Unsedated transnasal versus conventional oral endoscopy in endoscopy naïve patients

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Abstract

Background and study aims : **Unsedated transnasal upper endoscopy (TNE) has been suggested as a more comfortable and safer method than unsedated transoral endoscopy (TOE). However, the numbers of comparative trials are limited. The current study aimed to assess the tolerability, safety, and efficacy of TNE in endoscopy naïve patients.**

Patients and methods : **The current study was designed as a randomized, prospective, parallel arm trial including all eligible patients referred for upper endoscopy. Patients were randomized with a 1:1 ratio to undergo either unsedated TOE using a standard endoscope or unsedated TNE using an ultrathin endoscope. Post-procedure, all patients were asked to complete a questionnaire to assess pain, discomfort, distress and tolerability using a 10 cm visual analog scale (VAS). Patients' expectations and future preferences were also determined by multiple choice questions. Endoscope insertion rate, procedure duration, and side-effects were recorded for each patient.**

Results : **Each group included 200 patients. With the exception of nasal pain, mean VAS scores were significantly lower in TNE patients when compared to TOE patients (p = 0.0001). 85% and 54.5% of patients in TNE and TOE groups, respectively, found the procedure better than expected (p = 0001). A repeat procedure was significantly more acceptable for TNE than TOE (82.4% and 60.5%, respectively). Endoscope insertion failed in 3.5% of TNE patients. Mild epistaxis was observed in 4% of TNE patients.**

Conclusion : **Unsedated TNE was tolerated better in endoscopy naïve patients than unsedated TOE in a large parallel arm trial.** (Acta gastroenterol. belg., **2014**, 77, **224-228**).

Key words : transnasal endoscopy, ultrathin endoscope, unsedated oral endoscopy, tolerability.

Introduction

Sedated conventional transoral endoscopy (TOE) increases the risk of adverse cardio-respiratory events, requires careful patient monitoring and increased nursing time which can increase the cost of the procedure (1-3). Therefore, routine diagnostic upper endoscopy is currently being done in the absence of sedatives, using only topical pharyngeal anesthesia in some high-volume endoscopy centers. However, this approach increases patient discomfort and decreases the tolerability of the procedure (3,4). It might also potentially decrease the quality of examination as a result of retching and general discomfort. Unsedated transnasal upper endoscopy (TNE) with an ultrathin endoscope has been introduced as an alternative to both sedated and unsedated TOE (5-7). Potential advantages and disadvantages of TNE with ultrathin scopes compared to conventional TOE using standard scopes have been addressed in several studies (5-8). However, the numbers of head to head comparative trials are limited, particularly between unsedated TNE and conventional unsedated TOE. In addition, most trials were not powered sufficiently and included a relatively small number of patients. Lastly, no study was conducted exclusively in endoscopy naïve patients which allows for an unbiased evaluation of the procedure.

In the current study, we propose that unsedated TNE could be an important alternative to unsedated TOE. Therefore, our primary objective was to assess the tolerability of unsedated TNE versus unsedated TOE in a high-volume endoscopy center. Secondary objectives were to evaluate the ease of use and safety of the transnasal approach.

Patient and Methods

The study was designed as a randomized, prospective, parallel arm trial conducted in a high-volume endoscopy unit of the Gaziantep University Hospital, where > 20 endoscopies are performed daily. Participating in the study was offered to all eligible outpatient subjects who were scheduled for an upper endoscopic examination. Patients who wished to receive sedation or had received a previous endoscopy procedure were excluded from the trial. Other exclusion criteria included ; history of nasal or sinus surgery, planned or likely interventional endoscopy, the suspicion of active upper gastrointestinal (GI) bleeding, coagulopathy, and the inability to complete the study questionnaire. All patients were informed about both procedures and an informed consent was obtained if they agreed to participate to the trial. The study protocol was approved by the local ethical committee.

All eligible patients were randomly allocated with a 1:1 ratio to undergo either an unsedated TOE or unsedated TNE. TOE was performed using a standard gastroscope (OD : 9.3 or 9.8 mm, Fujinon EG-450 or Olympus GIF-Q 160) and TNE was performed using an ultrathin nasal endoscope (OD : 5.9 mm, Fujinon EG-530N). All

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procedures were carried out by three expert endoscopists who have been well-trained in both TOE and TNE. Patients in the TOE group received lidocaine spray to the pharynx just prior to the procedure. Patients in the TNE group received lidocaine spray to the pharynx and nostril which he or she can breathe better, and then a 14 or 16 F, 90 mm nasal catheter (Fujinon pretreatment delivery catheter) coated with lidocaine gel was placed into the nasal cavity for 3 minutes. The tip of nasal endoscope was also coated with a lubricant to ease insertion. All procedures aimed to reach the second section of the duodenum. If TNE failed, TOE was done using the ultrathin scope and TNE was considered unsuccessful. Biopsies were taken only where clinically indicated. Dyspeptic patients without an ulcer or any significant lesion have not been biopsied routinely for Helicobacter Pylori eradication based on our national guidelines. The working channel of ultrathin endoscopes is 2 mm. If any biopsy sample is needed, it is obtained by using a dedicated 1.8 mm biopsy forceps for ultrathin endoscopes. Blood oxygen saturation (SaO_2) and heart rate (HR) were monitored during all procedures. Heart rate over 100 beats per minute (bpm) was considered tachycardia, and a drop in SaO_2 below 90% was considered hypoxemia during the procedure. Supplemental oxygen was given by nasal cannula if hypoxemia lasted more than 30 seconds. The duration of procedure and the occurrence of any side-effects were recorded post-procedure in all patients. After the examination, all patients were asked to complete a questionnaire using a 10 cm (10 point) visual analog scale (VAS) (Table 1). The questionnaire included two multiple choice questions concerning patients' expectations and future preferences (Table 1). A senior nurse explained the questionnaire in detail prior to patients' completion.

The estimated sample size was calculated to detect a 1 point difference between mean VAS scores between groups. To detect this difference with 90% power at a 5% significance level, 190 patients were required in each study arm. This sample size also provided enough power to detect the differences in other data between groups. All data was expressed as mean ± standard deviation (SD). Comparisons between groups were done using independent Student *t* test. Categorical variables were tested with chi square test and Fisher's exact test. A two-tailed p value less than 0.05 was considered significant. SPSS 15.0 package program (2006 SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

During the 15 month study period ; nearly 6,000 upper endoscopies were done in the unit and 1,450 of them were eligible for the study. All eligible patients were offered to participate ; 400 accepted the terms of enrollment. Demographic characteristics were similar between groups (Table 2). Endoscopy was successful in all TOE patients. There were 7 unsuccessful attempts in the TNE group and procedures were completed via the oral route in these patients. The reasons for TNE insertion failure were ; narrow nasal passages (3 patients), severe nasal pain (2 patients), and epistaxis (2 patients). The duration of the procedure was shorter (almost 1 minute) in TOE patients than in TNE patients ($p = 0.001$, Table 2).

The anxiety prior to the procedure was moderate and not significantly different between groups ($p = 0.49$, Table 3). Generally, all first-time upper endoscopy patients have a bad impression about the procedure based on reports from other people which could account for their heightened anxiety levels. In general, women had greater anxiety than men (6.7 ± 3.2 vs. 4.9 ± 2.5, respectively, $p < 0.0001$). The female/male ratio was not different between groups (Table 2) and this finding did not affect study results.

Table 1. — **The queries included in the questionnaire form**

Queries	Evaluation
Please describe your apprehension, anxiety and concern before the procedure	VAS: 0-10
Please describe the pain you felt inside your nose during the procedure	VAS: 0-10
Please describe the pain you felt in your throat during the procedure	VAS: 0-10
Please describe the feeling of retching and breathlessness during the procedure	VAS: 0-10
Please describe the discomfort and pain in your abdomen during the procedure	VAS: 0-10
Please describe how tolerable is this procedure	VAS: 0-10
Please describe the overall distress and difficulty of the procedure	VAS: 0-10
If you think about the distress and difficulty of the procedure, it was ;	a. better than expected b. as I expected c. worse than expected
If it is required to repeat this procedure in future ;	a. accept b. hesitant c. do not want to accept

(VAS : 0 = none, 10 = unbearable).

Table 2. — **Demographic and clinical data of the patients**

Characteristics	TOE	TNE	p
Patients (n)	200	200	
Age (mean ± SD, years)	45.8 ± 12.8	47.2 ± 10.9	0.24[a]
Gender (male/female)	94/106	89/111	0.69[b]
Indication for upper endoscopy			
Dyspeptic symptoms	97	86	0.31[b]
Epigastric pain	35	41	0.52[b]
Pyrosis, regurgitation	38	32	0.51[b]
Anemia	13	17	0.57[b]
Screening	8	11	0.63[b]
Others	9	13	0.51[b]
Successful completion	200 (100%)	193 (96.5%)	0.01[c]
Duration of endoscopy (mean ± SD, minute)	6.4 ± 3.9	7.5 ± 2.7	0.001[a]
Biopsy during endoscopy (n)	37	29	0.34[b]
Complication s (n)	8	10	0.8[b]
Epistaxis	0	8	0.003[c]
Tachycardia	5	2	0.21[c]
Hypoxemia	3	0	0.24[c]

[a] : Unpaired student *t* test, [b] : Chi-Square test with Yates corrected, [c] : Fisher exact test.

Table 3. — **VAS results (mean ± SD) obtained from questionnaire in both groups**

Queries	TOE	TNE	p
Apprehension, anxiety and concern before the procedure	5.7 ± 2.7	5.9 ± 3.1	0.49[a]
Pain inside the nose	1.2 ± 0.7	3.4 ± 1.9	*0.0001*[a]
Pain in the throat	4.3 ± 2.5	1.7 ± 0.8	*0.0001*[a]
Retching and breathlessness feeling	5.4 ± 3.1	2.1 ± 1.4	*0.0001*[a]
Abdominal discomfort and pain	3.9 ± 1.7	2.3 ± 1.2	*0.0001*[a]
Tolerability	4.8 ± 2.4	2.6 ± 2.1	*0.0001*[a]
Overall distress and difficulty	4.4 ± 2.9	3.1 ± 1.8	*0.0001*[a]

[a]: Unpaired student *t* test.

Mean VAS scores for throat pain, retching, breathlessness, abdominal discomfort/pain, tolerability, and the overall distress and difficulty of the procedure were significantly lower in TNE patients when compared to TOE patients (p = 0.0001, Table 3). However, not surprisingly, mean VAS scores for nasal pain were greater in TNE patients when compared to TOE patients (p = 0.0001, Table 3). Patients' impression of the procedure based on prior expectations, and their tolerance for a possible repeat procedure in future was evaluated with 2 multiple choice questions. The majority of TNE patients (85%) found the procedure better than expected (Table 4), while only 54.5% of TOE patients found the procedure better than expected (p = 0.0001). The procedure was worse than expected in 7.2% and 27.5% of patients in TNE and TOE patients, respectively (p = 0.0001). A repeat procedure, if needed, was significantly more acceptable for TNE patients when compared to TOE patients (82.4% and 60.5%, respectively, p = 0.0001). In addition, significantly more patients who received unsedated TOE did not want a repeat procedure if it was required compared to patients who received unsedated TNE (31% and 11.4%, respectively, p = 0.0001).

Both methods were safe and no significant complications were observed over the course of the study. The most significant adverse side-effect in the TNE group was mild epistaxis (Table 1). It was observed in 8 patients, but no intervention was required. In 2 TNE patients, the procedure was unsuccessful due to blurred vision as a result of epistaxis during endoscope insertion. Tachycardia and hypoxemia was more frequent in TOE patients, but no significant cardiorespiratory event was detected. Operators reported that 5 patients with epistaxis had a more hyperemic and fragile nasal mucosa, and a second questioning of these patients revealed that they had a history of recent rhinitis.

Patients who had an unsuccessful transnasal insertion were also given a questionnaire (n = 7). Their responses were analyzed separately and not included in either group. The results were similar to TOE patients, but 2 patients complained from a moderate nasal pain.

Discussion

The advantage of unsedated TNE over both sedated and unsedated conventional TOE has been shown

Table 4. — **Patients' expectations and preferences for future**

Evaluation	TOE n, (%)	TNE n, (%)	p
The procedure was better than I expected	109 (54.5%)	164 (85%)	*0.0001*[a]
The procedure was as I expected	36 (18%)	15 (7.8%)	*0.004*[a]
The procedure was worse than I expected	55 (27.5%)	14 (7.2%)	*0.0001*[a]
If it is required to repeat the procedure, I accept	121 (60.5%)	159 (82.4%)	*0.0001*[a]
If it is required to repeat the procedure, I'm hesitant	17 (8.5%)	12 (6.2%)	0.5[a]
If it is required to repeat the procedure, I do not want to accept	62 (31%)	22 (11.4%)	*0.0001*[a]

[a]: Chi-Square test with Yates corrected.

previously in preliminary studies (5-8). However, many endoscopists, particularly in Western countries, are not aware of the potential benefits of utilizing the transnasal route and lack experience in this approach (9). A survey among 624 endoscopists from different European countries revealed that only 31% of respondents practice the procedure, and 34% lack any training in the transnasal approach (9). In addition, 74% of endoscopists practicing TNE use this technique in < 20% of all eligible patients. In this survey, the most common response for not adopting TNE into daily practice was uncertainties about its potential advantages and lack of training. This result suggests that more studies are required, especially in Western countries, to convince endoscopists of the utility of TNE.

In the current study, patients were asked to assess the important aspects of an upper endoscopy and results were significantly better for TNE than TOE group which could affect the standard of care in some GI problems while increasing the patients' compliance. One obvious disadvantage of TNE when compared to TOE was increased nasal pain. However, this pain was generally well tolerated and did not affect the overall difficulty of the procedure. The most important concern in nasal endoscopy, for both the endoscopist and patient, is passing the scope through the nasal passageway. This makes nasal pretreatment and application of local anesthesia one of the most critical parts of the procedure. Using a special nasal catheter coated with an anesthetic gel can achieve good local anesthesia through the passageway. The diameter of a 14/16 F catheter is very near the diameter of ultrathin endoscopes ; making it ideal for anesthetic gel application. Many studies addressing the utility of TNE have used only lidocaine spray to the nostril or cotton gauze/swap application rather than using catheters for pretreatment which makes good local anesthesia deep inside the nasal passage unlikely (5,7,10-12). We believe pretreatment using a 14/16 F catheter significantly affected the tolerability of the procedure in the current study.

There were no significant side-effects in this study. The rates of both tachycardia and hypoxemia were more frequent in TOE patients probably due to oral endoscope insertion and more frequent retching and breathlessness. The effects of TNE and TOE on cardiopulmonary functions were compared in a previous study, and a significant increase in heart rate and a significant decrease in oxygen saturation were observed only in TOE patients during endoscopy (13). Another recent study found systolic/diastolic blood pressure and pulse rate to be more stable in patients undergoing unsedated TNE than in patients undergoing sedated or unsedated TOE (14). Nevertheless, a number of studies have found epistaxis to be more frequent in TNE patients (6-8,15,16). The rate of epistaxis in the current study (4%) was comparable to what is published in the literature (17). We observed that epistaxis could be related to a recent history of rhinitis, which has not been reported previously. We suggest that patients with a recent history of rhinitis, TNE should be postponed or TOE should be preferred.

Endoscope insertion failure was 3.5% in the current study and the procedure was completed in these patients via oral route without delay. After oral insertion, the completion rate was 100% for both methods. It is important to acknowledge is that the failure rate may vary according to patient history, experience of endoscopist, scope diameter, nasal pretreatment, and other potential differences in procedural protocol from different institutions. In a large study, consisting of 1100 patients, the failure rate was 6.1% (18). They used both a 5.3 mm and 5.9 mm diameter endoscope and reported that larger endoscope diameter, as well as being female < 35 years, were predictive factors for TNE failure. However, these results have not been confirmed by other studies (15). In the current study, we did not detect an effect of age or sex on TNE failure rate. Importantly, while insertion failure may be thought as a drawback of TNE, it is quite easy to switch to the oral route and this imposes no negative effect on patients. Pharyngeal topical anesthesia during pretreatment makes such a switch easier. Mean examination time was longer in TNE than TOE, but it was only a minute and had no impact on the tolerability of the procedure.

Our study groups included only endoscopy naïve patients. In previous unpublished work, we observed that the first endoscopy usually affects peoples' concerns, apprehension, and anxiety in a positive way for the second procedure and increases the tolerability. The evaluation of patients who received TOE for their initial endoscopic procedure followed by TNE, or vice versa, would also be useful to assess the advantage/disadvantage of the second procedure. However, we believe this should be planned as a separate protocol since mixing naïve and experienced populations in the same group may cause bias.

Previous studies comparing unsedated transoral vs. transnasal endoscopy have included a limited number of patients, usually < 60 patients in each study arm, and were not powered sufficiently (5-8,12,13,16,19-23). Most did not calculate an estimated sample size. One study investigated the feasibility and tolerance of the TNE in 1100 consecutive patients across 3 institutions, but it was a single arm uncontrolled study without any comparable information (18).

In conclusion, the current study showed clearly the superiority of unsedated TNE to unsedated TOE, by reducing throat pain, retching, breathlessness, abdominal pain, and discomfort, and increasing overall tolerability and acceptability, in a large group of naïve endoscopy patients. Nasal pain and epistaxis were disadvantages of TNE, but could be handled easily if the patients were evaluated and pretreated cautiously prior to the procedure. All eligible patients for TNE should be informed about the advantages and disadvantages of this method, and offered as an alternative to standard oral endoscopy. We believe that more endoscopists, especially in Europe, should be aware of this method and hope that well-planned clinical studies will increase their interest and confidence to TNE.

References

1. PAMBIANCO D.J., VARGO J.J., PRUITT R.E., HARDI R., MARTIN J.F. Computer-assisted personalized sedation for upper endoscopy and colonoscopy : a comparative, multicenter randomized study. *Gastrointest. Endosc*., 2011, **73** : 765-772.
2. WANG C.Y., LING L.C., CARDOSA M.S., WONG A.K., WONG N.W. Hypoxia during upper gastrointestinal endoscopy with and without sedation and the effect of pre-oxygenation on oxygen saturation. *Anaesthesia*, 2000, **55** : 654-658.
3. ABRAHAM N.S., FALLONE C.A., MAYRAND S., HUANG J., WIECZOREK P., BARKUN A.N. Sedation versus no sedation in the performance of diagnostic upper gastrointestinal endoscopy : a Canadian randomized controlled cost-outcome study. *Am. J. Gastroenterol*., 2004, **99** : 1692-1699.
4. FAULX A.L., VELA S., DAS A., COOPER G., SIVAK M.V., ISENBERG G. *et al*. The changing landscape of practice patterns regarding unsedated endoscopy and propofol use : a national Web survey. *Gastrointest. Endosc*., 2005, **62** : 9-15.
5. DEAN R., DUA K., MASSEY B., BERGER W., HOGAN W.J., SHAKER R. A comparative study of unsedated transnasal esophagogastroduodenoscopy and conventional EGD. *Gastrointest. Endosc*., 1996, **44** : 422-424.
6. YAGI J., ADACHI K., ARIMA N., TANAKA S., OSE T., AZUMI T. *et al*. A prospective randomized comparative study on the safety and tolerability of transnasal esophagogastroduodenoscopy. *Endoscopy*, 2005, **37** : 1226-1231.
7. STROPPA I., GRASSO E., PAOLUZI O.A., RAZZINI C., TOSTI C., ANDREI F. *et al*. Unsedated transnasal versus transoral sedated upper gastrointestinal endoscopy : a one-series prospective study on safety and patient acceptability. *Dig. Liver Dis*., 2008, **40** : 767-775.
8. FRIELING T., SCHINDLER P., KUHLBUSCH-ZICKLAM R., HEISE J., HULSDONK A., KREYSEL C. Krefeld CONTRA study : conventional peroral Esophago-Gastro-Duodenoscopy (EGD) vs. transnasal EGD – a prospective and randomised study with independent evaluation of conscious sedation, endoscope diameter, and access path. *Z. Gastroenterol*., 2010, **48** : 818-824.
9. DUMONCEAU J.M., DUMORTIER J., DEVIERE J., KAHALEH M., PONCHON T., MAFFEI M. *et al*. Transnasal OGD : practice survey and impact of a live video retransmission. *Dig. Liver Dis*., 2008, **40** : 776-783.
10. CHO S., ARYA N., SWAN K., CIROCCO M., KANDEL G., KORTAN P, *et al*. Unsedated transnasal endoscopy : a Canadian experience in daily practice. *Can. J. Gastroenterol*., 2008, **22** : 243-246.
11. BAMPTON P.A., REID D.P., JOHNSON R.D., FITCH R.J., DENT J. A comparison of transnasal and transoral oesophagogastroduodenoscopy. *J. Gastroenterol. Hepatol*., 1998, **13** : 579-584.
12. ZAMAN A., HAPKE R., SAHAGUN G., KATON R.M. Unsedated peroral endoscopy with a video ultrathin endoscope : patient acceptance, tolerance, and diagnostic accuracy. *Am. J. Gastroenterol*., 1998, **93** : 1260-1263.
13. KAWAI T., MIYAZAKI I., YAGI K., KATAOKA M., KAWAKAMI K., YAMAGISHI T. *et al*. Comparison of the effects on cardiopulmonary function of ultrathin transnasal versus normal diameter transoral esophagogastroduodenoscopy in Japan. *Hepatogastroenterology*, 2007, **54** : 770-774.
14. AI Z.L., LAN C.H., FAN L.L., LAN L., CAO Y., LI P. *et al*. Unsedated transnasal upper gastrointestinal endoscopy has favorable diagnostic effectiveness, cardiopulmonary safety, and patient satisfaction compared with conventional or sedated endoscopy. *Surg. Endosc*., 2012, **26** : 3565-3572.
15. TATSUMI Y., HARADA A., MATSUMOTO T., TANI T., NISHIDA H. Current status and evaluation of transnasal esophagogastroduodenoscopy. *Dig. Endosc*., 2009, **21** : 141-146.
16. MURATA A., AKAHOSHI K., SUMIDA Y., YAMAMOTO H., NAKAMURA K., NAWATA H. Prospective randomized trial of transnasal versus peroral endoscopy using an ultrathin videoendoscope in unsedated patients. *J. Gastroenterol. Hepatol*., 2007, **22** : 482-485.
17. MAFFEI M., DUMONCEAU J.M. Transnasal esogastroduodenoscopy (EGD) : comparison with conventional EGD and new applications. *Swiss Med. Wkly*., 2008, **138** : 658-664.
18. DUMORTIER J., NAPOLEON B., HEDELIUS F., PELLISSIER P.E., LEPRINCE E., PUJOL B. *et al*. Unsedated transnasal EGD in daily practice : results with 1100 consecutive patients. *Gastrointest. Endosc*., 2003, **57** : 198-204.
19. CRAIG A., HANLON J., DENT J., SCHOEMAN M. A comparison of transnasal and transoral endoscopy with small-diameter endoscopes in unsedated patients. *Gastrointest. Endosc*., 1999, **49** : 292-296.
20. DUMORTIER J., PONCHON T., SCOAZEC J.Y., MOULINIER B., ZARKA F., PALIARD P. *et al*. Prospective evaluation of transnasal esophagogastroduodenoscopy : feasibility and study on performance and tolerance. *Gastrointest. Endosc*., 1999, **49** : 285-291.
21. AL KARAWI M.A., YASAWY M.I., SANAI F.M., MOHAMMED AEL S. Comparision between per-oral and ultrathin transnasal endoscopy in unsedated patients. *Saudi J. Gastroenterol*., 2001, **7** : 26-29.
22. PREISS C., CHARTON J.P., SCHUMACHER B., NEUHAUS H. A randomized trial of unsedated transnasal small-caliber esophagogastroduodenoscopy (EGD) versus peroral small-caliber EGD versus conventional EGD. *Endoscopy*, 2003, **35** : 641-646.
23. TREVISANI L., CIFALA V., SARTORI S., GILLI G., MATARESE G., ABBASCIANO V. Unsedated ultrathin upper endoscopy is better than conventional endoscopy in routine outpatient gastroenterology practice : a randomized trial. *World J. Gastroenterol*., 2007, **13** : 906-911.