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Dexamethasone for postoperative hyperbilirubinemia in patients after liver resection: An open-label, randomized controlled trial

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ABSTRACT

Background: Although prophylactic glucocorticoids have been used before liver resection to minimize liver dysfunction, it is unknown whether treatment with glucocorticoids will accelerates recovery from hyperbilirubinemia after liver resection.

Methods: In this open-label, randomized, controlled trial, patients with hyperbilirubinemia (>2.5 × and ≤5 × the upper limit of normal) within 7 days after hepatic resection were assigned randomly to the dexamethasone or control groups. For the dexamethasone group, 10 mg, 10 mg, and 5 mg dexamethasone were administered intravenously on days 0, 1, and 2, respectively, after randomization. For the control group, patients received standard treatment only. The primary outcome was time to recovery from hyperbilirubinemia defined as the period from the day of randomization to the day when serum bilirubin decreased to ≤1.5 times that of the upper limit of normal. Secondary outcomes were the prevalence of postoperative complications, postoperative hospital stay, and hospital expense.

Results: Between March 2016 and December 2017, 76 participants were enrolled (38 in each group). Median time to recovery from hyperbilirubinemia was less in the dexamethasone group than in the control group (2 vs 4 days, $P < .001$). Serum bilirubin levels were less in the dexamethasone group on days 1–3 after randomization ($P < .05$). The prevalence of infection, posthepatectomy liver failure, postoperative hospital stay, and hospital expense were not different between the groups.

Conclusion: Dexamethasone accelerated recovery from hyperbilirubinemia and decreased serum bilirubin levels without causing more side effects in patients after hepatectomy.

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Introduction

Posthepatectomy liver failure (PLF) is a serious complication of the operative treatment of benign and malignant liver tumors[1–4] and a predominant cause of hepatectomy-related mortality.[5] In 2011, the International Study Group of Liver Surgery proposed a definition for PLF based on increased international normalized ratio (INR) and hyperbilirubinemia on or after postoperative day 5 together with a grading system of severity based on the impact on patients' clinical management.[6] Although different authors and organizations still argue about the definition of PLF,[7,8] increased serum bilirubin remains 1 of the most reliable parameters in the criteria for the evaluation of PLF.[9–13]

The effect of glucocorticoids on short-term survival in patients with a variety of causes of severe hepatitis and liver failure is controversial.[14] Glucocorticoids, including dexamethasone, hydrocortisone, prednisolone, and methylprednisolone, improved the prognosis of patients with severe hepatitis or liver failure, alcoholic hepatitis, or autoimmune hepatitis and decreased serum bilirubin in patients with severe alcoholic hepatitis or drug-induced liver injury.[15–17] A meta-analysis showed that glucocorticoids improved the survival of patients with severe hepatitis B without inducing secondary infection or bleeding.[18] In contrast, another report showed that dexamethasone treatment did not improve the liver function or 12-week survival rate in patients with hepatitis B–related, acute-on-chronic liver failure.[19]

Perioperative glucocorticoid treatment decreased the incidence of postoperative complications and serum bilirubin. Four randomized, controlled trials showed that the perioperative use of methylprednisolone or hydrocortisone decreased the incidence of postoperative hyperbilirubinemia, probably through suppression of inflammation or ischemia-reperfusion injuries caused by the

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operative stress.[20–23] Indiscriminative prophylactic treatment with glucocorticoids, however, may potentially induce unnecessary side effects of the glucocorticoid, such as infection, increased blood glucose, impaired liver regeneration, immunosuppression, and the reactivation of hepatitis virus, in patients without liver dysfunction. It remains unknown whether glucocorticoid treatment after liver resection can accelerate recovery of liver function in those patients who have developed liver dysfunction. Therefore, we conducted a randomized, controlled trial to determine the efficacy and safety of postoperative dexamethasone administration in patients who developed increased serum bilirubin concentrations after liver resection.

Methods

Patients

All consecutive patients who received hepatic resection by the same group of surgeons in our department from March 15, 2016 to December 15, 2017 were screened. Inclusion criteria were age between 18 and 70 years, adequate functional reserves of important organ systems (i.e., heart, lungs, and kidneys), normal liver function or good compensation before operation (ie, Child–Pugh classes A or B with the score $\leq$7), preoperative liver stiffness $<$30 kPa as assessed by shear wave elastography,[24] and postoperative serum bilirubin concentrations of $>2.5\times$ but $\leq 5\times$ the upper limit of normal (ULN) within 7 days after liver resection. The ULN of serum bilirubin concentration in our hospital is 20.4 μmol/L or 1.2 mg/dL. Patients with obstructive jaundice, concomitant diseases (eg, peptic ulcer, alimentary tract hemorrhage, or massive ascites), or other contraindications for steroid therapy (eg, uncontrolled local or systemic infection, uncontrolled diabetes, or uncontrolled tuberculosis) were excluded, as were those with concomitant diseases treated with steroids.

Randomization

The patients were assigned randomly in a 1:1 ratio to the dexamethasone group or the control group on the day when they showed hyperbilirubinemia ($>2.5\times$ and $\leq 5\times$ ULN) for the first time after hepatectomy within the first 7 days postoperatively. Group allocation was sealed into sequentially numbered envelopes. When enrolled, a patient was assigned a sequential study number and allocated to a group after the investigators opened the corresponding envelope. Patients were masked to group allocation. This study was approved by the Zhongshan Hospital Research Ethics Committee. Informed consent was obtained from the patients before group allocation.

Therapeutic protocol

All patients received standard treatment after operation, including bed rest, fluid infusion with supplementation of glucose, human serum albumin infusion if serum albumin was $<$35 g/L, oral antihepatitis B virus (HBV) therapy if serum HBV–DNA was detectable, intravenous management of postoperative complications, and intravenous administration of ademetionine butanedisulfonate if their serum bilirubin was $>$ our ULN for serum bilirubin; ademetionine butanedisulfonate (Abbott Lab S.A., Shanghai, China) was approved in China for the patients with intrahepatic cholestasis in precirrhotic and cirrhotic states, therefore, ademetionine butanedisulfonate was used routinely for the patients with hyperbilirubinemia in our center. Patients in the dexamethasone group also received intravenous administration of 10 mg dexamethasone on day 0 (the same day of randomization) and day 1, and 5 mg on day 2; if patients' serum bilirubin did not decrease to $\leq 1.5\times$ ULN, another 5 mg dexamethasone were administered on day 3. All patients enrolled in this trial received laboratory tests once a day, including complete blood cell counts, blood biochemistry, and coagulation function tests, until serum bilirubin decreased to $\leq 1.5\times$ ULN. For patients with diabetes, preprandial blood glucose was monitored. This study was an investigator-initiated clinical study and did not receive support from pharmaceutical companies. The study was registered on ClinicalTrials.gov (NCT02991339).

Endpoints

The primary outcome was the time to recovery from hyperbilirubinemia (TTRH), which was defined as the duration from the day of randomization to the day when serum bilirubin decreased to $\leq 1.5\times$ ULN. The enrolled patients were divided into the fast recovery group (TTRH $\leq$3 days) or the delayed recovery group (TTRH $\geq$4 days) by the median value of TTRH. Then characteristics associated with fast or delay recovery were analyzed. Secondary outcomes were the incidence of postoperative complications associated with liver resection or steroids treatment, including PLF, postoperative infection, and gastrointestinal bleeding, as well as postoperative hospital stay and hospital expense. If serum bilirubin increased to $>5\times$ ULN after randomization, patients were given appropriate treatment at the physician's discretion including glucocorticoids administration. Infective complications included pneumonia diagnosed with imaging and leukocytosis, surgical site infection (including abdominal and wound infection), and bacteremia diagnosed with positive bacterial blood cultures during the hospital stay. Diagnosis of PLF was based on increased INR and hyperbilirubinemia on or after postoperative day 5.[6] In our hospital, the ULN for INR is 1.2. All patients were included in intention-to-treat analysis.

Calculation of sample size

We expected TTRH would be decreased by 1 day (standard deviation, 1.4 day) in the dexamethasone group compared with the control group. Thus, we estimated a sample size of 38 patients in each group to achieve an 80% statistical power at the 5% significance level with 15% dropout, using PS: Power and Sample Size Calculation program v. 3.1.2 (http://biostat.mc.vanderbilt.edu/wiki/Main/PowerSampleSize).

Statistical analysis

Statistical analyses were performed with PASW Statistics v. 18.0 for Windows (IBM Inc.). Quantitative variables were compared using Student *t*-tests or Mann–Whitney U tests and qualitative variables using chi-square tests or Fisher's exact tests. All statistical tests were 2-sided, and $P < .05$ was considered statistically significant.

Results

Patients

Between March 15, 2016 and December 15, 2017, 935 consecutive patients underwent liver resection, 859 patients were excluded because they did not meet the inclusion criteria of this study. A total of 76 participants were enrolled (Fig. 1). Of them, hepatectomy was performed for hepatocellular carcinoma in 66 patients; intrahepatic cholangiocarcinoma in 3; hepatic hemangioma or metastatic colorectal liver metastases in 2 each; and a mixed type of hepatocellular carcinoma/intrahepatic cholangiocarcinoma, hepatic dysplastic nodules, and hepatic angiomyolipoma in 1 each. Of these patients, 60 had a history of HBV infection, 3

Table 1
Preoperative and clinicopathologic characteristics of patients.

Parameter (mean ± SD unless stated otherwise)	Dexamethasone ($n = 38$)	Control ($n = 38$)	P value
Sex (male/female)	32/6	36/2	.262*
Age, y	56.3 (9.3)	55.2 (10.8)	.660
Diabetes (yes/no)	6/32	4/34	.497
Total bilirubin, μmol/L	16.7 (6.7)	18.9 (6.9)	.176
Alanine transaminase, U/L	46.0 (43.4)	44.5 (32.3)	.872
Aspartate aminotransferase, U/L	46.8 (33.4)	30.3 (23.0)	.330
γ-glutamyl transferase, U/L	107.1 (112.4)	109.6 (100.7)	.923
International normalized ratio	1.01 (0.08)	1.05 (0.08)	.040
Hemoglobin, g/L	140.7 (19.6)	147.0 (13.4)	.111
Platelets, $\times 10^9$/L	148.2 (64.5)	135.0 (58.8)	.356
Leukocytes, $\times 10^9$/L	5.5 (2.0)	5.4 (2.1)	.829
HBsAg (positive/negative)	30/8	30/8	1.000
HBeAg (positive/negative)	7/31	9/29	.574
Log(HBV–DNA)	2.2 (2.5)	1.6 (2.2)	.220
Liver stiffness, kPa	12.2 (4.4)	11.9 (3.6)	.764
ICG-R15, %	5.8 (5.2)	7.1 (9.9)	.544
Tumor size, cm	5.7 (4.1)	5.4 (4.0)	.722
Solitary tumor (yes/no)	28/10	24/14	.324
Intraoperative bleeding, mL	356.1 (467.5)	308.7 (390.7)	.633
Blood transfusion (yes/no)	5/33	5/33	1.000
Hilar occlusion time, min	15.5 (13.6)	11.3 (10.8)	.140
Extension of liver resection (major/minor)†	20/18	12/26	.063
Re-resection (yes/no)	5/33	7/31	.529
Scoring of chronic hepatitis			
Grade	1.89 (0.83)	1.89 (0.67)	.986
Stage	3.17 (1.34)	3.39 (1.05)	.448

* Fisher's exact test.
† Minor: 1–2 segment(s); major, ≥3 segments.

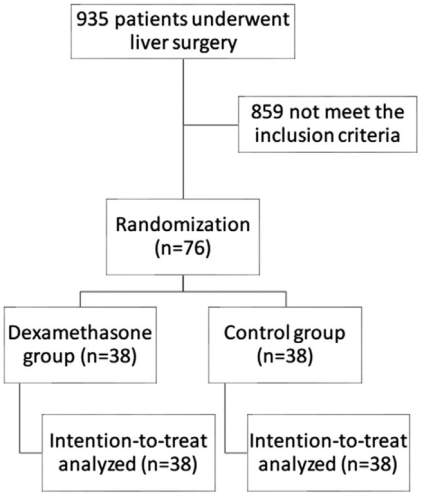

Fig. 1. CONSORT diagram.

a history of hepatitis C virus (HCV) infection, and 1 a history of co-infection with HBV and HCV. Of the patients who were positive for serum HBsAg ($n = 61$), 27 were on antiviral treatment before hospital admission, 27 started entecavir therapy within 2 weeks before operation, and 7 were not given entecavir therapy because of negative HBV–DNA. Of the patients who were positive for anti-HCV antibody ($n = 4$), 2 were negative for HCV–RNA (1 was treated with interferon-α and ribavirin) and 2 were positive for HCV–RNA. The characteristics of patients before or during operation (Table 1) and before randomization (Table 2) were well balanced between groups, except that the mean level of hemoglobin in the dexamethasone group was less on the day of randomization.

Efficacy of dexamethasone treatment

In all the enrolled patients, serum bilirubin concentrations increased to 2.5 × ULN on day 2.1 ± 0.9 postoperatively. The median TTRH of all these patients was 3 days (interquartile range [IQR], 2–4 days). When comparing the dexamethasone group with the control group, the median TTRH of 2 days (IQR, 2–3.25 days) in the dexamethasone group was less than in the control group (4 days, IQR, 3–5 days; $P < .001$; Table 3, Fig. 2, *A*).

The peak level of serum bilirubin tended to be less in the dexamethasone group (48.3 ± 18.9 μmol/L versus 55.4 ± 18.1 μmol/L, $P = .099$). Furthermore, serum bilirubin was less in the dexamethasone group on days 1, 2, and 3 after randomization ($P < .05$ for all), but was not different between groups on day 4 ($P = .615$; Fig. 2, *B*).

Serum bilirubin continued to increase in 4 patients in the dexamethasone group and 12 in the control group after randomization (14% vs 37%, $P = .024$; Fig. 2, *A*). Among these patients, from the dexamethasone and control group, the serum bilirubin increased to >5 × ULN in 1 and 2 patients, respectively; the 2 patients from the control group received dexamethasone administration and recovered uneventfully from hyperbilirubinemia.

Of note, 4 patients in the dexamethasone group had a rebound of serum bilirubin, which was defined as a >10% increase in serum bilirubin concentration after the dexamethasone treatment was stopped. Compared with other patients in the dexamethasone group, these 4 patients had a greater INR at randomization (1.6 vs 1.3, $P = .029$). Serum bilirubin in 3 patients returned to normal levels in 2 and 8 days without further dexamethasone treatment; for the other patient, serum bilirubin did not return to normal levels, and the patient died from liver failure on day 115 postoperatively.

The prevalence of PLF as defined by the International Study Group of Liver Surgery based on the bilirubin and prothrombin time on day 5 or later after liver resection, was not different between the groups (40% vs 50%, $P = .356$), both of which were greater than the prevalence of PLF we reported previously[24] because of the inclusion criteria of this study. No difference in INR was found between the 2 groups on days 1 to 4 after

Table 2
Patient characteristics on the day of randomization.

Parameter (mean ± SD)	Dexamethasone ($n=38$)	Control ($n=38$)	P value
Days from operation to randomization	2.3 (0.9)	1.9 (1.0)	.052
Days of oral intake after operation	2.6 (0.9)	2.9 (0.9)	.181
Total bilirubin, μmol/L	61.6 (9.3)	59.7 (7.0)	.330
Alanine transaminase, U/L	340 (281)	389 (361)	.514
Aspartate aminotransferase, U/L	282.6 (326.4)	346 (375)	.431
γ-glutamyl transferase, U/L	66 (68)	75 (56)	.535
International normalized ratio	1.3 (0.2)	1.3 (0.2)	.644
Hemoglobin, g/L	114.7 (23.2)	124.5 (17.9)	.043
Platelets, $\times 10^9$/L	107.1 (53.3)	111.0 (46.3)	.735
Leukocytes, $\times 10^9$/L	11.1 (4.4)	12.1 (4.5)	.351

Table 3
The characteristics of patients after randomization.

	Dexamethasone ($n=38$)	Control ($n=38$)	P value
TTRH, median (IQR)	2 (2–3.25)	4 (3–5)	<.001
Increased serum bilirubin after randomization n (%)	4 (11)	12 (32)	.024
Peak value of serum bilirubin after randomization, mean (SD), μmol/L	48.3 (18.9)	55.4 (18.1)	.099
No. of patients with serum bilirubin $>5\times$ ULN (%)	1 (2.6)	2 (5.3)	1.000*
PLF† (%)	15 (40)	19 (50)	0.356
Infectious complications, n	2	1	1.000*
Postoperative stay, mean (SD), d	9.4 (2.4)	8.6 (2.6)	.151
Hospital expense, mean (SD), CNY	$62,836 ($23,263)	$56,968 ($11,917)	.171

TTRH, time to recovery from hyperbilirubinemia; IQR, interquartile range; CNY, Chinese Yuan.
* Fisher's exact test.
† Posthepatectomy liver failure, according to the ISGLS criteria.

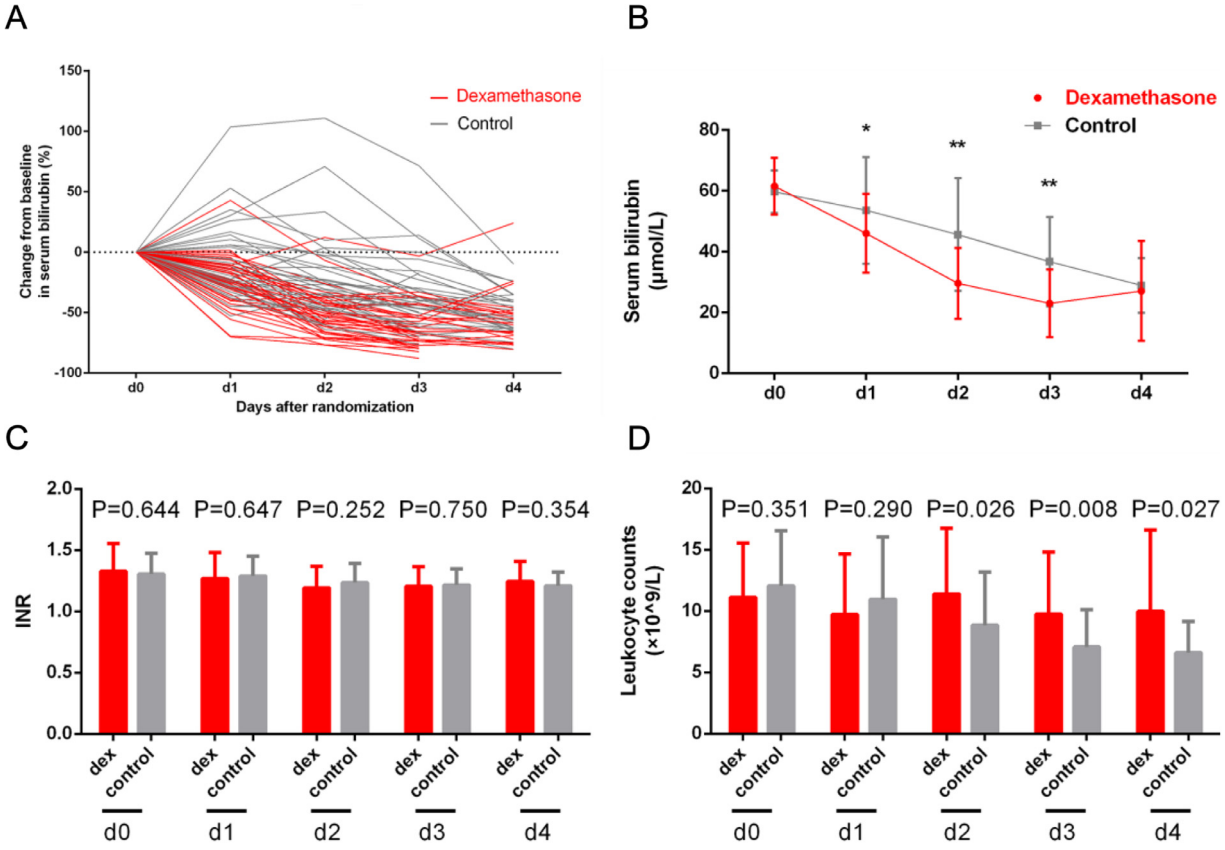

Fig. 2. Serum bilirubin, international normalized ratio (INR), and leukocyte counts in patients in the dexamethasone (dex) and control groups. Changes from baseline in serum bilirubin on day 0 to day 4 after randomization for each patient (*A*). Mean serum bilirubin (*B*), INR (*C*), and leukocyte counts (*D*) from day 0 to day 4 after randomization. Error bars, standard deviation.
*$P < .05$
**$P < .005$

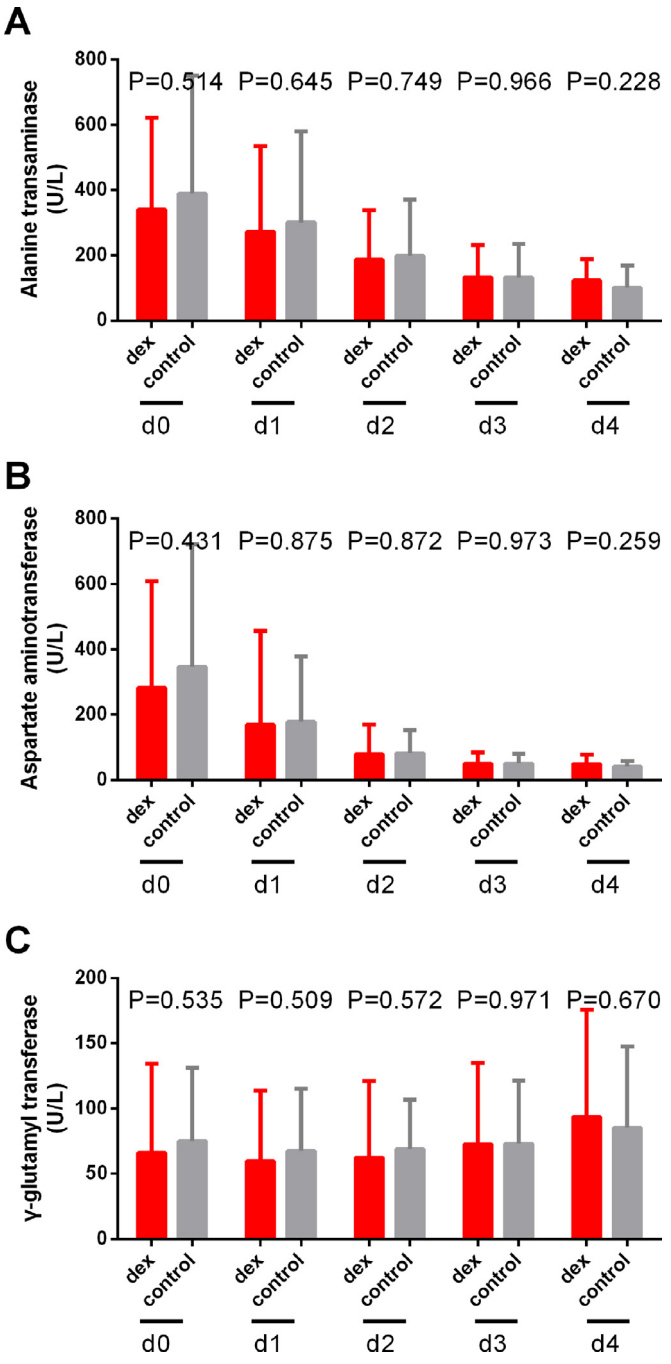

Fig. 3. Mean serum alanine transaminase (*A*), aspartate aminotransferase (*B*), and γ-glutamyl transferase (*C*) from day 0 to day 4 after randomization. Error bars, standard deviation.

randomization (Fig. 2, *C*), suggesting that dexamethasone treatment did not accelerate the recovery of coagulation function. Dexamethasone treatment did not decrease levels of the liver enzymes, including alanine transaminase, aspartate aminotransferase, and γ-glutamyl transferase (Fig. 3). Finally, the postoperative hospital stay (9.4 ± 2.4 vs 8.6 ± 2.6 days, $P=.151$) and hospital expense (62,836 ± 23,263 vs 56,968 ± 11,917 Chinese Yuan, $P=.171$) were not different between the groups.

Safety of dexamethasone treatment

There were no cases of gastrointestinal bleeding. A total of 2 patients experienced bacterial infection in the dexamethasone group, including 1 with a wound infection who was managed with changes of wound dressings and 1 with bacteremia who had a history of diabetes and was managed with antibiotics. One patient in the control group experienced bacteremia which was managed successfully with antibiotics. We also found that white blood cell counts on days 2 to 4 after randomization were greater in the dexamethasone group than in the control group (Fig. 2, *D*); however, the difference was not clinically relevant in most cases. Blood glucose was well controlled in the diabetic patients in the dexamethasone group. The prevalence of postoperative insulin administration did not differ between groups (16% vs 11%, $P=.497$).

Characteristics associated with normalization of bilirubin

We found that INR preoperatively or at randomization, the number of days from operation to randomization, and dexamethasone treatment, were associated with TTRH (Table 4). Patients a with lesser INR preoperatively or at randomization, or those with later onset of hyperbilirubinemia, showed a faster TTRH (≤3 days). Logistic regression analysis showed dexamethasone treatment was independently associated with a faster recovery of hyperbilirubinemia (odds ratio = 5.428, 95% CI, 1.777–16.584, $P=.003$). Increased INR at randomization was independently associated with a delayed recovery (TTRH ≥4 days; odds ratio = 0.036, 95% CI, 0.002–0.580, $P=.019$).

Follow-up 1 month after liver resection

A total of 31 patients in the dexamethasone group and 35 in the control group returned to our hospital 1 month after liver resection. We found no difference between the groups in serum bilirubin (15.0 ± 5.4 vs 16.6 ± 13.6 μmol/L, $P=.537$), alanine transaminase (41 ± 28 vs 38 ± 31 U/L, $P=.688$), aspartate aminotransferase (43 ± 26.0 vs 39 ± 30.3 U/L, $P=.587$), γ-glutamyl transferase (110 ± 110 vs 108 ± 100 U/L, $P=.918$), leukocyte counts (6.1 ± 2.2 vs 5.9 ± 1.6 $\times 10^9$/L, $P=.593$), or platelet counts (147.4 ± 70.2 vs 139.9 ± 68.3 $\times 10^9$/L, $P=.664$). There was no case of HBV reactivation in patients with a history of HBV infection examined by HBV–DNA test.

Discussion

In the present study, we found that the dexamethasone treatment appeared to accelerate the recovery from hyperbilirubinemia and decrease serum bilirubin concentrations without increasing complications in patients who developed elevated serum bilirubin after hepatectomy.

Perioperative glucocorticoid administration has been studied intensively, and many studies have shown that perioperative glucocorticoid use decreased complications and hospital stay for patients undergoing major abdominal surgery[25] as well as liver resection.[26,27] The largest and best-designed, randomized clinical trial reported by Hayashi et al[21] showed that perioperative glucocorticoid administration significantly decreased postoperative serum bilirubin after hepatectomy. In all these studies, glucocorticoids were administered in a prophylactic setting, but considering that only 3 of 105 patients had a bilirubin value >3 mg/mL after liver resection in Hayashi's study,[21] there is a concern that glucocorticoid treatment in most patients is unnecessary. Therefore, we aimed to evaluate the effect of glucocorticoid treatment in patients with emerging signs of liver dysfunction while sparing other patients from the side effects of glucocorticoid treatment. To our knowledge, this is the first randomized, controlled trial evaluating the efficacy of dexamethasone treatment in patients with jaundice after liver resection.

We found that dexamethasone treatment not only accelerated the recovery from hyperbilirubinemia, but also decreased serum bilirubin concentrations. Serum bilirubin is a reliable indicator for

Table 4
The association between perioperative characteristics and the recovery from hyperbilirubinemia.

	Fast recovery ($n = 44$)	Delayed recovery ($n = 32$)	P value
INR before operation, mean (SD)	1.0 (0.1)	1.1 (0.1)	.037
INR at randomization, mean (SD)	1.3 (0.2)	1.4 (0.2)	.036
Days from operation to randomization, mean (SD)	2.3 (0.9)	1.8 (1.0)	.009
Group allocation (dexamethasone/control)	29/15	9/23	.001

INR, international normalized ratio.

liver dysfunction, which is a clinical parameter in several criteria for postoperative liver dysfunction.[6,11,13] Moreover, increased serum bilirubin also appeared to alter liver regeneration capacity.[28] Ischemia-reperfusion injuries and inflammatory response are 2 major mechanisms involved in liver dysfunction after liver resection and result in increased serum levels of interleukin-6, interleukin-10, and tumor necrosis factor, which can be decreased by glucocorticoid treatment.[20–22] We did not evaluate these cytokines in our study, but the peak levels of interleukin-6 and tumor necrosis factor-α were found on days 1–3 after liver resection, as has been reported previously,[20–22] which seems consistent with the dynamic changes of serum bilirubin in our study (Fig. 2, *A*) and may support the postoperative use of dexamethasone in patients with hyperbilirubinemia.

Serum bilirubin continued to increase in 4 patients after the start of dexamethasone treatment; 1 of these patients died from liver failure, suggesting that non-responsiveness to dexamethasone treatment could be an early sign of impending PLF, especially when biliary tract obstruction or a persistent bile leak are excluded. More intensive observation and treatment may be needed for these patients. Takeda et al proposed the following 2 types of liver failure after liver resection based on histologic findings: the cholestatic type mainly induced by infection, and the nonregeneration type mainly induced by severe ischemia-reperfusion injury.[29] It would be interesting to investigate the response of these 2 types of liver failure to glucocorticoids. It has been reported that steroids suppress an excessive or uncontrolled systemic inflammatory response induced by major surgery and more specifically, ischemia-reperfusion injury caused by clamping of the portal triad during liver resection.[26] The overproduction of IL-6 during the inflammatory response may inhibit liver regeneration,[30] and steroids may decrease IL-6 production. In accordance with previous randomized controlled studies,[22,23,31] coagulation function was not improved by glucocorticoid treatment, which is incongruent with the results of Hayashi et al.[21] This discrepancy between studies may result from differences in study design, including drug selection, dosing schedule, and inclusion criteria.

Although 2 patients in the dexamethasone group had infective complications, both were well managed successfully. There was no statistical difference between groups in the prevalence of postoperative infection. Nevertheless, dexamethasone should be administered with caution in patients after a major operation like hepatectomy because of the risk of gastrointestinal bleeding.[32,33] With prophylactic use of proton pump inhibitors, we observed no gastrointestinal bleeding events in either group. Blood glucose was well controlled in all patients with an increased blood glucose. These results suggest that small doses and short-term use of dexamethasone is well tolerated in patients who undergo liver resection, even though most patients had concomitant liver cirrhosis.

Our study has several limitations. First, this trial was conducted in a single center and the number of patients was relatively small, which might explain why the effect of the dexamethasone treatment on serum bilirubin did not translate into a decreased prevalence of PLF or other clinical benefits. Second, although hyperbilirubinemia is a reliable parameter of liver failure, the patients with hyperbilirubinemia in the control group recovered without dexamethasone treatment. The prevalence of PLF was similar between the dexamethasone treatment group and the control group (40% vs 50%). It is also not clear whether the dexamethasone treatment decreased the true risk of fatal PLF because very few episodes of PLF will progress to a live-threatening event. Third, we did not monitor the various inflammatory cytokines reported by the previous studies;[20–22] these data could provide more insight into the mechanism(s) of dexamethasone treatment. The oncologic effect of the dexamethasone treatment needs to be followed because there may be some concern that the anti-inflammatory effect of dexamethasone may increase tumor recurrence. Most recently, Ogasawara et al[34] reported that prophylactic dexamethasone administration in patients undergoing transcatheter arterial chemoembolization alleviated the treatment-related complications without compromising the tumor response rate; this observation suggested that a short course of dexamethasone administration did not significantly affect tumor control. Fourth, ademetionine butanedisulfonate, which was approved in China for the patients with intrahepatic cholestasis, is usually administrated for patients with intractable hyperbilirubinemia. Therefore, the effects of dexamethasone alone are somewhat hard to evaluate based on the current protocol because all the patients received baseline treatment with ademetionine butanedisulfonate.

Conclusion

Dexamethasone treatment given postoperatively in patients with increased serum bilirubin after hepatectomy accelerated recovery from hyperbilirubinemia and decreased serum bilirubin, without causing more side effects, but did not decrease prevalence of PLF. Based on the current study, dexamethasone should not be administrated routinely for all patients after hepatectomy but should be considered for those who develop hyperbilirubinemia postoperatively and possibly as prophylactic treatment for patients at high risk of PLF.

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Conflicts of interest

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