



## Original Article



## Effect of Dexamethasone on Perioperative Lactate Levels in Donor Hepatectomy

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## ABSTRACT

The use of intravenous dexamethasone intraoperatively has been advocated for analgesia, prevention of nausea and vomiting, post-operative sore throat and inflammation. Hyperlactinemia associated with dexamethasone is a concern in patients undergoing hepatectomy. There is limited evidence to support safety or adversity of dexamethasone in terms of hyperlactinemia. **Objective:** To evaluate the effect of dexamethasone administration on perioperative lactate levels in living related donors undergoing liver donor right hepatectomies. **Methods:** The 60 patients who had donor hepatectomy appointments in total were divided into two groups at random. After the induction of anesthesia, Group B (n=30) got dexamethasone at a dose of 8 mg while Group A (n=30) received a placebo. Perioperative lactate levels were assessed at various time points, and statistical comparisons were made between the two groups' mean lactate levels. **Results:** The patients' mean age was 25.68 years, and their mean BMI was 21.48 kg/m<sup>2</sup>. At every time point, Group B displayed significantly higher mean lactate levels than Group A (p<0.001). Additionally, there were statistically significant differences between the groups, an hour after drug administration, and after graft extraction (p<0.001). The perioperative mean glucose level climbed steadily in both groups. **Conclusion:** The administration of dexamethasone in patients undergoing right living related donor hepatectomy was associated with significantly higher perioperative lactate levels compared to patients receiving placebo.

## INTRODUCTION

Living related donor hepatectomy is the surgical removal of right lobe of the liver for transplantation. This involves a number of physiological changes as well as the possibility of complications. Hemodynamic and metabolic alterations during the perioperative period can have a major impact on surgical outcomes [1]. Lactate is produced by most tissues in the human body, for example, in red blood cells, neurons, hepatocytes, and muscles. Muscles are primary site of lactate production. It is cleared by the liver, but the kidney also removes a small amount. Under conditions of cellular stress, glycolysis increases and results in increased lactate production [2, 3]. In anesthetized patients, lactic acidosis may occur due to an imbalance between lactate production and lactate utilization. It is frequently measured in critically

ill patients as a measure of tissue hypoxia and anaerobic metabolism. Blood lactate levels are extremely important in determining the patient's metabolic status as it signifies tissue hypoperfusion or decreased oxygen supply [2, 3]. Dexamethasone, a synthetic glucocorticoid, is used by anesthesiologist during surgery because of beneficial effects like analgesia and prevention of postoperative nausea and vomiting, suppression of inflammation, and reduction of the risk and severity of post-intubation sore throat [4]. However, dexamethasone also has some adverse effects, for example increasing blood glucose levels and type B hyperlactatemia [5]. The therapeutic benefit of perioperative dexamethasone treatment in hepatectomy has been evaluated [6, 7]. However, its effect

on perioperative lactate levels in living related donor hepatectomy patients remains unclear. Since liver is the primary organ for lactate clearance hence it is hypothesized that impairment of liver function as seen in patients undergoing hepatectomy may lead to lactic acidosis which may further be attenuated by intravenous dexamethasone administration [8]. Elevated lactate levels in perioperative period have been associated with worse clinical outcomes in terms of morbidity and mortality. [9, 10] In fact, lactate levels exceeding 3.8mmol/L have been linked to very high incidence of post hepatectomy liver failure and even death. [11,12] In majority of cases, lactic acidosis in perioperative period is a transient phenomenon that settles in most of the patients with conservative strategies yet some patients may need continuous renal replacement therapy for clearance of lactic acid. [13, 14]. Dexamethasone with all of its benefits in perioperative anesthetic management may be a factor contributing to lactate production. Usually cadaveric liver dissections are done in western world for liver transplantation where intravenous dexamethasone is omitted as all of its benefits are for living patient [15].

Living donor hepatectomy is a complex surgical procedure associated with significant metabolic and physiological alterations during the perioperative period. Dexamethasone is commonly administered intraoperatively for its anti-inflammatory and antiemetic effects; however, its potential role in increasing lactate levels and contributing to hyperlactatemia remains a concern, particularly in patients undergoing liver resection where lactate clearance may already be compromised. Although several studies have evaluated the benefits of dexamethasone in surgical settings, limited evidence exists regarding its specific impact on perioperative lactate levels in living liver donors. Therefore, further investigation is required to clarify its metabolic effects and safety in this population. Hence, its effect on lactate metabolism in said population is understudied and under reported. The aims and objective of this study was to evaluate the effect of dexamethasone administration on perioperative lactate levels in living related donors undergoing liver donor right hepatectomies.

## METHODS

This quasi-experimental study, with a prospective design was conducted from October 2019 to March 2020 following approval from the Institutional Review Board and Ethics Committee of Shifa International Hospital (IRB # 078-568-2019). A pilot study was conducted to calculate the sample size, to determine the effect of dexamethasone in donor hepatectomy. The following calculations with level of significance were carried out with the aid of the WHO sample size calculator: In a pilot research done at SIH, Islamabad, the test's 5% power was 95%, the population's

standard deviation was 1.22, and the test value of the population mean was 3.64 (lactate levels in mmol/L in placebo group patients against predicted population mean:5.32 (lactate levels in mmol/L in dexamethasone group patients). Each group's sample size (n) is 30 patients, for a total of 60 patients. A total of 60 adult donors over the course of 4 years scheduled to have Right living related donor hepatectomy with American Society of Anesthesiology status I and II were recruited from the Liver Transplant operation rooms. All living donors were healthy individuals and are free from any co-morbidities who underwent Right Hepatectomy with or without Middle Hepatic Vein. Patients who had received corticosteroids within last two weeks of surgery, patients allergic to dexamethasone, and patients suffering from any illness that elevates blood lactate levels, such as G6-PD deficiency, were excluded from the study. For general anesthesia, the anesthesiologist had followed the standard protocol used in hospital. Induction was obtained using midazolam 0.3 mg/kg, buprenorphine 0.03mg/kg and propofol 2mg/kg. Neuromuscular blockade was obtained with atracurium 0.5mg/kg, a loading dose followed by maintenance intermittent dosage guided by monitoring with train of four. Anesthesia was maintained using the inhalational agent Isoflurane 1 MAC with oxygen and air. Intraoperative monitoring consisted of a continuous electrocardiogram, invasive blood pressures using arterial line, peripheral oxygen saturation, end-tidal carbon dioxide (ETCO<sub>2</sub>), core temperature, urine output, and central venous pressure monitoring. The thoracic epidural catheter was inserted for pain control at T 7-8. The hospital protocol was used to strictly maintain mean arterial pressure above > 65 mm of Hg, CVP of < 5 mm of Hg, temperature above 36°C and urine output 0.5 ml/ hour. Patients were divided into two study groups using consecutive sampling technique. Group A: Conventional Care Patients in the control group received conventional care but did not get dexamethasone. Group B: Patients in the experimental group received 8 mg of intravenous dexamethasone after anesthesia induction, as per regular institutional policy. The primary outcome measure was perioperative lactate levels, assessed at predefined time points during perioperative period i.e., 1 hour after dexamethasone administration, lobe resection, graft extraction, incision closure and at PACU. Lactate levels were measured using arterial gas analysis. Data were collected and analyzed using the computer software SPSS version 21.0. Mean and calculated standard deviation of continuous variables, e.g. age, BMI, blood loss, blood sugar levels, and postoperative and perioperative lactate levels in all the patients. Categorical variables, i.e. gender, were presented as frequency and percentage. An independent sample t-test was applied to compare mean lactate levels in both groups. P-value < 0.050 was considered statistically significant.

## RESULTS

Donors had an average age of 25.68±6.43 years and a BMI of 21.48 ± 2.13 kg/m<sup>2</sup>. There were 37 (61.7%) males and 23 (38.3%) females. Table 1 displayed descriptive statistics broken down by group which suggest that patients in both study groups were standardized in terms of hemodynamics and volume status in terms of central venous pressure. In table 1 comparisons between age, BMI, duration of surgery, MAP and CVP in Group A and Group B were described by using Mean (M) and Standard Deviations (SD) and its statistical significance was determined by student t Tests. A p value ≤0.050 was considered statistically significant (n=60).

**Table 1:** Comparison of Demographic and Hemodynamic Variables Between Groups

Variables	Group A Mean ± SD	Group B Mean ± SD	p-Value
Age (Years)	24.67 ± 6.08	26.70 ± 6.71	0.450
BMI (kg/m <sup>2</sup> )	21.55 ± 2.20	21.41 ± 2.09	0.160
Duration of surgery (hours)	9.08 ± 1.33	9.32 ± 1.18	0.890
MAP before drug administration	79.98 ± 9.93	83.10 ± 9.96	0.120
MAP one hour after drug administration	86.30 ± 9.57	83.42 ± 9.44	0.210
MAP at lobe resection	82.60 ± 8.27	83.78 ± 8.27	0.470
MAP after graft extraction	81.66 ± 8.26	84.58 ± 9.06	0.100
MAP at incision closure	81.80 ± 9.70	81.94 ± 8.99	0.940
MAP in PACU	85.84 ± 11.36	85.12 ± 11.04	0.740
CVP before drug administration	5.94 ± 2.84	5.16 ± 2.41	0.140
CVP one hour after drug administration	5.28 ± 2.6	5.96 ± 3.34	0.540
CVP at lobe resection	4.60 ± 1.78	5.10 ± 1.45	0.140
CVP at graft extraction	5.84 ± 2.16	5.56 ± 1.47	0.360
CVP at incision closure	7.02 ± 2.22	6.46 ± 2.00	0.110
CVP in PACU	7.82 ± 1.88	8.30 ± 1.03	0.100

In group A, the mean blood loss was 470 ± 134.93ml versus 480 ± 136.83 (p=0.73). The liver remnant in group A was 35.47 ± 3.81, whereas in group B it was 33.77 ± 3.02. The liver attenuation index was 9.94 ± 3.87 in group A versus 9.92 ± 3.07 in group B (p=0.970). It was observed that mean blood lactate levels in patients of Group B were higher as compared to group A at all intervals. The difference was very highly statistically significant (p<0.001). In table 2 comparisons between perioperative lactate levels in Group A and Group B were described by using Mean (M) and Standard Deviations (SD) and its statistical significance was determined by student t Tests. A p-value ≤0.050 was considered statistically significant (n=60).

**Table 2:** Effect of Intraoperative Dexamethasone on Perioperative Lactate Levels in Donor Hepatectomy

Lactate Levels (mmol/L)	Group A Mean ± SD	Group B Mean ± SD	p-Value
1 hour of drug administration	1.89 ± 0.41	2.36 ± 0.72	0.002
After lobe resection	1.94 ± 0.17	2.95 ± 0.80	<0.001
After graft extraction	2.15 ± 0.18	3.63 ± 1.05	<0.001

After incision closure	2.31 ± 0.18	4.46 ± 1.20	<0.001
In PACU	2.60 ± 0.18	5.71 ± 1.40	<0.001

The difference in mean blood glucose levels between the study groups was variable. Mean blood glucose levels were statistically higher in Group A at 1 hour of dexamethasone administration and after graft extraction. However, the difference between study groups in terms of blood glucose levels was comparable at all other stages of surgery as it is apparent in Table 3. Comparisons between perioperative sugar levels in Group A and Group B were described by using mean (M) and standard deviations (SD) and its statistical significance was determined by student t Tests. A p-value ≤0.050 was considered statistically significant (n=60).

**Table 3:** Comparison of Perioperative Blood Glucose Levels between Dexamethasone and Placebo Groups in Donor Hepatectomy

Sugar Level (mg/L)	Group A Mean ± SD	Group B Mean ± SD	p-Value
1 hour of drug administration	155.10 ± 21.62	129.07 ± 24.64	0.001
After lobe resection	146.73 ± 31.34	139.63 ± 25.52	0.340
After graft extraction	154.40 ± 33.39	133.40 ± 25.89	0.009
After incision closure	135.80 ± 21.78	143.33 ± 21.23	0.100
In PACU	142.30 ± 19.14	144.67 ± 17.12	0.610

## DISCUSSION

According to the findings of this study, mean lactate levels were higher in the group of living related liver donor hepatectomies patients who got dexamethasone than in the group who did not. These findings were true across all time intervals studied, from medication delivery until the PACU. Dexamethasone may raise lactate levels by increasing gluconeogenesis, which is the process of turning non-carbohydrates into glucose. The metabolic pathway gluconeogenesis is frequently stimulated in response to low blood sugar levels during surgeries as patients are fasting for eight hours before surgery. It can, however, be activated in reaction to trauma, such as surgery. These effects are hypothesized to contribute to the stress response and subsequent increase in lactate levels [2]. Similarly, it was reported in a randomized controlled trial called Dexamethasone for Cardiac Surgery (DECS), in which one group of patients received a single intravenous (IV) bolus of Dexamethasone (20 mg/mL, 1 mg/kg, maximum 100 mg). Another group received a placebo (NaCl 0.9%) immediately after induction of general anesthesia. The effect of Dexamethasone on perioperative lactate levels was observed, and they found that the lactate levels were significantly higher in the dexamethasone group than in the placebo group, i.e. lactate levels 25.8±13.1 versus 19.9±11.2 mmol/L × hour, P <0.001 [16]. In contrast to present study, a higher dose of Dexamethasone was used along with extracorporeal circulation. This was not the case in our study. DREAMS Trial advocates use of

intravenous dexamethasone for prevention of post-operative nausea and vomiting [17]. However, transient worsening of glycemic control has been reported by various studies which is incoherent with findings of present study which can be explained by difference in study population as patients with impaired glucose levels preoperatively or diabetics were excluded from the study [18]. Clinicians must weigh benefits of dexamethasone in accentuation of systemic inflammatory response syndrome against potential of confounding rise in lactic acidosis [19, 20]. In addition, the rise in perioperative glucose levels found in both groups reflects a metabolic response to surgery, however there were no significant differences between groups except at certain time periods. Further research is needed to identify the clinical implications of these glucose level changes on patient outcomes. There are a few limitations of this study. First off, this study was performed in a single center, and the sample size was quite small. Therefore, the results of future studies with greater sample sizes and multi-center designs would be more generalizable. Despite the fact that none of the patients had serum lactate levels in the potentially harmful range, the study also did not evaluate the long-term clinical effects linked to the observed variations in lactate levels.

This study has certain limitations, including a relatively small sample size and its single-center design, which may limit the generalizability of the findings. Additionally, the study focused only on short-term perioperative lactate changes and did not assess long-term clinical outcomes related to hyperlactatemia. Variations in patient characteristics and perioperative management may also influence metabolic responses. Future multicenter studies with larger sample sizes and extended follow-up are recommended to better evaluate the long-term clinical implications of dexamethasone administration on metabolic parameters and postoperative outcomes in donor hepatectomy patients.

## CONCLUSIONS

In conclusion, donor hepatectomy patients who received dexamethasone had significantly higher perioperative lactate levels than those who had not received it.

## Authors' Contribution

Conceptualization: R

Methodology: R, MHF, MA, MZA

Formal analysis: ZAR

Writing and Drafting: MA, ZAR, MNAK, SAN

Review and Editing: MA, ZAR, MNAK, SAN, MZA, R

All authors approved the final manuscript and take responsibility for the integrity of the work

## Conflicts of Interest

All the authors declare no conflict of interest.

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