Comparison of intraocular pressure change in patients under sedation-assisted and sedation-free upper gastrointestinal endoscopy

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Intraocular pressure in endoscopy

Abstract

Aim: The study aimed to compare the intraocular pressure (IOP) in patients with upper gastrointestinal endoscopy (UGE) under sedation and without sedation.

Material and Methods: This study was performed prospectively. Among patients with indications for upper gastrointestinal endoscopy, we included in the study fifty subjects who wanted the procedure to be performed without sedation and fifty subjects who wanted the procedure to be performed with sedation. All participants were aged between 18-60 years, with a body mass index (BMI) of less than 30 kg/m² and did not have any systemic and ocular disease. Demographic data of all patients were recorded. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were recorded before and during the procedure. IOP was measured 5 times in all patients.

Results: There was no significant difference between the two groups in terms of age, BMI, gender, IOP values prior to the procedure, IOP values 60 minutes after the procedure (p=0.066, p=0.057, p=0.230, p=0.749, respectively). It was found that the IOP values were significantly lower in the sedated group during, at 15 and 30 minutes after the procedure(p<0.001). While there was no statistically significant difference between the two groups in terms of SBP, DBP and HR values before the procedure (p=0.688, p=0.538, p=0.494, respectively), these values measured during the procedure were significantly higher in the non-sedated group (p<0.001).

Discussion: The increase of IOP can be prevented during the procedure by performing UGE with sedation. Complications related to acute IOP increase may be prevented by performing sedation-assisted UGE, especially in patients with glaucoma and those undergoing ocular surgery due to glaucoma and eye perforation.

Keywords
Endoscopy; Glaucoma; Intraocular pressure; Propofol; Sedation
Introduction

Upper gastrointestinal endoscopy (UGE) is a powerful diagnostic tool because it provides direct mucosal imaging and is widely used in the treatment of many gastrointestinal diseases [1]. During UGE, full-time imaging of the oropharynx, pharynx, esophagus, stomach and proximal duodenum is provided with an esophagogastroduodenoscope (EGD). During the oropharynx and pharynx transition at the beginning of the procedure, the gag reflex, which is one of the normal reflexes, is produced by contraction of the pharyngeal muscles as a result of stimulation of the pharynx and velar region [2]. Although local lidocaine was administered to prevent this reflex during UGE, it was shown that the gag reflex occurred during the procedure [3]. Also, intraabdominal pressure increases abruptly with retching caused by the gag reflex [4]. In this case, the Valsalva reflex, which is defined as forced exhalation when the glottis is closed, may occur due to a sudden increase in intrathoracic and/or intrabdominal pressure [5]. The Valsalva reflex has been shown to cause an increase in intraocular pressure (IOP) [6].

On the other hand, previous studies have shown that laryngopharynx or epilarynx contact during direct laryngoscopy before endotracheal intubation leads to sympatho-adrenergic discharge [7,8]. As with laryngoscopy, the sympathetic discharge may occur due to the pressure of the EGD on the laryngopharynx area during UGE. Therefore, many hemodynamic changes may occur, including hypertension, tachycardia, and cardiac arrhythmia [9]. Moreover, the sympathetic-adrenergic discharge has been reported to cause a sudden increase in IOP, independent of hemodynamic changes [8].

An acute IOP increase may have negative effects in some patient groups and may cause various complications in healthy adults. For example, acute IOP elevation in adults without a history of the ocular disease has been reported to cause permanent visual field defects due to optic nerve damage [10,11]. Besides, orbital hematoma that occurs during UGE, and is thought to be caused by Valsalva reflex, has been reported as a complication of UGE [12]. Also, an acute IOP increase, especially in patients with a history of glaucoma and ocular surgery due to glaucoma, may have some negative results. For example, in a study performed by Tun et al., especially in open-angle glaucoma, it was shown that visual field loss occurred due to an acute elevation of IOP [13].

We anticipate that with sedation-assisted UGE, the pressure on the laryngopharynx area will be reduced and adrenergic discharge will be relatively low in these patients, with a reduction in the gag reflex and minimal retching, and consequently, there will be no increase in IOP. Therefore, this study aimed to compare the IOP in patients with UGE under sedation and the IOP in patients without sedation.

Material and Methods

Ethics committee approval was obtained from the local Clinical Research Ethics Committee (approval no: 2017-KAEK-189_2019.05.29_03). The study was conducted prospectively in accordance with the Declaration of Helsinki. Signed informed consent forms were obtained from all patients. Before starting the study, the sample size was determined using power analysis.

Between June 2019 and September 2019, patients admitted to the general surgery outpatient clinic with various complaints and indicated for UGE, aged between 18 and 60 years, and whose body mass index (BMI) was below 30 kg/m², were included in the study. Patients with any systemic disease were excluded from the study. Then all patients underwent an ophthalmologic examination by an ophthalmologist. Patients with any ocular disease (such as glaucoma, vernal conjunctivitis, valve deformity) and any history of ocular surgery for any reason were excluded from the study. Then 50 people who wanted to perform UGE with sedation were included in the study as the sedated group, and 50 people who did not want to take sedation were included as the non-sedated group.

The sociodemographic characteristics of all patients were recorded.

Anesthesia Protocol

Sedation was performed without an anesthesiologist (accompanied by a physician experienced in intensive care and resuscitation and a trained nurse) to achieve an adequate level of sedation and ensure the continuity of sedation. Propofol (1 mg/kg) (propofol-lipuro %1 Braun, Istanbul, Turkey) was administered just before the procedure. Subsequently, if necessary, sedation was maintained with repeated doses of propofol (10–20 mg). During sedation, oxygen was given through a nasal cannula at 2 L/min.

UGE Protocol

All patients were taken to the endoscopy room and their heart rate (HR), blood pressure, oxygen saturation, and respiration rate were monitored. First, systolic blood pressure (SBP), diastolic blood pressure (DBP) and HR were recorded. In all patients, topical anesthesia was applied with 3 puffs of lidocaine (Xylocaine pump spray 10%, AstraZeneca Inc., Turkey). Then all patients underwent the standard UGE procedure by the same physician with the same fiber optic EGD (Fujifilm Corporation, Tokyo, Japan). In addition, blood pressure and HR were recorded during gastric mucosa examination of all patients during the procedure.

IOP Evaluation

The IOP measurement was performed by the same ophthalmologist with the I-Care Pro tonometer (Tiolat Oy, Helsinki, Finland), which works on the principle of rebound tonometry. The measurement was performed in the right eye of all patients and, a total of 5 times. The mean value was recorded from three consecutive measurements during each evaluation. The first measurement was taken 2 minutes before the initiation of UGE in the non-sedated group and before the propofol administration in the sedated group (T1). The second measurement was taken when examining the gastric mucosa, as it was filled with air (T2). The third measurement was taken 15 minutes after the end of the UGE process (T3). The fourth measurement was taken 30 minutes after the end of UGE (T4). The final, fifth, measurement was taken 60 minutes after the end of UGE (T5).

Statistical Analysis

SPSS 22.0 (Statistical Package for Social Sciences, IBM Inc., Chicago, IL, USA) was used for statistical analysis of the data. The Kolmogorov–Smirnov test was used to test the distribution of normality. The chi-square test was used to
Intraocular pressure in endoscopy

compare categorical variables. The Student’s t-test was used for the comparison of two groups for parametric data, and the Mann-Whitney U test was applied for nonparametric data. Comparisons of the changes in variables in the same group were performed using the Wilcoxon test for nonparametric data. The Pearson correlation test was used for correlation analysis of normally distributed data, and the Spearman correlation test was used for non-normally distributed data. A P-value of less than 0.05 was considered statistically significant.

**Results**

In our study, while the mean age in the non-sedated group was 41.10 ± 9.44 years, the mean age in the sedated group was 44.72 ± 10.02 years. There was no statistical difference between the groups in terms of average age (p = 0.066). Similarly, no significant difference was found between the groups in terms of BMI (p = 0.057). In addition, 21 (42%) patients in the non-sedated group were women, while 27 (54%) patients in the sedated group were women. However, this situation did not create a statistical difference (p = 0.230). The sociodemographic characteristics of the patients are shown in Table 1.

The mean propofol dose used in the sedation group was 82.40±13.78 mg.

There was no statistically significant difference between the IOP values at T1 and T5 in both groups. However, T2, T3, and T4 IOP values were significantly higher in the non-sedated group. The IOP measurement values are shown in Table 2. In addition, the mean values of the IOP measurements are shown in Figure 1. On the other hand, when T1 and T2, T3, and T4 values were compared in the non-sedated group, T2, T3, and T4 values were found to be significantly higher than T1 (p<0.001). However, there was no statistically significant difference between T1 and T5 values in the non-sedated group (p=0.151). In the sedation group, T2, T3, and T4 values were statistically significantly lower than T1 values (p<0.001). No statistically significant difference was found between T1 and T5 values in the sedated group (p=0.118). Furthermore, no statistically significant difference was found between the two groups in terms of SBP, DBP and HR values recorded before the procedure. However, SBP, DBP and HR values measured during the procedure in the non-sedated group were found to be significantly higher than those measured in the sedated group. Data for SBP, DBP, and HR are shown in Table 2. Additionally, SBP, DBP and HR values measured during the procedure in the non-sedated group were significantly higher than those measured before the procedure (p<0.001). However, in the sedated group, there was no significant difference between SBP, DBP and HR values measured during the procedure and pre-procedural values (p=0.069, p=0.139, p=0.092, respectively).

Also, our correlation analysis did not reveal any correlation between age and BMI and any of the measured values. Correlation data are shown in Table 3.

| Table 1. Sociodemographic Characteristics |
|------------------------------------------|
| Non-sedated Group | Sedated Group | p value |
| Age* | 41.10±9.44 | 44.72±10.02 | 0.066 |
| BMI* (kg/m²) | 24.92±2.30 | 25.82±2.37 | 0.057 |

| Gender |
|------------------------------------------|
| Female (%) | 21 (42) | 27 (54) | 0.230 |
| Male (%) | 29 (58) | 23 (46) | |

BMI: Body mass index. * mean±standard deviation.

| Table 2. Data for IOP Measurement Values, SBP, DBP, and HR |
|------------------------------------------|
| Non-sedated | Sedated |
|---|---|---|---|
| T1 (mmHg) | 15.26±2.35 | 15.50±2.11 | 0.593 |
| T2 (mmHg) | 41.82±6.01 | 13.38±1.64 | <0.001 |
| T3 (mmHg) | 33.52±4.28 | 13.72±1.51 | <0.001 |
| T4 (mmHg) | 25.42±3.20 | 14.86±1.72 | <0.001 |
| T5 (mmHg) | 15.46±2.45 | 15.32±1.87 | 0.749 |

Pre-procedural SBP* | 113.50±8.97 | 112.82±7.86 | 0.688 |
| Pre-procedural DBP* | 74.92±8.58 | 73.94±7.19 | 0.538 |
| Pre-procedural HR** | 74.52±6.32 | 73.70±5.58 | 0.494 |
| During procedure SBP* | 146.24±15.49 | 114.46±6.44 | <0.001 |
| During procedure DBP* | 108.68±17.37 | 75.14±6.54 | <0.001 |
| During procedure HR** | 91.88±7.94 | 75.54±6.28 | <0.001 |

IOP: Intraocular pressure. T1: Pre-procedure measurement. T2: Measurement during operation. T3: Measurement taken 15 minutes after the procedure. T4: Measurement taken 30 minutes after the procedure. T5: Measurement taken 60 minutes after the procedure. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. HR: Heart rate. Data are shown as mean±standard deviation. *Blood pressures were given in millimetres of mercury. **Heart rate was given in beats / minute. Bold p<0.05

| Table 3. Correlation Analysis |
|------------------------------------------|
| Age | BMI |
|---|---|---|---|
| T1 | 0.034 | 0.739 | 0.021 | 0.836 |
| T2 | -0.132 | 0.191 | -0.185 | 0.065 |
| T3 | -0.162 | 0.108 | -0.194 | 0.053 |
| T4 | -0.149 | 0.140 | -0.193 | 0.055 |
| T5 | 0.033 | 0.743 | -0.013 | 0.901 |

T1: Pre-procedure measurement. T2: Measurement during operation. T3: Measurement taken 15 minutes after the procedure. T4: Measurement taken 30 minutes after the procedure. T5: Measurement taken 60 minutes after the procedure.
Discussion
In our study, it was found that the IOP was significantly increased during the procedure as compared to the pre-procedure in patients, who underwent UGE without sedation. Moreover, IOP was high even 30 minutes after the procedure, but regressed to pre-procedural levels by 60 minutes after the procedure. We think that one of the reasons for this increase in IOP during the procedure may be the retching that occurs during the pharynx transition. Intra-abdominal pressure may increase suddenly and the Valsalva reflex may occur [5]. In the literature, it has been shown that the Valsalva reflex causes an increase in IOP [14,15]. Additionally, it has been reported that an increase in intraabdominal pressure caused either by the gag reflex or intragastric air insufflation, independent of the Valsalva reflex, may lead to an increase in intracranial pressure [16,17].

A positive correlation has been shown between increased intracranial pressure and increased intraocular pressure [18]. We also believe that another reason for the high IOP in non-sedated UGE patients was that retching was intense due to the procedure being performed without sedation, and consequently, intense pressure of the EGD on the laryngopharynx region. In the literature, it has been shown that sympatho-adrenergic discharge occurs as a result of compression to the laryngopharynx region [19]. Furthermore, sympatho-adrenergic discharge has been reported to cause a sudden increase in IOP [8]. The following situation in our study supports this information: in patients who underwent UGE without sedation, SBP, DBP, and HR were significantly higher during the procedure than before the procedure, and in the same group of patients, the IOP during the procedure was higher than before the procedure. Regardless of the mechanism underlying the IOP increase during UGE, this increase may cause complications in some special patient groups (such as glaucoma) and may result in significant complications in adults without any ocular disease. For example, in a study conducted in a healthy adult, Valsalva retinopathy, which is thought to result from multiple and continuous retching during UGE, has been reported [5]. However, in the literature, we have not come across a study of acute glaucoma attack due to increased IOP after UGE. In order to elucidate this issue, we plan to investigate this issue in our next study. On the other hand, it has been shown in the literature that retinal and vitreous hemorrhage occurs as a result of strong and continuous retching for various reasons [20]. Also, transient IOP elevation after oral surgery has been shown to cause glaucoma progression, particularly in patients with advanced glaucoma [21,22]. On the other hand, Chai et al. reported that a sudden IOP increase in patients with a history of eye perforation may have negative consequences [23]. In our study, it was found that the IOP during, at 15 and 30 minutes after the procedure was significantly lower in patients with UGE under sedation compared to those without sedation. In fact, in patients with UGE performed with sedation, the IOP during, at 15 and 30 minutes after the procedure was significantly lower than the IOP measured before the procedure. Moreover, although the IOP increased gradually after the procedure, it remained low compared to the pre-procedure, even after 15 and 30 minutes; however, it was found to reach the level before UGE by 60 minutes after the procedure. We propose that one of the causes of this condition is the use of propofol for sedation, because topical anesthesia using lidocaine combined with propofol sedation has been shown to reduce the retching reflex in UGE [24]. Thus, the intraabdominal pressure does not increase abruptly due to the absence of, or reduced, retching and, therefore, the Valsalva reflex does not occur. Consequently, there was no increase in the IOP during the process. In addition, propofol has been reported to reduce IOP regardless of changes in HR, SBP, and DBP [25]. In our study, in patients with UGE performed under sedation, it was observed that the IOP was low during and after the procedure compared to the pre-procedure, supporting findings presented in the literature. Also, in our study, it was found that there was no significant difference between pre-procedure and during the procedure values of SBP, DBP, and HR in patients with UGE under sedation. This is due to the fact that the retching reflex is lower when performing the procedure with sedation; therefore, we think that the EGD is relatively less compressive to the laryngopharynx region, and thus less sympatho-adrenergic discharge occurs. However, we would like to emphasize the need for further studies on sympatho-adrenergic discharge during UGE due to the limited number of studies in the literature. Furthermore, the fact that our study was conducted in a single center and with a relatively small number of patients can be considered a limiting factor. In addition, the fact that our study was not a randomized study is another limiting factor. However, according to our literature research, we have not come across a study that measured IOP during the UGE and, therefore, the work that we have carried out fills this gap in the literature. We also believe that our work will provide a basis for future work on this subject.

Conclusions
In conclusion, it should be noted that a sudden increase in IOP during UGE without sedation may lead to several complications in glaucoma patients, people with a history of eye perforation and ocular surgery due to glaucoma, as well as in healthy individuals. In these patients, the increase in IOP can be prevented by performing UGE accompanied by sedation using propofol. Therefore, we suggest that UGE should be performed with sedation using propofol in patients with a history of glaucoma, eye perforation and ocular surgery due to glaucoma.

Scientific Responsibility Statement
The authors declare that they are responsible for the article’s scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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