showed a significantly lower NGAL value than the placebo group at T1 and T2. Also, there were statistically significant differences between pre-operative and postoperative values in each group **(Table 4).**

As regards Heart rate, there was a non-statistically significant difference between groups at baseline and day 1. However, the heart rate was significantly lower in the DEX group than in both NAC and placebo groups on day 2. Also, there were non-statistically significant differences between pre-operative and postoperative values in each group.

There were non-statistically significant differences between groups at baseline and day 2 measures regarding mean arterial blood pressure. The DEX group showed a significantly lower mean arterial blood pressure value than the placebo group at day 1 postoperatively. Also, there were statistically significant differences between pre-operative and postoperative values in each group.

As regards central venous pressure, there were no statistically significant differences between groups at baseline, day 1, and day 2 postoperative measures. Also, there were no statistically significant differences between pre-operative and postoperative values in each group (**Table 5).**

**Table 4. Comparison of urinary NGAL of Studied Groups**

| NGAL (ng/ml) | DEX group (n=30) | NAC group (n=30) | Placebo group (n=30) | P value |
|---|---|---|---|---|
| **T0** | 8.45±1.85 | 9.18±2.53 | 8.94±2.31 | 0.443 |
| **T 1** | 89.63±53.11 | 111.26±55.18 | 123.37±56.43 | **0.014***<br>P1= 0.071<br>**P2< 0.001***<br>P3= 0.280 |
| **T 2** | 47.67±35.13 | 59.33±33.17 | 75.44±31.43 | **0.007***<br>P1= 0.168<br>**P2= 0.030***<br>P3= 0.098 |
| **PX** | **< 0.001*** | **< 0.001*** | **< 0.001*** | |

**Chi-square test,One Way ANOVA Test.**
**PX: Comparison between basal and final values P1: Significance between DEX group and NAC group**
**P2: Significance between the DEX and Placebo group P3: Significance between the NAC and Placebo group**
***P<0.05 significant comparison between the groups.**
**(T0): baseline before induction; (T1):6 hour postoperative; (T2):24 hr postoperative.**

**Table 5: Comparison of the Intra-Operative Hemodynamic Parameters of Studied Groups**

| Variable | DEX group (n=30) | NAC group (n=30) | Placebo group (n=30) | P Value |
|---|---|---|---|---|
| **Heart rate (bpm)** | | | | |
| **Baseline** | 76.24±8.13 | 74.54±10.23 | 74.93±10.24 | 0.372 |
| **Day 1** | 74.21±8.63 | 77.88±11.52 | 76.72±11.66 | 0.186 |
| **Day 2** | 72.44±10.77 | 79.52±13.44 | 80.35±14.17 | **0.037***<br>**P1= 0.036***<br>**P2= 0.028***<br>P3= 0.626 |
| **PX** | 0.094 | 0.078 | 0.058 | |
| **Mean arterial blood pressure (mmHg)** | | | | |
| **Baseline** | 98.34±11.64 | 101.42±12.31 | 105.31±11.37 | 0.077 |
| **Day 1** | 94.62±12.19 | 98.45±13.15 | 101.82±13.64 | **0.044***<br>P1= 0.194<br>**P2= 0.038***<br>P3= 0.442 |
| **Day 2** | 92.32±11.28 | 95.51±12.71 | 97.62±10.15 | 0.201 |
| **PX** | **0.042*** | **0.046*** | **0.028*** | |
| **CVP (cm H20)** | | | | |
| **Baseline** | 10.28±1.58 | 11.71±1.62 | 11.23±1.53 | 0.381 |
| **Day 1** | 12.40±1.69 | 12.24±1.51 | 11.47±1.44 | 0.133 |

| | | | | |
|---|---|---|---|---|
| **Day 2** | 13.27±1.35 | 12.62±1.39 | 11.62±1.36 | 0.127 |
| **PX** | 0.062 | 0.674 | 0.992 | |

**Chi-square test, •: One Way ANOVA Test**
**PX: Comparison between basal and final values**
**P1: Significance between DEX group and NAC group. P2: Significance between DEX group and Placebo group. P3: Significance between NAC group and control group *P<0.05 significant comparison between the groups.**

DEX group had lower non-significant CPB and cross-clamping time compared with NAC and placebo. IABP insertion requirements were nearly equal in both DEX and NAC groups and lower than the placebo group without significant differences. Also, the blood losses and fluids requirements intraoperatively were almost similar among all groups without significant differences **(Table 6).**

**Table 6. Intra-Operative Data of Studied Groups**

| Variable | DEX group (n=30) | NAC group (n=30) | Placebo group (n=30) | P |
|---|---|---|---|---|
| **CPB time (min)** | 114.25±21.46 | 119.42±20.72 | 126.16±23.25 | 0.087 |
| **Cross clamping time (min)** | 73.22±11.63 | 75.15±10.57 | 79.46±10.86 | 0.168 |
| **IABP insertion** | 2 (6.7%) | 2 (6.7%) | 3 (10%) | 0.656 |
| **Intraoperative blood loss (mL)** | 1027.25±238.13 | 951.23±218.42 | 921.25±227.11 | 0.065 |
| **Intraoperative fluids: Crystalloids (mL)** | 1672.12±625.30 | 1583.41±735.12 | 1536.42±518.31 | 0.701 |
| **Hesteril 6 (%) (ml)** | 612.50±138.21 | 638.11±283. 30 | 651.12±163.27 | 0.760 |

**IABP: intra-aortic balloon pump, CPB: Cardiopulmonary bypass**

The amount of postoperative blood loss and fluids infused was nearly equal among all groups without significant difference.

DEX group showed significantly lower postoperative AKI value than placebo group but non-significantly lower than NAC group. At the same time, the NAC group showed a lower postoperative AKI value than the placebo groupwith no significant difference.

There were non-statistically significant differences between groups regarding postoperative ARF, dialysis, reoperation, postoperative MV, ICU admission, hospitalization period, and mortality rate **(Table 7).**

**Table 7. Postoperative Variables and Outcomes of Studied Groups**

| Variable | DEX group (n=30) | NAC group (n=30) | Placebo group (n=30) | P |
|---|---|---|---|---|
| **Postoperative blood loss (mL/24 h)** | 554.32±148.22 | 533.11±145.15 | 593.28±163.54 | 0.306 |
| **Postoperative fluids/24h Crystalloids (ml)** | 2532.42±826.31 | 2481.65±824.46 | 2676.73±921.21 | 0.160 |
| **Hesteril 6 (%) (ml)** | 473.18±381.22 | 377.11±371.18 | 514.52±419.34 | 0.381 |
| **MV 48 h** | 2 (6.7%) | 3 (10%) | 3 (10%) | 0.817 |
| **Reoperation within 24h** | 1 (1.3%) | 1 (1.3%) | 2 (6.7%) | 0.769 |
| **Acute kidney injury** | 3 (10%) | 6 (20%) | 8 (26.7%) | **0.015***<br>P1= 0.078<br>**P2=0.010***<br>P3=0.345 |
| **Acute renal failure** | 6 (20 %) | 8 (26.7%) | 9 (30%) | 0.346 |
| **Postoperative dialysis** | | | | |
| **Temporarily** | 2 (6.7%) | 4 (13.3%) | 5 (16.7%) | 0.386 |
| **Permanent** | 1 (3.3%) | 2 (6.7%) | 2 (6.7%) | 0.482 |
| **ICU length of stay (days)** | 4.82±1.23 | 5.23±1.72 | 5.37±1.84 | 0.396 |
| **Hospital stay (days)** | 7.52±2.42 | 8.56±2.77 | 8.13±2.84 | 0.325 |
| **Mortality** | 1 (3.3%) | 2 (6.7%) | 2 (6.7%) | 0.482 |

**P1: Significance between DEX group and NAC group P2: Significance between DEX group and Placebo group**
**P3: Significance between NAC group and control group *P<0.05 significant comparison between the groups.**
**MV: mechanical ventilation**

## Discussion

AKI is a common complication following cardiac surgeries associated with poor outcomesincluding elevated healthcare costs, hospitalization, short and long-term mortality rates**(Vives et al., 2019).**

This randomized, double-blind, placebo-controlled trial was performed at Qena University Hospital and Sohag Cardiac Institute in period between October 2019 to October 2021; the study included 90 cases listed for elective on pump open-heart surgery.

Here, serum creatinine, BU and creatinine clearance results revealed no statistically significant differences between groups at baseline, T1, T2, T3, and T4. Also, there were non-statistically significant differences between pre-operative and postoperative values in each group.

These findings agree with the study done by**Jannati et al. (2021),** who reported no significant differences in serum creatinine levels between the DEX and Placebo groups. However, a significant difference in serum blood urea levels was observed between the studied groups except for the third day. Also, **Göksedef et al. (2013)** reported no positive impact of low-dose Dexmedetomidine on UOP or other kidney functiontests such as blood urea, Serum Creatinine, and creatinine clearance rate. Further studies confirmed these observations. Contrary to such results,**Soliman and Hussien (2017)**had observed a significant reduction of blood urea and serum creatinine with a significant higher creatinine clearancevalue till the fifth day after CPB when Dexmedetomidine was administered through the surgery. Similarly, **Cho et al. (2016)**observed a reduction in the occurrence and severity of postoperative AKI (according to Acute Kidney Injury Network) after infusion of Dexmedetomidine at a rate of 0.4 mcg/kg/h beginning immediately after anesthesia and sustained for 24 hours, among 200 patients with valvular heart disease. However, Serum Creatinine, estimated GFR and UOP were not significantly different among the included groups.

Regarding the dose, **Balkanay et al., (2015)**revealed a significant change in the mean values of (NGAL)for the 1st day post CABG among high (8 mcg/kg) and low (4 mcg/kg) DEX dose, signifying that DEX had clear impacts on reno protections in a dose-dependent way**.**

Until now, the best dosage of DEX needed to recover kidney functions after cardiac operations isn't clear. The best dosage of DEX to improve postoperative renal conditions can't be drawn due to absence of full access to case information **(Balkanay et al., 2015).**

DEX was accompanied by an elevated risk of bradycardia treatment requirements in studies that utilized both a loading dosage and maintenance dosage > 0.7 mcg /kg/hr. **(Tan and Ho, 2010)**.

As regards timing, DEX was applied postoperatively and not pre-emptively in most preceding clinical reports.

Using routine laboratory examinations, including the blood urea, serum creatinine levels, UOP estimation, and creatinine clearance rate to determine AKI may lead to a delay in the detection of kidney with subsequent false-negative findings (in comparison with measurement of urinary NGAL levels)**(Vaidya et al., 2008)**.

NGAL is a highly sensitive, specific, predictive, and rapid biomarker for AKI following various surgeries. It can be distinguished in serum as well as urine. Measurement of NGAL is helpful in the prediction of tubular stress; its concentrations increase dramatically in response to tubular injuries and frequently precede the elevation of S. Cr by more than a day. Serum or urine NGAL levels reached maximum values in the 1st two hours postoperatively. This elevation continued for 48 hours. For the reasons mentioned above, NGAL is considered more reliable than other renal function tests in detecting kidney impairment earlier**(Mishra et al., 2005).**

A meta-analysis performed on 24 studies revealed a 0.68 (95% confidence interval (CI), 0.65–0.70) sensitivity and a 0.79 (95% CI, 0.77–0.80) specificity of NGAL measurement. Performance characteristics were superior in children than adults and among those without a history of CKD (**Massoth and Zarbock, 2021**).

In our study, as regards urinary NGAL, there were no statistically significant differences between groups at baseline. Still the DEX group showed significantly reduced NGAL levels than placebo group at T1 and T2 postoperatively. Also, there were statistically significant differences between pre-operative and postoperative values in all groups.

In agreement with our results, **Zhai et al. (2017)**revealed that DEX impacted properly the renal functions of patients scheduled for cardiac valve replacement under CPB. 72 cases were randomly allocated into 2 groups; DEX and placebo. DEX group used 0.6 mcg/kg bolus dosage over 15 minutes before induction, followed by 0.2 mcg/kg/h till the end of the operation. The authors revealed a non-significant difference among study groups regarding BUN and Serum Creatinine at all-time points, except on the third day postoperatively as the DEX group resulted in significantly lower levels. Furthermore, Serum NGAL values were elevated at 12 and 24 hours postoperatively in the placebo groupwith significantly lower levels in the DEX group. The intra-operative urine output was significantly elevatedand the postoperative occurrence of AKI was significantly reduced in the DEX group according to (RIFLE) criteria (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney).

Contrary to such results, **Anantachote Vimuktanandana et al. (2018)**reported that differences in both serum creatinine and urinary NGAL at 6 and 24 h weren't significantly changed among groups. while, serum NGAL in DEX group was significantly reduced than the control group at 6 and 24 h (149.5 versus 291.4; P value= 0.016 and 118.5 versus 201.5; P value= 0.004, respectively). Furthermore, the DEX group showed significantly elevated urine output during the surgery.

Lately, studies on NAC have increased because of its protective effect against organ injuries caused by oxidative stress. However, there are several inconsistent reports regarding this effect on the kidney **(Šalamon et al., 2019).**

Numerous reports were performed to assess the protective effect of NAC on vital organs and tissue among cases undergoing cardiac surgeries.

**Savluk et al. (2017)** reported that intravenous NAC administration was accompanied by improved serum creatinine and eGFR in the first and second postoperative days among cases with pre-existing moderate renal insufficiency with a statistically significant difference in comparison with either placebo or Dopamine groups**.**

**Santana-Santos et al. (2014)**and his colleagues reported an association between high-dose IV NAC administration (150 mg/kg bolus followed by 50 mg/kg infusion for 6 h) and reduced risk of AKI, eliminated

oxidative stress and minimizing the negative effect of CPB on renal functions among 70 subjects with stage 3 or 4 Chronic kidney Disease (CKD) who were scheduled for coronary artery bypass graft surgery (CABG)**(Santana-Santos et al., 2014)**.

In concordance with our results,**Aldemir et al. (2016)** studied the effect of intravenous NAC which given at the induction of anesthesia and continued 20 hour postoperative on post-CABG renal functions among elderly patients. Serum Creatinine levels at 1$^{st}$day postoperatively were significantly elevated in the placebo group in comparison to the NAC group. Also, the mean serum NGAL level at 3 hours postoperatively was statistically high in the placebo group compared to the NAC group.

The findings of our work revealed that as regard UOP, there were non-statistically significant differences between groups at baseline. At the same time, the DEX group showed statistically significant higher UOP values compared with NAC and placebo groups at day1 postoperatively. but on day2postoperatively, the DEX group had statistically significantly higher UOP values than the placebo grouponly. Also, there were no statistically significant differences between pre-operative and postoperative values in all groups.

Also in our study, we found that the DEX group had significantly lower postoperative AKI incidence (guided by Acute Kidney Injury Network criteria)(AKIN)than the placebo group.

**Zhai et al. (2017)** revealed that post bypass DEX infusion was accompanied by a significant decrease in the occurrence of AKI followingcardiac valve replacement surgeryunder CPB.

On the other hand, one more retrospective study revealed that DEX was accompanied by an elevated incidence of renal failures while decreasing mortalities and other side effects**(Ji et al., 2013)**.

In our study DEX infusion resulted in a non-significant reduction in thepostoperative mechanical ventilation rate than NAC and placebo groups. Also, there were no statistically significant differences between groups regarding postoperative ARF, postoperative dialysis, reoperation, ICU admission, hospitalization period, and mortality rate.

In addition to the mechanisms mentioned above of DEX, the sedative action without respiratory depressions can also contribute to a decline in ventilation interval and thus a shorter period of ICU admission and better outcomes as reported by a previous investigation **(Turunen et al., 2015)**.

**Gerlach and Dasta (2007)** showed that continuous infusion of DEX for sedation caused significantly lower entire ICU costs than midazolam, primarily because of reduced ICU period and decreased mechanical ventilations prices.

## Conclusion

We found that DEX could have a more reno-protective effect among cardiac surgery patients than Acetyl Cysteine. This effect was reflected by lower urinary NGAL

levels, improved UOP, and reduced risk of postoperative AKI among those who received DEX.

**Abbreviations**: BU: blood urea , CBC: complete blood count, Scr: serum creatinine, UOP: urine output, NGAL: neutrophil gelatinase-associated lipocalin, GFR: glomerular filtration rate, eGFR: estimated glomerular filtration rate, CPB: cardiopulmonary bypass, CABG: coronary artery bypass graft, RRT: renal replacement therapy, AKI: acute kidney injury,AKIN :acute kidney injury network, ARF: acute renal failure, MV: mechanical ventilation, ICU: intensive care unit,IABP:intra-aortic balloon pump, CKD: chronic kidney disease , DEX:Dexmedetomidine, NAC: N Acetylcysteine, RIFLE: risk,injury, failure,loss and end stage renal disease.

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