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Research Article

Factors affecting acid base status during hepatectomy in cirrhotic patients

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Abstract *Objective:* To study acid base changes during hepatectomy in cirrhotic patients and their relations to intraoperative variables and different preoperative scoring systems used to asses hepatic patients.

Methods: After obtaining approval of the Ethics and Research Committee of the National Liver Institute – Menoufia University and written informed patient consent, 80 patients scheduled for hepatectomy for hepatocellular carcinoma were included in the study. Anesthesia was induced with propofol, fentanyl, and rocuronium then maintained with desflurane and 50% O_2 in air. Samples for arterial blood gases and serum lactate were withdrawn from a left radial artery catheter just before the start of resection of liver parenchyma and immediately after its completion. Intraoperative events were recorded including use of Pringle maneuver and fluids and blood products infusions.

Results: No differences were found in study parameters between Child class A and B patients except for the preresection lactate ($p = 0.02$). Patients with MELD score <11 had higher preresection HCO_3 ($p = 0.004$), higher BE ($p = 0.002$), and lower lactate ($p = 0.001$) than patients with MELD score ⩾11. These findings were true also for patients with MELD-Na score <11 as they had higher preresection HCO_3 ($p = 0.001$), higher BE ($p = 0.001$), and lower lactate ($p < 0.001$) than patients with MELD-Na score ⩾11. All patients had significant decrease in pH ($p < 0.001$), HCO_3 ($p < 0.001$), and BE ($p < 0.001$) and significant increase in lactate ($p < 0.001$). These changes were augmented by intraoperative RBCs and FFP transfusion, using Pringle maneuver, but type of hepatectomy had significant effect only on HCO_3 and BE. Again these changes in pH, HCO_3, BE, and lactate were more obvious in patients with preoperative MELD score ⩾11, and this was also true in patients with preoperative MELD-Na score ⩾11 only with HCO_3, BE, and lactate, but not with pH.

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Conclusion: Changes occurred in acid base status during hepatectomy in cirrhotic patients are affected by the preoperative condition of the patient (MELD and MELD-Na scores) as well as by intraoperative transfusion of blood products, use of Pringle maneuver and to a lesser extent by major versus minor hepatectomy.

1. Introduction

Hepatic resection is the main management for hepatocellular carcinoma (HCC) in the world. There is a strong correlation between the hepatocellular carcinoma and the presence of liver cirrhosis [1–3].

The risk of hepatic failure in a cirrhotic patient undergoing hepatectomy remains high due to the compromised function of the liver remnant. So, proper evaluation of hepatic functional reserve is essential prior to hepatectomy. The minimal liver mass needed for adequate postoperative liver function in cirrhotic patients is estimated to be about 40% at least [4–6].

Child–Turcotte–Pugh (CTP) classification was the first score used for determining the severity of liver cirrhosis, and the extent of resection that a cirrhotic patient can tolerate. CTP class C cirrhosis is considered an absolute contraindication for hepatic resection, and only minor resection could be done for CTP class B cirrhosis [7–9].

The Model for End-stage Liver Disease (MELD) score was designed for selection of cirrhotic patients for the Transjugular Intrahepatic Portosystemic Shunt (TIPS) procedure and for predicting mortality between them [10–13]. It is used also for detecting priority in the waiting list for liver transplantation [13,14].

It has the advantage over CTP score in using three objective and easily measured parameters: total bilirubin, serum creatinine level, and international normalized ratio (INR), unlike CTP score which has two subjective parameters (ascites and encephalopathy). In addition to the MELD score, the Model for End-Stage Liver Disease and serum sodium concentration score (MELD-Na) incorporates serum sodium concentration as the serum sodium concentration is an important predictor of mortality especially in patients with a low MELD score [10,15,16].

The liver plays an important role in lactate metabolism. When the liver blood flow is reduced to 25% of normal, the lactate clearance is reduced and delivers less lactate for metabolism. Under anaerobic conditions, glycolysis becomes the main source for hepatic energy production, so the liver becomes a lactate producing organ rather than using lactate for gluconeogenesis [17].

So, the metabolic acid–base balance in cirrhotic patients could be lost during episodes of hepatic decompensation, hemorrhage and when become critically ill. Lactic acidosis and acidemia are associated with increased incidence of ICU morbidity and mortality [18–20].

In this study, we aimed to investigate the acid–base changes during hepatectomy procedure in cirrhotic patients and their affection by the different surgical events, intraoperative variables, and the different preoperative scoring systems (CTP, MELD, and MELD-Na scores) used to asses hepatic patients.

2. Methods

The study performed in the hospital of the National Liver Institute – Menoufia University – Egypt, which is a tertiary center specialized in liver diseases. After approval by the institution Research and Ethics Committee and informed patient consent, 80 patients scheduled for elective liver resection completed this study. We excluded patients undergoing emergency surgery for ruptured HCC, and we excluded also patients with chronic renal insufficiency, which did not allow a reliable measurement of the acid–base parameters and calculation of the MELD and MELD-Na scores. Full preoperative work-up was done including assessment of the severity of the underlying liver disease by calculating CTP class, MELD, and MELD-Na scores.

A 20 gauge intravenous cannula was inserted in the non-dominant arm and used for induction of anesthesia. Afterward, at least two large peripheral venous lines (16 gauge or larger) and a multi-lumen central venous catheter in the right internal jugular vein were inserted. After performing modified Allen's test, an arterial catheter was inserted in the left radial artery to be used for hemodynamic monitoring and taking blood samples for acid–base parameters measurement.

General anesthesia was induced by fentanyl in a dose of (2–3 μg/kg), propofol (1.5–2.5 mg/kg), and rocuronium (0.9 mg/kg). After endotracheal intubation, patients were ventilated to maintain $ETCO_2$ between 35 and 40 mmHg, and anesthesia was maintained with a mixture of desflurane, oxygen, and air ($FiO_2 = 0.5$) at a fresh gas flow of about 1 liter/min. Top up doses of rocuronium were administered according to the train of four response, end tidal desflurane concentration was adjusted guided with entropy within the range of 40–60, and mean arterial blood pressure (MAP) and heart rate (HR) were kept within 20% of the pre-induction baseline values.

Intravenous crystalloids in the form of Ringer's acetate were infused at a rate of 6 ml/kg/hr to replace fluid deficit and basal fluid requirements. Colloid (6% hydroxyethyl starch in saline, 6% HES130/0.4 Voluven; Fresenius-Kabi, Bad Homburg, Germany) bolus administration was used depending on the Doppler estimations of stroke volume and corrected flow time (FTc). Incremental doses of ephedrine were given if the mean arterial blood pressure decreased by more than 25% of the base line value with poor response to bolus fluid therapy or no need to fluid therapy as indicated by FTc, and Packed RBCs were administered to keep hematocrit more than 25%. Other blood products were given, if at all, guided by the coagulation laboratory intraoperative findings and/or the use of Rotational Thromboelastometry (ROTEM) (Pentapharm, Munich, Germany).

Venous blood samples for lactate measurement and arterial blood samples from the radial artery for pH, bicarbonate (HCO_3), and base excess (BE) measurement with a blood gas analyzer (Rapid Lab® 1265, Siemens , Germany) were collected immediately before the start of parenchymal transection and at the end of resection. The presence of intraoperative events as using Pringle maneuver or transfusion of blood products was recorded, and we recorded also the extent of hepatectomy (excision of more than two hepatic segments was considered major hepatectomy, while excision of two hepatic segments or less was considered minor hepatectomy).

3. Statistical analysis

Variables are presented as mean ± SD, independent samples *T*-test was used to test differences between data in different groups, while paired samples *T*-test was used to test preresection versus postresection data, $p < 0.05$ was considered significant.

4. Results

Eighty-five patients included in this study with subsequent exclusion of five cases; two cases did not complete the surgery as proved to be inoperable after laparotomy (in spite of thorough preoperative diagnostic work). In the third case, the mass was originating from the suprarenal gland and only indenting the liver without true invasion, another two cases had massive uncontrolled intraoperative hemorrhage which necessitated – in addition to massive blood transfusion and vasopressor therapy – hyperventilation and administration of large amount of sodium bicarbonate, both largely affected the ABG results. The last two cases had a dramatic postoperative course which ended eventually with death in the fifth and seventh postoperative day respectively.

Eighty patients completed this study, the mean age was 53.8 ± 5.8 years, there were 66 male patients forming 82.5% of the study group while females were 14 patients (17.5%), and 10 patients (12.5%) were classified CTP class B all of which had minor hepatectomies, while there were 70 patients classified as CTP class A (87.5%). Mean MELD score was 8.53 ± 1.74, 64 patients had MELD score < 11 (80%), and 16 patients had MELD score ⩾11 (20%). Mean MELD-Na score was 11.53 ± 3.09, only 65% of patients had a score < 11, and the remaining 35% had a MELD-Na score ⩾11. The demographic and preoperative data involving albumin, bilirubin, creatinine, and INR levels are shown in Table 1.

The mean operative time was 4.57 ± 1.11 h. Sixteen patients (20%) received RBCs transfusion with a mean amount 2.69 ± 0.87 unit, while eight patients (10%) received FFP with a mean amount 4.75 ± 0.89 unit (Table 2). Pringle maneuver was used in 18 patients (22.5%), 28 patients (35%) undergone major hepatectomy while 52 patients (65%) undergone minor hepatectomy (Table 2).

The preresection acid base parameters in relation to the preoperative CTP class, MELD and MELD-Na scores are shown in (Table 3), where there were no significant differences between child A and B classes regarding the acid base parameters except for the lactate level, which was significantly higher in CTP class B patients ($p = 0.02$). Patients with MELD and MELD-Na scores < 11 had significantly higher bicarbonate level, higher base excess, and lower lactate level than patients with MELD and MELD-Na scores ⩾11 (Table 3).

There were significant changes between the preresection and postresection values regarding all the parameters, as lactate increased while pH, bicarbonate, and base excess decreased (Table 4).

The postresection acid base parameters were not affected with the CTP class but affected by MELD and MELD-Na scores, as pH, bicarbonate, and base excess were significantly higher, while lactate was significantly lower in the low MELD group compared to the high MELD group. The same results were true with MELD-Na score except for pH, as patients with low MELD-Na score had significantly higher bicarbonate and base excess and significantly lower lactate than patients with high MELD-Na score (Table 5).

The group of patients who had Pringle maneuver during surgery showed significantly lower pH, bicarbonate, and base excess levels and significantly higher lactate level. The same was shown in patients received RBCs and/or FFP transfusion (Table 5).

Only bicarbonate and base excess were affected by the extent of hepatectomy, as patients who undergone major resection had significantly lower bicarbonate and base excess levels than patients who undergone minor resection (Table 5).

5. Discussion

The liver is considered to play an essential role in lactate clearance and utilization as it is the principal organ for lactate metabolism accounting for 40% to 50% of the whole body lactate clearance, so it participates in the regulation of plasma lactate concentration as well as acid–base balance, and the increase in lactate level and acid–base imbalance may reflect the liver function [18,19].

Our results demonstrated that all the preresection acid–base parameters affected by the severity of the underlying liver dis-

Table 1 Preoperative data of the study group.

Age	53.58 [5.79] Year
Weight	76 [8.36] kg
Gender	Male: 66 (82.5%) and Female: 14 (17.5%)
Albumin	3.42 [0.52] g/dl
Bilirubin	1.19 [0.29] mg/dl
Creatinine	0.92 [0.15] mg/dl
INR	1.13 [0.12]
CTP	A 70 (87.5%) B 10 (12.5%)
MELD	All patients: 8.53 [1.74] < 11: 64 (80%) ⩾ 11: 16 (20%)
MELD-Na	All patients: 11.53 [3.09] < 11: 52 (65%) ⩾ 11: 28 (35%)

INR indicates International Normalized Ratio; CTP, Child–Turcotte–Pugh; MELD, Model for end-stage liver disease. Data are presented as mean and [SD] and/or number and (percentage).

Table 2 Intraoperative data of the study group.

Operative time	4.57 [1.11] h
Colloids	1.01 [0.36] l
Crystalloids	4.13 [0.95] l
RBCs transfusion	No 64 (80%) Yes 16 (20%) Amount 2.69 [0.87] Unit
FFP transfusion	NO 72 (90%) Yes 8 (10%) Amount 4.75 [0.89] Unit
Hepatectomy	Minor 52 (65%)
	Major 28 (35%)
Pringle	No 62 (77.5%) Yes 18 (22.5%)

RBCs, red blood cells; FFP, fresh frozen plasma, data are presented as mean and [SD] and/or number and (percentage).

Table 3 Preresection parameters in relation to preoperative CTP class, MELD, and MELD-Na scores.

Variable	No	(%)	pH	HCO_3 (mmol/L)	BE (mmol/L)	Lactate (mg/dl)
All patients	80	100%	7.37 [0.04]	24.25 [0.92]	−0.74 [0.89]	13.58 [2.68]
CTP class						
A	70	87.5%	7.37 [0.04]	24.24 [0.90]	−0.75 [0.87]	13.31 [2.59]
B	10	12.5%	7.39 [0.04]	24.28 [1.08]	−0.70 [1.09]	15.4 [2.72]
P Value			0.233	0.906	0.874	0.020
MELD score						
Low	64	80%	7.38 [0.04]	24.39 [0.86]	−0.59 [0.82]	12.59 [1.88]
High	16	20%	7.37 [0.03]	23.66 [0.95]	−1.34 [0.95]	17.50 [1.55]
P Value			0.634	0.004	0.002	0.001
MELD-Na score						
Low	52	65%	7.37 [0.04]	24.48 [0.79]	−0.51 [0.75]	12.19 [1.77]
High	28	35%	7.38 [0.03]	23.80 [0.99]	−1.20 [0.99]	16.30 [1.99]
P Value			0.715	0.001	0.001	0.001

CTP: Child–Turcotte–Pugh, MELD: Model for End-Stage Liver Disease, MELD-Na: Model for End-Stage Liver Disease and serum sodium concentration, HCO_3: bicarbonate, BE: base excess, data are presented as mean and [SD].

Table 4 Preresection and Postresection ABG and Lactate.

Variable	pH	HCO_3 (mmol/L)	BE (mmol/L)	Lactate (mg/dl)
Before	7.37 [0.04]	24.25 [0.92]	−0.74 [0.89]	13.58 [2.68]
After	7.34 [0.03]	22.16 [1.24]	−2.78 [1.14]	32.95 [5.89]
P value	0.001	0.001	0.001	0.001

HCO_3: bicarbonate, BE: base excess, data are presented as mean and [SD].

ease expressed by MELD and MELD-Na. On the other hand, the CTP class affected only the lactate level. MELD score has been demonstrated to correlate with the preoperative risk. In addition to the MELD score, the serum sodium concentration has been considered as an important prognostic factor in patients with liver cirrhosis. Several studies demonstrated that it is an important predictor of mortality in patients on the waiting list for liver transplantation [7,15].

Postresection acid–base parameters were affected by the preoperative MELD and MELD-Na scores. That could be due to the already affected preresection acid–base parameters, or it could be explained as the more severe underlying liver disease resulted in more affection by liver surgery, as many previous studies reported that the MELD score is an excellent predictor of both short and medium term survival, and an increase in MELD score is associated with a decrease in the residual liver function [13,21,22].

Surgical maneuvers as the use of Pringle maneuver resulted in an increase in the lactate level and a decrease in pH, bicarbonate (HCO_3) and base excess (BE) levels, and this may be due to its metabolic effect on hepatocytes due to the potential hypoxemia.

Increased times of ischemia and surgical manipulations of hepatocytes may lead to ischemia reperfusion injury which activates a complex cascade that triggers an inflammatory reaction mediated by cytokines; Interleukin-6 (IL6), and Tumor Necrosis Factor-Alpha (TNFα), and cells; Kuppfer cells, neutrophils [4,5]. Although this maneuver involves clamping of the hepatic inflow intermittently or continuously up to one hour [4,23], it is primarily intended to maintain hemostasis. Uncontrolled activation may become destructive inducing necrosis and apoptosis of hepatocytes and affect the hepatic sinusoidal blood flow leading to potential hypoxia of hepatocytes and consequently metabolic derangement [24].

Transfusion of blood and blood products was associated with changes in lactate level and acid base parameters similar to that occurred with using Pringle maneuver, i.e. lactate level increased while pH, BE, and bicarbonate decreased. Stored

Table 5 Postresection parameters in relation to preoperative scores and intraoperative variables.

Variable	No	(%)	pH	HCO_3 (mmol/L)	BE (mmol/L)	Lactate (mg/dl)
All Pts	80	100	7.34 [0.03]	22.16 [1.24]	−2.78 [1.14]	32.95 [5.89]
Hepatectomy						
Minor	52	65	7.34 [0.03]	22.47 [0.89]	−2.51 [0.87]	32.16 [6.14]
Major	28	35	7.34 [0.04]	21.76 [1.54]	−3.11 [1.36]	33.79 [5.14]
P value			0.939	0.011	0.021	0.239
Pringle						
No	62	77.5	7.35 [0.03]	22.53 [0.86]	−2.45 [0.85]	31.42 [4.42]
Yes	18	22.5	7.31[0.04]	20.89 [1.51]	−3.92 [1.31]	38.22 [7.29]
P value			0.001	0.001	0.001	0.001
RBCs transfusion						
No	64	80	7.35 [0.03]	22.59 [0.77]	−2.38 [0.74]	30.75 [3.92]
Yes	16	20	7.30 [0.02]	20.44 [1.28]	−4.41 [1.02]	41.75 [3.86]
P value			0.001	0.001	0.001	0.001
FFP transfusion						
No	72	90	7.34 [0.03]	22.43 [0.89]	−2.54 [0.87]	31.78 [4.80]
Yes	8	10	7.30 [0.01]	19.75 [1.39]	−4.98 [0.99]	43.50 [4.03]
P value			0.001	0.001	0.001	0.001
MELD score						
Low	64	80	7.34 [0.03]	22.45 [0.92]	−2.52 [0.90]	31.25 [4.77]
High	16	20	7.32 [0.03]	21.00 [1.66]	−3.85 [1.41]	39.75 [5.03]
P value			0.019	0.004	0.002	0.001
CTP class						
A	70	87.5	7.34 [0.03]	22.14 [1.30]	−2.80 [1.18]	32.80 [6.06]
B	10	12.5	7.34 [0.02]	22.28 [0.75]	−2.68 [0.83]	34.00 [4.66]
P value			0.703	0.745	0.764	0.550
MELD-Na score						
Low	52	65	7.34 [0.04]	22.45 [0.90]	−2.52 [0.88]	31.08 [4.58]
High	28	35	7.34 [0.02]	21.63 [1.58]	−3.27 [1.41]	36.43 [6.52]
P value			0.329	0.016	0.014	0.001

CTP: Child–Turcotte–Pugh, MELD: Model for End-Stage Liver Disease, MELD-Na: Model for End-Stage Liver Disease and serum sodium concentration, HCO_3: bicarbonate, BE: base excess.
Data are presented as mean and [SD].

blood contains citrate which then metabolized by the liver to bicarbonate, but in this study, bicarbonate level was lower in patients who received blood products (packed red blood cells and fresh frozen plasma), this may be due to the fact that those patients exposed to more blood loss, hypotensive episodes and hemodynamic instability (which necessitated blood transfusion), all these factors caused a decrease in hepatic blood flow and its metabolic function.

It was reported that intraoperative blood loss more than 1 l increases the postoperative morbidity. It may be due to the fluid shift which occurs after excessive blood loss and/or the systemic inflammation caused by bacterial transmission [6].

Our results demonstrated that only bicarbonate and base excess levels were affected by the extent of hepatectomy, as major hepatectomy was associated with lower HCO_3 and BE levels than with minor hepatectomy, while there were no changes in pH and lactate levels.

Major hepatectomy was commonly associated with more blood loss, longer duration of surgery, increased incidence of Pringle maneuver, and increase in exposure of hepatocytes for surgical manipulation that could affect the hepatic and systemic perfusion and be reflected by the acid base imbalance state.

Answering the question why the extent of hepatectomy had less effect on acid base parameters (compared to other factors), this may be due to the advancement in surgical equipments and techniques.

All the study parameters changed significantly after resection (when compared with the preresection level), i.e. lactate increased, while pH, HCO_3, and BE decreased. This is in agree with Shin et al., that they found that transient hyperlactemia and decrease in pH and base excess occurred one and three hours after resection in right donor hepatectomy procedure [25].

Also, Kato et al. found that lactate profile was a reliable indicator of postoperative liver function in cirrhotic patients undergoing liver resection, and the increase in lactate profile during hepatectomy procedure may be caused by direct liver damage and hypoperfusion during surgery in addition to that the rate of elimination of lactate correlated with the extent of preoperative liver function [26].

Orii et al. studied lactate concentration with the indocyanine green elimination rate (ICG-K) in liver resection in cirrhotic patients, they found that the lactate level increased during the ischemic phase reaching its maximum level just after resection then started to decrease during the post-ischemic phase and these changes correlated conversely with the changes of indocyanine green elimination rate [27].

In addition, the base excess continued to decline until it reached its maximum decline just after liver resection then its level started to increase [27].

Our results coincided with Cucchetti et al. results in their study where all patients showed a significant reduction in pH, bicarbonate, and base excess at the end of hepatectomy worsened by intraoperative blood loss and MELD score >11. Also, they found that patients with postresection bicarbonate <19.4 mmol/L were at high risk of postoperative liver failure, whereas levels >22.1 mmol/L had a more peaceful postoperative course [28].

6. Conclusion

The changes in acid–base status during hepatectomy in cirrhotic patients are affected by the preoperative condition of the patient as expressed by MELD and MELD-Na scores as well as by intraoperative transfusion of blood products, use of Pringle maneuver and to a lesser degree by extent of hepatectomy.

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