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Research Article

Does the use of Bispecteral Index reduce the oxidative stress in Endoscopic Retrograde Pancreoticocolangiography?

Abstract

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

Aim: Our aim was to evaluate the effects of the depth of anesthesia on oxidative stress provided via Bispecteral Index (BIS) monitorisation during the ERCP procedure by analyzing the biochemical parameters. And also was the effects of anesthesia depth on propofol consumption and postoperative sedation status.

Methods: 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.

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 glutathione system induce the increasing lipid peroxidation that causes this imbalance [1-3]. Biliary obstruction may cause acute hepatocellular injury and lead to progressive fibrogenesis, although the mechanism is not clearly understood, oxidative stress is known to be involved in this process [4].

Endoscopic Retrograde Cholangiopancreatography (ERCP) is an important way in diagnosis and treatment of illnesses of the pancreas, gall bladder and choleductal duct, and is performed for resolving cholestasis by sphincterotomy and/or stone retraction. ERCP can be done under general anesthesia and deep or superficial sedation [5]. Excessive or inadequate sedation affect the success of the process for it cause unresponsiveness or discomfort of the patient [6]. During this procedure, while providing sufficient analgesia and immobility, avoiding coughing and retching without suppression of protective airway reflexes is desirable. Briefly anesthesia during ERCP requires art. Therefore the doses of sedative drugs to be used should be good titrated and patients should be followed closely with monitoring procedures. Bispecteral Index (BIS) is one of the noninvasive method of measuring the depth of anesthesia that shows the activity in the deep cortical structure [7,8]. To perform a bispecteral analysis, data measured by EEG are taken through a number of steps to calculate a single number that correlates with depth of anesthesia. BIS values of 65-85 have been advocated as a measure of sedation, whereas values of 40-65 have been recommended for general anesthesia. Bispecteral index may reduce patient awareness during anesthesia [9].

We aimed to investigate the effects of anesthesia with monitoring the depth of anesthesia using BIS on oxidative stress, propofol consumption, postoperative recovery during ERCP procedures in this study.

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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 (O_2) 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 remaining plasma samples were 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* value < 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, 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.

	Group R (n=25)	Group B (n=25)	Total (n=50, %)	p
Gender (Female/Male),n	16-Sep	Nov-14	27(54%)/23(46%)	0.156*
Age(year)	57.52±14.83	55.72±13.90	56.62±14.25	0.660#
Weight(kg)	70 (60-94)	70 (60-85)	70 (60-94)	0.313&
Height (cm)	165 (155-176)	160 (155-180)	160 (155-180)	0.776&
Comorbidities (yes/no)	Nov-14	13-Dec	24(48%)/26(52%)	0.571*
Cigarette (yes/no)	May-20	Jun-19	11(22%)/39(78%)	0.733*
Alcohol (yes/no)	Feb-23	Feb-23	4(8%)/46(92%)	1.000*

Data presented as mean±standart deviation or median (min-max). p<0.05 was accepted statistically significant *Chi-Square, #T-test,&Mann-Whitney U

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

	Grup R (n=25)	Grup B (n=25)	Total (n=50, %)	p
Duration of sedation(minute)	35(20-60)	35 (25-45)	35 (20-60)	0.373&
Postoperative awakening time(minute)	7 (5-10)	5 (4-7)	5.50 (4-10)	0.000&
Ramsey 1st minute	4.08±1.26	3.20±0.91	3.64±1.17	0.007#
5th minute	3.12±0.97	2.48±0.65	2.80±0.88	0.009#
10th minute	2.32±0.99	2.04±0.20	2.18±0.72	0.117#
15th minute	2.28±0.84	2.00±0.10	2.14±0.60	0.110#
Propofol consumption (mg)	140.16±33.16	107.40±22.23	123.78±32.46	0.001#

Data presented as mean±standart deviation or median (min-max). P<0.05 was accepted statistically significant , #t-test, &Mann-Whitney U

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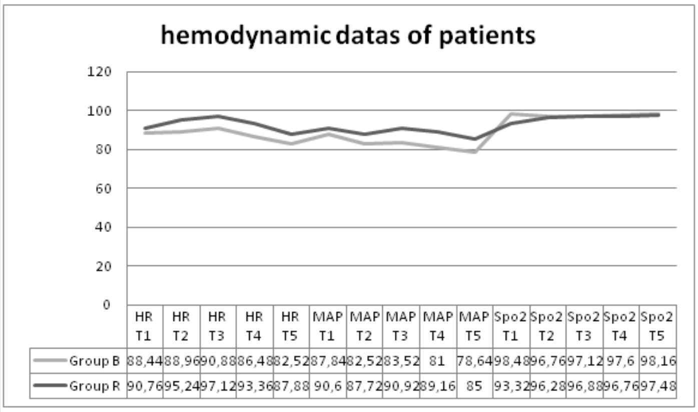

Figure 1: Perioperative hemodynamic variables of patients. HR; heart rate, beat/minute, Spo2; saturation %, MAP; mean arterial pressure, mmHg
p is statistically significant (P<0.05) at heart rate of T2-T4-T5, MAP of T2-T3-T4-5 and Spo2 of T5.

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 (mMH_2O_2Equiv./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&

Data presented as mean±standart deviation or median (min-max). p<0.05 was accepted statistically significant , #t-test, &Mann-Whitney U. TAS ; total antioxidant status, TOS; total oxidant status, OSI; oxidative stress index

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 simple, stable, 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 antioxidant-oxidant status during the different anesthesia techniques for elective caesarian 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 both in mothers and infants, they found 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 oxidant 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-analgesic 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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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.

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