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BRIEF ARTICLE

Safety of same-day endoscopic ultrasound and endoscopic retrograde cholangiopancreatography under conscious sedation

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Abstract

AIM: To assess the tolerability and safety of same-day tandem procedures, endoscopic ultrasound (EUS) followed by endoscopic retrograde cholangiopancreatography (ERCP) under conscious sedation.

METHODS: A retrospective review was conducted at Loma Linda University Medical Center, a tertiary-care center. All 54 patients who underwent EUS followed by ERCP (group A) from 2004 to 2006 were included in the study. A second group of 56 patients who underwent EUS only (group B), and a third group of 53 patients who underwent ERCP only (group C) during the same time period were selected consecutively as control groups for comparison.

RESULTS: Conscious sedation was used in 96% of patients in group A. Mean dosages of meperidine and midazolam used in group A were significantly higher than in group B or C. Mean recovery time in group A was not statistically longer than in group B or C. There was no significant difference in the incidence of sedation-related and procedural-related complications.

CONCLUSION: Tandem EUS/ERCP procedure can be safely performed under conscious sedation with minimal adverse events. Combined procedures, however, are associated with higher dosages of sedatives, and slightly longer recovery time.

Key words: Conscious sedation; Safety; Same-day; Endoscopic ultrasound; Endoscopic retrograde cholangiopancreatography

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INTRODUCTION

Endoscopic ultrasound (EUS) and/or EUS-guided fine needle aspiration (EUS-guided FNA) is increasingly utilized for the diagnosis of pancreatico-biliary diseases including malignancies and choledocholithiasis. The diagnostic accuracy in reported studies of EUS or EUS-guided FNA in the diagnosis of obstructive jaundice is from 80% to 98%[1,2]. In addition, EUS is associated with lower morbidity compared to endoscopic retrograde cholangiopancreatography (ERCP), with an overall EUS-FNA complication rate of 1%-2%[2-4]. EUS is now being performed

first for evaluation in patients with suspected pancreaticobiliary diseases, especially those with obstructive jaundice[5]. Based on EUS findings, therapeutic ERCP interventions, such as stent placement for biliary drainage or stone extraction can then be performed in a tandem fashion.

The literature is scarce on the safety of same-day tandem EUS and ERCP procedures done under conscious sedation. The tandem procedure approach is believed to reduce procedure time and be cost-effective[6]. Potential risks associated with such a strategy are unknown. There are only 2 reported cases in the medical literature of bile leakage into the peritoneum as a result of performing ERCP immediately after EUS-guided FNA[7]. In 2007, Tarantino *et al*[8] evaluated the safety of performing ERCP immediately after EUS in 25 patients done under general anesthesia using propofol. In 1999, Duchmann *et al*[9] also examined the feasibility of performing EUS and ERCP in 57 patients during the same general anesthesia session. Although widely practiced, the safety of performing tandem procedures under conscious sedation is unclear. At our institution, a tandem approach with EUS and/or EUS-guided FNA is sometimes performed for patients with suspected obstructive jaundice, followed by therapeutic ERCP if indicated.

MATERIALS AND METHODS

From October 2004 to November 2005, 54 patients underwent same-day tandem EUS followed by ERCP procedures for the indication of obstructive, or post-hepatic jaundice. This cohort was designated as group A.

From the above time period, 60 consecutive patients who underwent EUS-only and 60 consecutive patients who underwent ERCP-only for the indication of jaundice were chosen as the EUS and ERCP control groups. Of the 60 EUS-only procedures reviewed, only 56 procedures had complete data for analysis (group B). Of the 60 ERCP-only procedures reviewed, only 53 procedures had complete data for analysis (group C).

This retrospective review included: demographics, indications, completion rate of procedures, sedation medication dosages, procedure and recovery times, and adverse events. Vital signs recorded during each procedure and during post-procedure recovery were reviewed. Adverse events included hypotension (defined as systolic blood pressure < 90 mmHg requiring intravenous fluids), bradycardia (heart rate < 60 bpm, or in patients with a baseline heart rate under 60 bpm, heart rate < 45 bpm), and oxygen desaturation (pulse oximetry reading < 90%). The use of reversal agents such as flumazenil and/or naloxone due to oversedation was examined. Post-ERCP pancreatitis was defined as amylase and lipase over five times normal values with abdominal pain and/or leukocytosis persisting 24 h after ERCP. Some of the patients in this study were inpatients, whereas the majority were outpatients. For those who underwent outpatient procedures, it was not standard practice to bring them back for scheduled follow-up laboratory tests.

Statistical analysis

Statistical analysis was performed using StatView version 5.0 for Windows. Numeric variables were expressed as mean ± SD. Differences between groups were analyzed using student's *t*-test for continuous variables. Fisher's exact test was performed for categorical variables but was not done if there was zero in a cell. All differences were considered statistically significant at the *P*-value of < 0.05.

Informed consent was waived for this retrospective study and the research committee at Loma Linda University Medical Center approved the study.

RESULTS

A total of 163 patients were included in this study: tandem EUS/ERCP (group A: $n = 54$), EUS-only (group B: $n = 56$), and ERCP-only (group C: $n = 53$). Mean age, gender, indication, and procedure completion rate are shown in Table 1. There were significantly less males in group A compared to group B, but not significantly different compared to group C. All procedures were performed for the indication of obstructive jaundice. When cholangitis was presumed to be the cause of jaundice, ERCP only, as it should be, was performed. Patients with jaundice and abnormal pancreatico-biliary imaging underwent EUS as part of the work-up.

All patients who underwent EUS in group A and in group B completed the procedures. There was no significant difference in the number of patients who had EUS-FNA in groups A *vs* B (57% *vs* 68%, $P = 0.32$). In group A, ERCP was not completed in five patients compared to seven patients in control group C. Two patients (one each from group A and C) had difficult anatomy and the ampulla was not reached. Eight patients (four from both group A and C) had failed deep cannulation of the desired duct. Two patients from group C had cardiac dysrhythmias (atrial fibrillation and ventricular tachycardia) necessitating early abortion of the procedures.

The amount and type of sedation used is displayed in Table 2. Conscious sedation was used in 96% of group A patients, 100% of group B and 98% of group C patients. General anesthesia and/or propofol were used in three patients, two patients in group A and one patient in group C. The mean total dose of meperidine used in group A was significantly higher than in group B (151.1 ± 64.0 mg *vs* 104.0 ± 43.6 mg, $P < 0.0001$) or in group C (151.1 ± 64.0 mg *vs* 104.5 ± 32.5 mg, $P < 0.0001$). The mean total dose of midazolam used in group A was significantly higher than in group B (8.5 ± 3.2 mg *vs* 6.3 ± 2.4 mg, $P = 0.0001$), or in group C (8.5 ± 3.2 mg *vs* 6.9 ± 3.4 mg, $P = 0.01$).

Procedure and recovery time data are shown in Table 3. The total procedure time for group A was 93.5 ± 36.1 min (range: 30-185 min), 59.0 ± 35.0 min (range: 10-129 min) for group B, and 40.1 ± 20.4 min (range: 20-170 min) for group C. The mean procedure time for EUS in group A, when compared as a separate procedure to the EUS procedure time in group B was not statistically significant (48.0 ± 28.0 min *vs* 59.0 ± 35.0 min, $P = 0.07$). Similarly, the mean procedure time for ERCP in group A, when compared as a

Table 1 Patient demographics, indications, and procedure completion rates *n* (%)

	Tandem (group A) (*n* = 54)	EUS only (group B) (*n* = 56)	*P*-value[1]	ERCP only (group C) (*n* = 53)	*P*-value[2]
Demographics					
Age (yr) (mean ± SD) (Range)	65.2 ± 15.6 (18-93)	63.4 ± 15.7 (19-85)	0.54	54.7 ± 21.3 (14-96)	0.004
Sex, male (%)	43%	66%	0.02	59%	0.12
Indications					
Pancreatic mass	10 (19)	16 (29)	0.26	3 (6)	0.07
Cholangiocarcinoma	3 (6)	1 (2)	0.36	0 (0)	0.24
CBD stones	3 (6)	2 (4)	0.68	6 (11)	0.32
CBD stricture	1 (2)	10 (18)	0.01	1 (2)	1.00
Cholangitis	0	0	NA	8 (15)	NA
Abnormal imaging	10 (19)	10 (18)	1.00	2 (4)	0.03
Pancreatitis	4 (7)	4 (7)	1.00	1 (2)	0.36
Completion					
Completion of procedures	EUS 54 (100) ERCP 49 (91)	56 (100)	1.00	46 (87)	0.56

[1]*P*-value of group A *vs* group B; [2]*P*-value of group A *vs* group C. EUS: Endoscopic ultrasound; ERCP: Endoscopic retrograde cholangiopancreatography; CBD: Common bile duct; NA: Not available.

Table 2 Sedation medication used and dosages *n* (%)

	Tandem (group A) (*n* = 54)	EUS only (group B) (*n* = 56)	*P*-value[1]	ERCP only (group C) (*n* = 53)	*P*-value[2]
Sedation type					
Conscious sedation	52 (96)	56 (100)	0.24	52 (98)	0.22
GA/propofol	2 (4)	0	0.24	1 (2)	0.22
Medications used for sedation					
Meperidine	49 (91)	56 (100)	0.03	44 (83)	0.27
Midazolam	54 (96)	56 (100)	0.24	53 (98)	1.00
Diphenhydramine	16 (30)	4 (7)	0.003	28 (53)	0.02
Promethazine	5 (9)	4 (7)	0.74	0	0.06
Fentanyl	7 (13)	0	0.01	8 (15)	0.12
Total dosage of sedatives used (mean ± SD) (range)					
Meperidine (mg)	151.1 ± 64 (25-325)	104 ± 43.6 (25-250)	< 0.0001	104.5 ± 32.5 (25-175)	< 0.0001
Midazolam (mg)	8.5 ± 3.2 (0-16)	6.3 ± 2.4 (2-13)	0.0001	6.9 ± 3.4 (0-16)	0.01
Diphenhydramine (mg)	50 ± 15.8 (25-100)	50 ± 0 (50)	1.00	51.8 ± 9.45 (50-100)	0.64
Promethazine (mg)	25 ± 0 (25)	25 ± 0 (25)	1.00	0	NA
Fentanyl (mcg)	100.0 ± 55.9 (25-175)	0	NA	146.9 ± 54.2 (75-200)	0.12

[1]*P*-value of group A *vs* group B; [2]*P*-value of group A *vs* group C. GA: General anesthesia.

separate procedure to the ERCP procedure time in group C was not significantly different (45.1 ± 20.7 min *vs* 40.1 ± 20.4 min, $P = 0.20$). The mean recovery time in group A was slightly longer than in group B (105.1 ± 74.8 min *vs* 84.0 ± 51.7 min, $P = 0.06$) or in group C (105.1 ± 74.8 min *vs* 84.5 ± 42.6 min, $P = 0.07$).

The complications among the three study groups are reported in Table 4. There was no significant difference in the number of patients who had hypotension, bradycardia, or desaturation among the groups. Reversal agents (flumazenil and/or naloxone) were used in 2% of patients in group A *vs* 0% in group B ($P = 1.00$) *vs* 6% in group C ($P = 0.36$). The number of patients with post-ERCP pancreatitis when comparing group A and group C was similar. One patient in group A was hospitalized due to rectal bleeding that was unrelated to the procedures; a colonoscopy during hospital stay revealed colon cancer. Two patients were hospitalized in group C, one due to oversedation and another due to ventricular tachycardia. The patient admitted for oversedation returned home the following day with no complications. Hypokalemia was the cause of ventricular tachycardia in one patient with metastatic colon cancer who died a month later due to septic pneumonia unrelated to the ERCP procedure.

DISCUSSION

More patients with suspected pancreatico-biliary diseases are now first undergoing EUS with possible EUS-guided FNA. Some of these patients will also undergo ERCP and interventions based on EUS findings. Performing tandem procedures starting with EUS followed by ERCP is logical and is being done at many centers. However, there is little data on its safety when done under conscious sedation. There have been 2 reported cases of bile leak with ERCP following immediately after EUS-guided FNA[7]. Mergener *et al*[10] described a case of massive pneumoperitoneum in a patient who underwent ERCP immediately after EUS-

Table 3 Procedure and recovery times (mean ± SD) (range)

	Tandem (group A) (*n* = 54)	EUS only (group B) (*n* = 56)	*P*-value[1]	ERCP only (group C) (*n* = 53)	*P*-value[2]
EUS time (min)	48 ± 28 (8-110)	59 ± 35 (10-129)	0.07	NA	NA
ERCP time (min)	45.1 ± 20.7 (10-105)	NA	NA	40.1 ± 20.4 (7-90)	0.20
EUS and ERCP time (min)	93.5 ± 36.1 (30-185)	NA	NA	NA	NA
Recovery time (min)	105.1 ± 74.8 (15-350)	84.0 ± 51.7 (9-252)	0.06	84.5 ± 42.6 (20-170)	0.07

[1]*P*-value of group A *vs* group B; [2]*P*-value of group A *vs* group C.

Table 4 Procedure complications *n* (%)

	Tandem (group A) (*n* = 54)	EUS only (group B) (*n* = 56)	*P*-value[1]	ERCP only (group C) (*n* = 53)	*P*-value[2]
Hypotension	4 (7)	7 (13)	0.53	3 (6)	1.00
Bradycardia	12 (22)	14 (25)	0.82	14 (26)	0.66
Desaturation	1 (2)	0	NA	3 (6)	0.36
Use of reversal agent	2 (4)	0	NA	2 (4)	1.00
Post procedure pancreatitis	2 (4)	0	NA	4 (8)	0.68
Hospitalization	1 (2)	0	0.49	2 (4)	0.62

[1]*P*-value of group A *vs* group B; [2]*P*-value of group A *vs* group C.

FNA. Despite this, two other studies have reported the safety of tandem procedures when done under general anesthesia[8,9]. The objective of our study was to assess safety in a retrospective review of tandem cases done under conscious sedation at our center.

Our study reviewed 54 patients with tandem procedures EUS/ERCP along with 56 control patients with EUS only and 53 control patients with ERCP only. Appropriately, patients with presumed cholangitis underwent ERCP only and more patients with obstructive jaundice and abnormal pancreatico-biliary imaging underwent EUS, EUS-FNA as part of the evaluation.

Almost all (96%) of the procedures in the tandem group were done under conscious sedation with meperidine and midazolam. The procedure time for the tandem group was longer than either the EUS or ERCP alone control groups. This is intuitive because two procedures were done at the same setting in the tandem group. Given longer procedures, the amount of meperidine and midazolam was higher in the tandem group as compared to the controls. However, a similar amount of time was needed for EUS and ERCP when the procedures were compared separately to each control group.

In our setting, EUS is performed in the GI Lab at the medical center and ERCP is done at a different location in the radiology suite under fluoroscopy. The total time reported for the tandem group would be even shorter if EUS and ERCP were performed in one place, eliminating patient transfer and transport times.

Given the higher amount of sedation used, the recovery time was slightly longer (although not statistically significant) in the tandem group compared to the two control groups. Despite the longer procedure and recovery time, no significant difference in sedation-related and procedure-related complications were noted in the tandem group compared with the controls. There was no difference in hemodynamic adverse events, use of reversal agents, or rate of hospitalization post procedures. None of the patients with bradycardia required atropine, and none of the patients were intubated due to oxygen desaturation. The post-ERCP pancreatitis rate was 4% in the tandem group, which was statistically similar to the ERCP control group and is within the accepted level. In a large prospective study by Freeman *et al*[11], post-ERCP pancreatitis occurred after 6.7% procedures. No bile leaks were noted with the tandem group.

Nonetheless, there are limitations to our study. Given that the study was a retrospective review, we were unable to assess patient tolerability through direct patient questionnaire. It was not known whether patients were comfortable during the procedures, if they had any recollection of the procedures, or if they would undergo the tandem procedure again. Another limitation was the lack of uniform follow-up of patients to evaluate long-term adverse events due to the tandem procedure. In this study, the few patients who were admitted for observation and those who were already inpatients were all discharged home without complications. It appears that tandem procedures may be safely done under conscious sedation. With the size of groups studied here, no significant complications were noted in the tandem group compared to either study alone. However, it would seem reasonable that a prospective study should be carried out, where a larger number of patients were included and patient tolerance was assessed. Overall, our study is the first of its kind to try to assess issues concerning the safety and feasibility of performing tandem EUS/ERCP procedures under conscious sedation.

In conclusion, a tandem EUS/ERCP procedure can be safely performed under conscious sedation with minimal adverse events. The combined procedure, however, is associated with higher dosages of sedatives and with slightly longer recovery time.

COMMENTS

Background

Same-day endoscopic ultrasound (EUS) followed by endoscopic retrograde cholangiopancreatography (ERCP) is performed at many medical centers for pancreatico-biliary diseases. Little data exists regarding the safety of performing tandem procedures under conscious sedation.

Research frontiers

Efficiency and cost savings are important issues in our current healthcare system, however, this should not be done at the expense of patient safety.

Innovations and breakthroughs

Several studies have examined the safety of combined procedures under propofol or general anesthesia but none, to date, have evaluated the safety of combined procedures under conscious sedation.

Applications

In medical centers where propofol or general anesthesia is not readily available, same-day combined EUS and ERCP under conscious sedation can be performed safely.

Peer review

It is a good manuscript comparing the retrospective data of the procedures (EUS, ERCP and EUS + ERCP) including a good number of patients. This manuscript will be of use for the medical fraternity.

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