Introduction

Imbalance in cellular oxidative status is one of the most important mechanisms in the pathophysiology of liver diseases. Oxygen-derived free radicals and impaired functioning of the glutathione system induce the increasing lipid peroxidation and glutathione system that causes this imbalance [1-3]. Biliary obstruction may cause glutathione system induce the increasing lipid peroxidation and impaired functioning of the important mechanisms in the pathophysiology of liver diseases.

Endoscopic Retrograde Cholangiopancreatography (ERCP) is performed for resolving cholestasis by sphincterotomy and/or stone extraction and is done with deep sedation or general anesthesia.

Method:

50 patients undergoing ERCP procedure were randomly allocated in two groups. Propofol was given to provide the patients Ramsey sedation scale as 3 and 4 in Group R (n=25) patients whereas it was given to Group B (n=25) patients to provide BIS values between 65 to 85. The levels of total oxidant status (TOS), total antioxidant status (TAS), and OSI were measured. Hemodynamic signs, propofol consumption, postoperative recovery time were recorded.

Results:

TAS and OSI values were similar between the groups but TOS levels were significantly lower in Group B (p=0.027). Heart rate and mean arterial pressures of Group R were significantly higher than Group B. Propofol consumption and postoperative recovery time were smaller in Group B patients (p=0.001, p=0.000).

Conclusion:

In patients undergoing ERCP, using adequate sedation by BIS monitoring, may not only allow us to avoid unnecessary anesthetic drug consumption but also decrease the oxidant status.

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Methods

This study was approved by the Ethics Committee of the University and written informed consent was obtained from each patient. Fifty patients with American Society of Anesthesiologists physical status I–II, between 18 and 65 years of age, undergoing ERCP procedure were enrolled in this study. Patients with uncontrolled comorbidities (hypertension, diabetes mellitus, kidney–liver failure), difficulty in communication (language problems, such as deafness), who are allergic to the drugs used and pregnant women were excluded. Patients were randomized into two groups (Group R and Group B) using a sealed envelope system.

All patients were premedicated with 1mg Midazolam 5 minutes before the procedure. Standard monitoring was performed with electrocardiography, pulse oximetry and noninvasive blood pressure. Additionally, BIS (Aspect Medical Systems, Natick, MA) electrodes were connected to Group B patients. Ringer Lactat was administered during the procedure to all patients via an intravenous catheter. 4lt/min Oxygen (O2) was given via a nasal mask. After giving 1 mcg/kg fentanyl, loading dose of propofol 1mg/kg was administered to all patients intravenously. Then propofol infusion at a rate of 12.5–100 mcg/h was administered to provide Ramsey Sedation Scale 3–4, in Group R or to maintain the BIS level between 60 and 85 in Group B. At the end of the procedure propofol infusion was stopped. Demographic characteristics of all patients were noted. Hemodynamic parameters of saturation (SpO2), heart rate (HR) and mean arterial pressure (MAP) were recorded at before the procedure (T1), 10th minute (T2), 20th minute (T3), 30th minute (T4) intraoperatively and at the end of the procedure (T5). Duration of sedation, awakening time, postoperative Ramsey scores, propofol consumption were also recorded.

Blood samples for Total oxidant status (TOS) and Total antioxidant status (TAS) were applied using a 5 ml disposable syringe from cephalic vein of the patients after the procedure. And the samples were centrifuged at 3000 rpm for 10 min and stored at -80°C until analysis of plasma TAS and plasma TOS levels. Oxidative stress index (OSI) were calculated by a ratio of TOS to the TAS.

Statistical Analysis

The SPSS software version 21.0 (Statistical Package for the Social Sciences Inc, Chicago, IL, USA) was used for all statistical analysis. The Kolmogorov–Smirnov test was used to determine whether the variables were distributed normally or not. Continuous variables were expressed as mean (±) standard deviation (SD) or median according to distribution state. Categorical variables were compared with Fischer exact-test or Chi–square test according to number of cases. Statistically significance was set at \( p < 0.05 \).

Results

In our study, demographic characteristics were similar between the groups (Table 1). Although there was no significance in terms of duration of sedation between the groups, postoperative awakening times were significantly lower in Group B (\( p=0.000, \text{Table 2} \)). There was a significant difference in Ramsey scores of 1st and 5th minutes postoperatively (Table 2). Total propofol consumption during the procedure was significantly lower in Group B (Table 2).

Perioperative hemodynamic variables of the patients were seen in Figure 1. Heart rates were significantly higher at 10th minutes (T2), 30th minutes (T4) and at the end of the procedure (T5) in Group R. And also mean arterial pressures were higher at 10th (T2), 20th (T3), 30th (T4) minutes and at the end of the procedure (T5) in Group R.

When we compared the TAS and TOS values between the groups; TAS and OSI values were similar in both groups whereas TOS values were significantly lower in Group B (\( p=0.027 \)) (Table 3).

Discussion

ERCP plays an important role in the diagnosis and treatment of pancreaticobiliary pathologies. There are many in vivo and in vitro studies that show the role of oxidative stress in the pathogenesis of cholestasis produced by acute biliary obstruction [1–3]. In the present study we compared the effects of physician controlled sedation versus BIS controlled sedation on oxidative stress during ERCP. To the best of our knowledge there is no study in the literature that investigate the effects of BIS on oxidative stress during ERCP. The main findings of the current study include the following; 1) TOS values were

Table 1: Demographic data of the patients.

| Gender (Female/Male), n | Group R (n=25) | Group B (n=25) | Total (n=50, %) | \( \chi^2 \) | \( p \) |
|------------------------|----------------|----------------|----------------|-----------|-------|
| Male                   | 14             | 16             | 30             |           |       |
| Female                 | 11             | 9              | 20             |           |       |
| Gender                 |                |                |                | 0.269     | 0.600 |

Table 2: Duration of sedation, awakening time, Ramsey scores, propofol consumption.

| Duration of sedation (minute) | Group R (n=25) | Group B (n=25) | Total (n=50, %) | \( \chi^2 \) | \( p \) |
|-------------------------------|----------------|----------------|----------------|-----------|-------|
| 35 (20-60)                    | 7              | 10             | 17             | 0.000     | 0.034 |
| Postoperative awakening time (minute) |                |                |                |           |       |
| 5th minute                    | 3.12±0.76      | 3.80±0.57      | 3.51±0.67      | 0.500     | 0.009 |
| 10th minute                   | 2.32±0.99      | 2.04±0.20      | 2.10±0.72      | 0.117     |       |
| Propofol consumption (mg)     | 140.16±33.16   | 107.40±22.23   | 123.78±32.46   | 0.001     |       |

Data presented as mean ± standard deviation or median (min-max). P<0.05 was accepted statistically significant *Chi-Square, *T-test, *Mann-Whitney U
Figure 1: Perioperative hemodynamic variables of patients. HR; heart rate, beat/minute, Spo2; saturation %, MAP; mean arterial pressure, mmHg

Table 3: TAS and TOS values of the groups.

|                  | Grup R (n=25) | Grup B (n=25) | Total (n=50) | P       |
|------------------|---------------|---------------|--------------|---------|
| TAS (mmol Trolox Equiv./L) | 1.74±0.67     | 1.79±0.79    | 1.77±0.73   | 0.809   |
| TOS (mMHO2.Equiv./L)    | 15.18 (6.32-65.47) | 12.25 (3.57-22.55) | 12.70 (3.57-65.47) | 0.027   |
| OSI (arbitrary unit)   | 10.45 (3.02-57.69) | 6.18 (1.33-79.07) | 8.04 (1.33-79.07) | 0.090   |

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Data presented as mean±standard deviation or median (min-max). p<0.05 was statistically significant (P<0.05) at heart rate of T2-T4-T5, MAP of T2-T3-T4-T5 and Spo2 of T5.

significantly lower in Group B (p=0.027), 2) heart rate and mean arterial pressures were lower in Group B, 3) propofol consumption were lower in Group B, 4) recovery period was more favorable in Group B.

The body has a defense system against oxidative stress. The cellular, extracellular, and membranous antioxidant substances included in the antioxidant system react very rapidly with radicals in order to prevent the progression of auto-oxidation/ peroxidation [10]. Since different oxidant and antioxidant species may have additive effects, serum concentrations of different oxidant and antioxidant species may be measured separately but this method is not practical and can achieve false results. Nowadays total antioxidant and oxidant levels can be measured by a stable, simple, reliable and sensitive method [11,12]. We preferred the assessment of oxidative stress by measurement of the TAS, TOS and calculating the value of OSI instead of measurement of several oxidant and antioxidant molecules. In a recent study the researchers investigate the effects of fetal oxidant-oxidant status during the different anesthesia techniques for elective caesarion sections, they found no change in the levels of TAS and TOS in umbilical artery blood levels whereas the OSI values were significantly lower in general anesthesia group [13]. In another study that investigate the effects of mode of delivery on oxidative-antioxidative balance in both mothers and infants, they found TAS and TOS levels were higher in patients delivering with C/S while vice versa for TAC [10]. There are so many studies about the effects of laparoscopy on oxidative stress [14–16]. In a review about the effects of laparoscopic surgery on oxidative stress response, highly discordant results were seen; some studies suggested less pronounced oxidative status after laparoscopy, some of them suggested potentiation of OS whereas some studies demonstrated no difference in OS between open and laparoscopic surgery [15]. Erçin et al. evaluated the role of oxidative stress in the cholestatic liver disease, they found an increase in oxidative stress and significant alterations in the different part of the antioxidant system in extrahepatic cholestasis [17].

In our study, the levels of both OSI and TAS were not statistically significant, but TOS levels were statistically lower in Group B. When we looked at the hemodynamics of the patients, heart rate and mean arterial pressures were higher in Group R. Sedation levels were maintained more uniform in Group B and also hemodynamic response were avoided better in Group B. Most likely, sympathetic activity might cause high oxidative status in Group R patients.

Deterioration of the balance between the oxidant and antioxidant systems is the main cause of tissue damage. Under some conditions, increases in oxidants and decreases in antioxidants cannot be prevented, and the oxidative/antioxidative balance shifts toward the oxidative status [10]. Ischemia, hemorrhage, trauma in addition to this factors such as cigarette smoke, dirty air, and sulfur increases the amount of oxidizing agents. Alcohol, drugs and other addictive substances also increase the oxidants formation due to disturb the homeostasis [18]. There is a growing evidence of the beneficial protective effect of fruit and vegetables in cancer and cardiovascular diseases. Recently, it was suggested that the effect of fruit and vegetables is superior to a single antioxidant in producing total antioxidant potential [19]. In our study smokers and alcohol users were similar in both groups, but its our limitation that we did not query the patients diets or any drug abuse. Another limitation was the small number of patients and then didnot show enough power.

The administration of sedative-analgetic medications should not be based on anticipated distress but rather on that which is observed; otherwise, there will be an increased risk of over sedation which has been shown to worsen clinical outcomes. A study by Monk et al. [20], suggests that intraoperative anesthetic management, particularly depth and blood pressure control may influence the mortality in up to one year. The maintenance of pharmacological sedation requires that patients be reassessed frequently to determine whether their agitation and underlying distress are being adequately managed. Monitoring anesthetic depth is now possible thanks to use of EEG digital signal processing techniques. The most commonly used the Bispectral Index (BIS), the Patient Safety Index (PSI), Narcotrend, and Entropy [21]. Conscious sedation applications were made not only to facilitate the work of physician and patient comfort but also to increase the success rate during ERCP procedures [22–23]. Nowadays propofol is widely used in both adult and children’s anesthesia induction, maintenance and sedation [24]. Propofol has been shown to have important advantages such as ability of better titration and shorter recovery times according to benzodiazepines and

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048
opioids in a large prospective study [25]. In this study we also used propofol for sedation. Although duration of sedation were similar between the groups postoperative awakening times were significantly lower in Group B. Also propofol consumption was lower and recovery times were smaller in Group B.

As a result anesthetic depth monitoring allows the use of exact dosages of anesthetics and decreases the oxidant status during ERCP.

References

1. Gonzales-Correa JA, De La Cruz JP, Martin-Aurioles E, Lopez-Egea MA, Ortiz P, et al. (1997) Effects of S-adenosyl-L-methionine on hepatic and renal oxidative stress in an experimental model of acute biliary obstruction in rats. Hepatology 26: 121-127. Link: https://doi.org/10.1002/hep.

2. Muriel P, Suarez OR, Gonzales P, Zuniga L (1994) Protective effect of S-adenosyl-L-methionine on liver damage induced by biliary obstruction in rats: a histological, ultrastructural and biochemical approach. J Hepatol 21: 95-102. Link: https://doi.org/10.1016/0168-8278(94)90093-8.

3. Singh S, Shackleton G, Ah-Sing E, Chacraborty J, Bailey ME (1992) Antioxidant status during ERCP. J Surg Arts 5: 31-34. Link: https://doi.org/10.1016/0930-7040(92)90002-A.

4. Neuschwander-Tetri BA, Nicholson C, Wells LD, Tracy TF Jr (1996) Cholestatic extrahepatic cholestasis. Anatol J Clin Invest 2: 150-154.

5. Manukyan MN, Deveci U, Kebudi A, 3. Singh S, Shackleton G, Ah-Sing E, Chacraborty J, Bailey ME (1992) Antioxidant defences in the bile duct-ligated rat. Gastroenterology 103: 1625-1629. Link: https://doi.org/10.1016/0016-5085(92)90470-V.

6. Çelebi S (2007) COMPLICATIONS OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY. Türkiye Klinikleri J Int Med Sci 3: 33-36. Link: https://doi.org/10.5505/tkjem.2007.15191.

7. Balco C, Svacci RG, Saka O, Akbulut G (2006) Comparison of recovery times of desflurane and sevoflurane with bispectral index values. Journal of Anesthesia-JARSS 14: 32-36.

8. Ma PL, Zhao JZ, Su JW, Li Q, Wang Y (2006) Comparison of reliability of BIS and sedation - agitation scale in assessing the depth of sedation in patients treated with mechanical ventilation. Zhongguo Wei Zhong Bing Ji Jiu Yi Xue 18: 323-326. Link: https://doi.org/10.1016/S1005-7730(06)63124-4.

9. Butterworth JF, Mackey DC, Wasnick JD Noncardiovascular Monitoring. Morgan&Mikhail’s Clinical Anesthesiology 5th edition. McGraw Hill Companies, United States Lange 123-142.

10. Mutlu B, Aksoy N, Çakır H, Celik H, Erel Ö (2011) The effects of mode of delivery on oxidative-antioxidative balance. The Journal of Maternal Fetal and Neonatal Medicine 24: 1367-1370. Link: https://doi.org/10.3109/14767058.2010.527234.

11. Erel O (2004) A novel automated method to measure total antioxidant response against potent free radical reactions. Clin Biochem 37: 112-119. Link: https://doi.org/10.1016/j.clinbiochem.2003.12.005.

12. Erel O (2005) A new automated colorimetric method for measuring total oxidant status. Clin Biochem 38: 1103-1111. Link: https://doi.org/10.1016/j.clinbiochem.2004.12.005.

13. Karabayrik S, Keskin EA, Kaya A, Koca C, Erel O, et al. (2015) Assessment of fetal antioxidant and oxidant status during different anesthetic techniques for elective cesarean sections. J Res Med Sci 20: 739-744. Link: https://doi.org/10.22038/jrms.2015.4849.

14. Aran T, Unsal MA, Guven S, Kart C, Cotin EC, et al. (2012) Carbon dioxide pneumoperitoneum induces systemic oxidative stress: a clinical study. European Journal of Obstetrics&Gynecology and Reproductive Biology 161: 80-83. Link: https://doi.org/10.1016/j.ejogrb.2011.08.009.

15. Yiannakopoulou EC, Nikitas N, Perrea D, Tsigris C (2013) Effect of Laparoscopic Surgery on Oxidative Stress Response:Systematic Review. Surg Laparosc Percutan Tech 23: 101-108. Link: https://doi.org/10.1097/SLT.0b013e318275d9f6.

16. Koksal H, Kurban S (2010) Total oxidant status, total antioxidant status, and paraoxonase and arylesterase activities during laparoscopic cholecystectomy. Clinics 65: 285-290. Link: https://doi.org/10.6061/clinics/2010/65/2/285.

17. Erçin CE, Bağcı S, Yesilova Z, Aydin A, Sayal A, et al. (2008) Oxidative stress in extrahepatic cholestasis. Anatol J Clin Invest 2: 85-90.

18. Yerer MB, Aydoğan S (2000) Oxidative stress and antioxidants. E.U. Journal of Health Sciences 9: 49-53.

19. Lavy A, Karban A, Suissa A, Yassin K, Hermesh I, et al. (2004) Natural β-Caroten for the prevention of post-ERCP pancreatitis. Pancreas 29: 45-50. Link: https://doi.org/10.1097/01.PAN.0000111709.53472.5E.

20. Monk TG, Saini V, Weldon BC, Sigl JC (2005) Anesthetic management and one-year mortality after noncardiac surgery. Anesth Analg 100: 4-10. Link: https://doi.org/10.1213/01.ANE.0000152585.73199.4B.

21. Brown EN, Solt K, Purdon PL, Johnson-Akeju O (2015) Monitoring brain state during general anesthesia and sedation. In: Miller, Ronald D. Miller’s Anesthesia, eight edition, ‘015 by Saunders, 1524-1540.

22. Standart of Practice Committee of the American Society for Gastrointestinal Endoscopy, et al. (2008) Sedation and anesthesia in GI endoscopy. Gastrointest Endosc 68: 815-826. Link: https://doi.org/10.1016/j.gie.2008.07.051.

23. Chen WX, Lin HJ, Zhang WF, et al. (2005) Sedation and safety of propofol for therapeutic endoscopic retrograde cholangiopancreatography. Hepatobiliary Pancreat Dis Int 4: 437-440. Link: https://doi.org/10.2147/HPD.S121.

24. Benedict P,Tremper K (2008) The anesthetic plan for healthy patients. In: Longnecker D, Brown D. Anesthesiology, First edition. Pennsylvania: The McGraw-Hill Company, 68-87.

25. Koshy G, Nair S, Norkus EP, Hertan HI, Pitchumoni CS (2000) Propofol versus midazolam and Meperidine for conscious sedation in GI endoscopy. Am J Gastroenterol 95: 1476-1479. Link: https://doi.org/10.1111/j.1572-0241.2000.000045.x.