

# Risk Management for Gastrointestinal Endoscopy in Elderly Patients: Questionnaire for Patients Undergoing Gastrointestinal Endoscopy

Eiji Umegaki<sup>1,2,\*</sup>, Shinya Abe<sup>2</sup>, Satoshi Tokioka<sup>1</sup>, Nozomi Takeuchi<sup>1</sup>, Toshihisa Takeuchi<sup>1</sup>, Yukiko Yoda<sup>1</sup>, Mitsuyuki Murano<sup>1</sup> and Kazuhide Higuchi<sup>1</sup>

<sup>1</sup>Second Department of Internal Medicine, Osaka Medical College, 2-7 Daigaku-machi, Takatsuki-shi, Osaka 569-8686, Japan

<sup>2</sup>Osaka Medical College Hospital Endoscopy Center, 2-7 Daigaku-machi, Takatsuki-shi, Osaka 569-8686, Japan

Received 9 June, 2009; Accepted 8 August, 2009

**Summary** More elderly patients now undergo gastrointestinal endoscopy following recent advances in endoscopic techniques. In this study, we conducted a high-risk survey of endoscopies in Japan, using a questionnaire administered prior to upper gastrointestinal tract endoscopy (UGITE), and identified anticholinergic agents and glucagon preparations as high-risk premedication. We also evaluated the cardiovascular effects of anticholinergic agents and glucagon through measurements of plasma levels of human atrial natriuretic peptide (hANP) and human brain natriuretic peptide (hBNP). The subjects were 1480 patients who underwent UGITE. Nurses administered a pre-endoscopy questionnaire, questioning subjects regarding heart disease, hypertension, glaucoma, and urinary difficulties as risk factors for anticholinergic agents, and Diabetes mellitus as a risk factor for glucagon preparations. Evaluation of subjects divided into under 65 and over 65 age groups revealed that in subjects aged 65 and over, risk factors for anticholinergic agents were significantly more high than those for glucagon. Analysis of the cardiovascular effects of anticholinergic agents and glucagon, in the elderly patients showed that hANP levels were significantly higher following administration of anticholinergic agents, but the change was not significant for glucagon premedication. Taking a detailed history before UGITE with the aid of a questionnaire at the same time as informed consent is obtained, is extremely useful in terms of risk management and selection of the appropriate premedication.

**Key Words:** risk management, gastrointestinal endoscopy, questionnaire, hANP, hBNP

## Introduction

Gastrointestinal endoscopic investigation and treatment have contributed greatly to improved quality of life for Japanese patients in recent years, through innovations in endoscopic techniques, marked improvement in endoscopes and accessories, and enhancements to the medical insurance

system. Gastrointestinal endoscopy is used in wide variety of situations, from everyday investigation to highly complex diagnostic and therapeutic applications. A certain level of complications appears to be unavoidable; both adverse drug reactions to antispasmodic premedication, including allergic reactions and anaphylactic shock, and intraoperative haemorrhage or perforation [1–4]. Reports from Japan of endoscopic complications appear regularly in the literature; in a survey of the age distribution of deaths due to endoscopic premedication and endoscopy itself, Kaneko *et al.* found a rapid increase in deaths from both causes over the age of 60 years [5].

\*To whom correspondence should be addressed.  
Tel: +81-72-683-1221 Fax: +81-72-684-6532  
E-mail: in2038@poh.osaka-med.ac.jp

Accompanying the aging of the general population in Japan, the proportion of elderly patients undergoing gastrointestinal endoscopy is also increasing, making less invasive and safer investigations desirable from the risk management point of view. Okamura *et al.* reported increased use of antithrombotic therapy in elderly patients, and examples of inadequate history-taking resulting in hemorrhagic complications due to an inadequate washout period for the antithrombotic therapy, or no washout at all [6]. The choice of anticholinergic agents and glucagon, administered as antispasmodic premedication prior to gastrointestinal endoscopy, needs to be carefully considered in the elderly because of the high incidence of conditions such as prostatic hypertrophy, glaucoma and heart disease, for which anticholinergic agents are contraindicated.

With these considerations in mind, we developed a questionnaire for assessing patient background factors prior to gastrointestinal endoscopy, and investigated the proportions of patients with risk factors for anticholinergic agents and glucagon, and how these correlated with age. We also

evaluated the cardiovascular effects of anticholinergic agents and glucagon used as premedication in gastrointestinal endoscopy.

## Subjects and Methods

Patients who underwent upper gastrointestinal tract endoscopy (UGITE) at the Osaka Medical College Hospital Endoscopy Center between June and December 2001 were included in the retrospective study. The World Health Organization (WHO) definition of elderly patients, i.e., those aged 65 years or older, was used for this study.

A doctor or nurse administered the oral pre-endoscopy questionnaire, which is shown in Figure 1. The questions were developed to detect background factors, including underlying conditions and medication, in each subject to help in risk management and reducing endoscopy complications. The <65 (younger) and ≥65 age groups (elderly) were compared for five characteristics or clinical conditions deemed high-risk for complications: 1) first-time endoscopy;

		Date :    /    /	
		Name : _____	
The following questions are designed to facilitate the examination procedure. Please circle the responses that apply to you.			
1. Do you feel well in yourself today? -----	Yes	No	
2. Have you had a gastrointestinal investigation before (including endoscopy)? ----- If Yes, when was the last time? (including at another hospital) -----	Yes	No	
3. If Yes, did you feel unwell in any way during or after the examination? -----	Don't remember	Date: _____	
4. Have you ever had a bad reaction to an anaesthetic used in dental treatment? -----	No	Sweating	No
5. Have you ever had a bad reaction to an injection for reduce gastrointestinal activity? ---	Nausea	Dizziness	No
6. Have you ever had a reaction to a medication or suffered from any allergies? -----	Heart palpitations	Urination problems	No
If Yes, please specify the type of medication: _____	Other		No
7. Which medicine do you take ? -----	Warfarin	Ticlopidine	No
If so, did you stop for the medicine? -----	Low-dose Aspirin	Other [    ]	No
If Yes, how many days ago did you stop it? -----	Yes		_____ days ago
8. Do you have any heart disease? -----	No	Arrhythmia	No
9. Do you take medicine for heart disease? -----	Angina	Myocardial infarction	No
10. Do you have hypertension? -----	Other [    ]		No
11. Do you have Glaucoma? -----	Yes		No
12. Do you have enlarged prostate? -----	Yes		No
13. Do you have Diabetes? -----	Yes		No
14. Do you want to be informed if the result of test is cancer? -----	Yes		No
<For female> Is there a possibility that you may be pregnant? -----	Yes	No	Unknown
<For colonoscopy> When did you last open your defecation? -----			_____ days ago
Have you opened your defecation today? -----	Yes		No
Osaka Medical College Gastrointestinal Endoscopy Center			

Fig. 1. Detail of pre-endoscopy questionnaire developed at Osaka Medical College Gastrointestinal Endoscopy Center.

Table 1. Comparison of contraindications and precautions for use associated with anticholinergic agents and glucagon used as premedications for gastrointestinal endoscopy

	Glucagon	Anticholinergic
Contraindications	Patients with suspected pheochromocytoma	Patients with haemorrhagic colitis
	Patients with a history of hypersensitivity to this drug	Patients with glaucoma Patients with impaired micturition due to prostatic hypertrophy Patients with serious heart disease Patients with paralytic ileus Patients with a history of hypersensitivity to this drug Patients with bacterial diarrhoea (relative contraindication)
Precautions with use	Patients with an insulinoma	Patients with prostatic hypertrophy
	Elderly patients with known heart disease	Patients with congestive heart failure
	Diabetic patients	Patients with cardiac arrhythmias
	Patients with hepatic disease associated with impaired glucose release, such as cirrhosis	Patients with ulcerative colitis
		Patients with hyperthyroidism Patients in high temperature environments

2) lignocaine allergy; 3) antithrombotic therapy (e.g., warfarin, ticlopidine, aspirin); 4) heart disease (arrhythmia, ischemic heart disease), hypertension, glaucoma, prostatic hypertrophy; and 5) Diabetes mellitus.

We injected anticholinergic agents (15 mg of prifinium bromide) or glucagon (1 mg of Glucagon G Novo) muscularly according to Table 1 (Comparison of contraindications and precautions for use associated with anticholinergic agents and glucagon used as premedications for gastrointestinal endoscopy) and then evaluated the cardiovascular effects of anticholinergic agents and glucagon through measurements of plasma levels of human atrial natriuretic peptide (hANP) and human brain natriuretic peptide (hBNP), which are indices of cardiovascular load [7, 8]. hANP and hBNP were measured before and after UGITE using chemiluminescent enzyme immunoassay (CLEIA) in the above period, between June and December 2001. The levels of hANP and hBNP at baseline and after endoscopy were compared in the <65 and ≥65 age groups, and the elderly group (≥65 years) was further stratified according to the presence of cardiovascular disease.

#### Analysis

All data were expressed as mean ± SD. Analyses were conducted using Fisher's exact method (chi-square test) or Student's *t* test, with  $p < 0.05$  considered statistically significant.

## Results

### Baseline patient characteristics

The baseline patient characteristics are shown in Table 2.

Table 2. Baseline patient characteristics

Number of subjects	1480
Age (yrs, mean ± SD)	59.2 ± 14.3
Elderly (over 65 yrs)	40.3% (597)
Gender (M/F)	805/675
First time for endoscopy	26.6% (402)
Lignocaine allergy	2.1% (31)
Antithrombotic therapy	16.6% (245)
Concurrent conditions	
Heart disease (arrhythmias, ischemic heart disease)	28.0% (414)
Hypertension	23.4% (347)
Glaucoma	3.6% (54)
Urinary difficulties	8.6% (128)
Diabetes mellitus	8.1% (119)

The study included 1480 patients, of which over half were aged <65 years.

#### Analysis of risk groups

*Subjects undergoing their first endoscopy.* First-time endoscopy cases accounted for 26.6% of all subjects and the proportion of first endoscopy procedures was significantly lower in the elderly subjects ( $p = 0.0042$ , Table 3).

*Subjects with lignocaine allergy.* Subjects allergic to lignocaine accounted for 2.8% (25/883) of subjects aged <65 years and 1.0% (6/597) of those ≥65 years, making lignocaine allergy significantly less common in elderly subjects ( $p = 0.016$ , Table 3).

Table 3. Analysis of risk factors for endoscopy-related complications or premedication contraindications according to age

	<65 years old (n = 883)	≥65 years old (n = 597)	p value
First time endoscopy	29.9% (264)	23.1% (138)	0.0042
Lignocaine allergy	2.8% (25)	1.0% (6)	0.0160
Antithrombotic therapy	11.1% (98)	24.6% (147)	<0.0001
Heart disease	19.8% (175)	40.0% (239)	<0.0001
Hypertension	15.1% (133)	35.8% (214)	<0.0001
Glaucoma	2.5% (22)	5.4% (32)	0.0046
Prostatic hypertrophy	4.8% (42)	14.4% (86)	<0.0001
Diabetes	5.8% (51)	11.4% (68)	<0.0001

All data were expressed as mean. Analyses were conducted using Fisher's exact method (chi-square test).

*Subjects on antithrombotic therapy.* Subjects on antithrombotic therapy accounted for 11.1% (98/883) of subjects <65 years, and 24.6% (147/597) of those ≥65 years, with significantly more elderly subjects on antithrombotic therapy ( $p<0.0001$ , Table 3).

*Subjects with risk factors for use of anticholinergic agents.* The proportions of subjects with conditions where anticholinergic agents should be avoided (heart disease, hypertension, Glaucoma and/or prostatic hypertrophy) are shown in Table 3. The proportion of subjects ≥65 years in whom anticholinergic agents were contraindicated was therefore 66.2% (395/597), significantly higher than that of 33.0% (291/883) for the <65 age group ( $p<0.0001$ , Table 3).

*Subjects with risk factors for glucagon.* The proportions of diabetic subjects, for whom glucagon is contraindicated, was 5.8% (51/883) of subjects <65 years, and 11.4% (68/597) of those ≥65 years, with diabetes significantly more common in elderly subjects ( $p<0.0001$ , Table 3).

*Subjects with risk factors for anticholinergic agents and/or glucagon.* Almost half the study population had no contraindications for anticholinergic agents or glucagon (Table 4). More patients had contraindications for anticholinergic agents than glucagon, and less than 5% of the study group had contraindications for both anticholinergic agents and glucagon (Table 4).

Stratifying the risk groups according to age shows that patients in the ≥65 years old group were less likely than

Table 4. Incidences of risk factors for anticholinergic agents and glucagon in patients undergoing gastrointestinal endoscopy

	Risk (n = 1480)
No risk	49.9% (738)
Anticholinergic	41.6% (616)
Glucagon	3.8%* (56)
Anticholinergic & Glucagon	4.7%** (70)

All data were expressed as mean. Analyses were conducted using Fisher's exact method (chi-square test).

\*Anticholinergic Group vs Glucagon group ( $p<0.001$ )

\*\*Anticholinergic Group vs Anticholinergic & Glucagon group ( $p<0.001$ )

younger patients to have no contraindications (Table 5). This difference is largely driven by a higher proportion of patients with risk factors for anticholinergic agents in the elderly group, as there was no significant difference between the groups in the proportion of patients with risk factors for glucagon.

#### *Cardiovascular effects of endoscopic premedication*

In the younger group, there were no significant changes from baseline in hANP (Fig. 2) or hBNP (Fig. 3) levels measured after endoscopy. However, in the elderly group,

Table 5. Incidences of risk factors for anticholinergic agents and glucagon by age group in patients undergoing gastrointestinal endoscopy

	<65 years old (n = 883)	≥65 years old (n = 597)	p value
No risk	63.3% (559)	30.0% (179)	<0.0001
Anticholinergic	30.5% (269)	58.1% (347)	<0.0001
Glucagon	3.7% (33)	3.9% (23)	>0.9999
Anticholinergic & Glucagon	2.5% (22)	8.0% (48)	<0.0001

All data were expressed as mean. Analyses were conducted using Fisher's exact method (chi-square test).

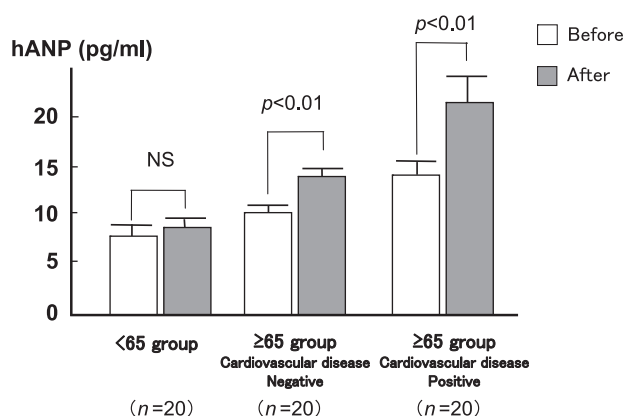


Fig. 2. Baseline and post-endoscopy human atrial natriuretic peptide (hANP) levels in patients aged <65 years and patients ≥65 years with and without cardiovascular disease. All data were expressed as mean ± SD. Analyses were conducted using Student's *t* test. In the ≥65 year age group, hANP level post-endoscopy was significantly greater than at baseline ( $p<0.01$ ), regardless of whether cardiovascular disease was present or not.

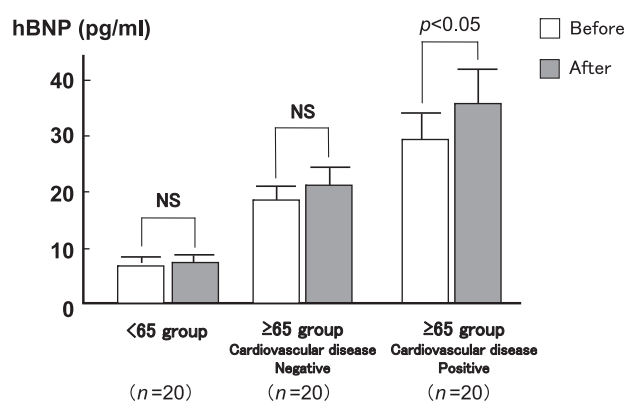


Fig. 3. Baseline and post-endoscopy human brain natriuretic peptide (hBNP) levels in patients aged <65 years and patients ≥65 years with and without cardiovascular disease. All data were expressed as mean ± SD. Analyses were conducted using Student's *t* test. In the ≥65 year age group with cardiovascular disease, hBNP level was significantly greater than at baseline ( $p<0.05$ ).

regardless of whether cardiovascular disease was present or not, hANP level post-endoscopy was significantly greater than at baseline ( $p<0.01$ ), indicating an increased atrial load associated with endoscopy (Fig. 2). In contrast, the increase from baseline in hBNP level, indicating an increased ventricular load, was only statistically significant ( $p<0.05$ ) in elderly patients with cardiovascular disease (Fig. 3).

Analysis of the cardiovascular effects of anticholinergic agents and glucagon, administered as antispasmodic premedication prior to endoscopy, in the elderly patients showed that hANP levels were significantly higher following administration of anticholinergic agents, but the change was not significant for glucagon premedication ( $p<0.05$ ) (Fig. 4). No statistically significant changes from baseline were observed for hBNP levels after either anti-

cholinergic or glucagon premedication in elderly patients (Fig. 5).

## Discussion

The Japanese population is ageing rapidly. The Ministry of Internal Affairs and Communications estimates that in 2008 there will be 27,790,000 Japanese aged over 65 years, 21.8% of the total population [9], and every year the number and proportion of elderly sets a new record. Declining physiological function accompanies the aging process, arteriosclerosis and various degenerative changes. At the same time, the prevalence of other comorbid diseases increases, so special consideration is required to ensure the safety of elderly patients when performing gastrointestinal

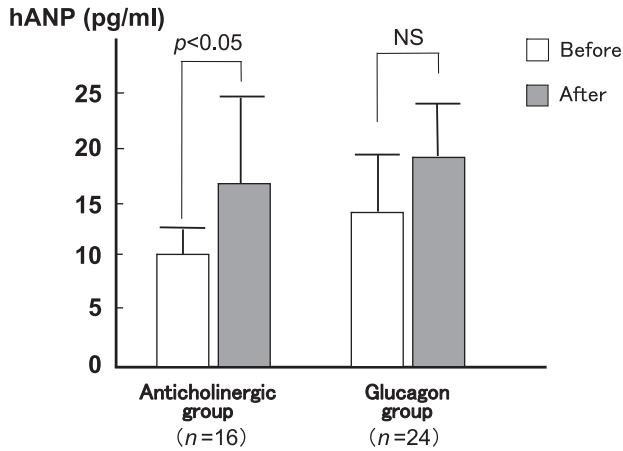


Fig. 4. Baseline and post-endoscopy human atrial natriuretic peptide (hANP) levels in patients aged  $\geq 65$  years following premedication with anticholinergic agents or glucagon. All data were expressed as mean  $\pm$  SD. Analyses were conducted using Student's *t* test. In the elderly patients ( $\geq 65$  year age group) showed that hANP levels were significantly higher following administration of anticholinergic agents ( $p < 0.05$ ).

endoscopy.

We developed this questionnaire from the viewpoint of risk management associated with endoscopy. Questions relating to known risk factors were included to identify five groups considered high-risk during UGITE:

- 1) subjects undergoing their first endoscopy, who are thought to be at increased risk for complications;
- 2) subjects allergic to lignocaine who are more likely to develop anaphylactic shock, allergic reactions, or toxicity [10];
- 3) subjects taking antithrombotic therapy (e.g., warfarin, ticlopidine, aspirin), prone to hemorrhage during investigations or treatment [11];
- 4) subjects with heart disease (arrhythmia, ischemic heart disease), hypertension, glaucoma, or prostatic hypertrophy, for whom anticholinergic agents are contraindicated according to the Japanese Guidelines for Endoscopy in Elderly Patients [12]; and
- 5) subjects with Diabetes mellitus, for whom glucagon is contraindicated.

The patient's cardiorespiratory load is a major risk associated with gastrointestinal endoscopy [13]. In this study, no significant changes in hANP and hBNP, markers of cardiac load, were seen before and after endoscopy in younger subjects. In elderly subjects, however, hANP levels increased significantly following the procedure, regardless of whether cardiovascular disease was present or not, indicating an increased atrial load associated with endoscopy. A significant rise in hBNP level was observed following the procedure in elderly subjects with cardio-

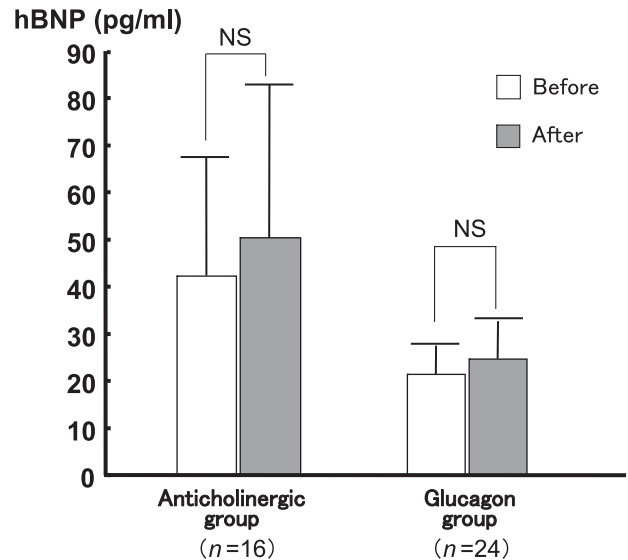


Fig. 5. Baseline and post-endoscopy human brain natriuretic peptide (hBNP) levels in patients aged  $\geq 65$  years following premedication with anticholinergic agents or glucagon. All data were expressed as mean  $\pm$  SD. Analyses were conducted using Student's *t* test. No statistically significant changes from baseline were observed for hBNP levels after either anticholinergic or glucagon premedication in the elderly patients ( $\geq 65$  year age group).

vascular disease, indicating an increased ventricular load in addition to the abovementioned atrial load.

If tissue biopsies are required during an endoscopic procedure, it is important to consider whether the patient is taking anticoagulant medication. In recent years, the use of anti-thrombotic agents has increased markedly, particularly in elderly patients, and the duration of the washout period for these medications prior to an endoscopy has become a major problem [14]. In this study, we were able to prevent gastrointestinal hemorrhage associated with endoscopy by confirming patients' current medications using the pre-procedural questionnaire.

Caution is also required to prevent problems associated with endoscopic premedication. Reported complications include anaphylaxis and allergic reactions caused by lignocaine used for pharyngeal anesthesia [10], sudden hemodynamic changes caused by anticholinergic agents administered to inhibit gastrointestinal motility [15], and secondary hypoglycemia caused by glucagon in diabetic patients [16]. Apart from these complications, a number of conditions have been identified as contraindications, or requiring caution with use, for anticholinergic agents and glucagon (Table 1).

Due to their parasympathetic blocking activity, anticholinergic agents are contraindicated in patients with glaucoma, prostatic hypertrophy, and cardiac conditions

such as arrhythmias. When anticholinergic agents are contraindicated, glucagon is used as an alternative premedication. However, glucagon should be used with caution in diabetic patients due to its hyperglycemic effect [16]. Like anticholinergic agents, glucagon acts directly on the smooth muscle of the gastrointestinal tract to inhibit peristaltic activity [17–19], and should be administered with caution to patients with cardiac disease. Compared with anticholinergic agents, however, the effects of glucagon on hemodynamic parameters such as blood pressure and heart rate are minimal [20]. In this study, we measured hANP and hBNP levels to compare the cardiovascular effects of anticholinergic agents and glucagon, both used as antispasmodic premedication for gastrointestinal endoscopy. We found the rise in hANP levels, indicating increased atrial load, was significant in elderly patients given anticholinergic agents, but not in those given glucagon. Accordingly, the premedication best suited to the individual patient's medical condition should be selected in accordance with the information provided by the questionnaire, and informed consent obtained before performing gastrointestinal endoscopy [21].

Saito *et al.* applied a preprocedural questionnaire similar to ours, defining the contraindications for anticholinergic agents as “hypertension, arrhythmia, ischemic heart disease, glaucoma and prostatic hypertrophy”, with glucagon contraindicated in patients with “diabetes mellitus” [22]. Of 416 subjects who underwent investigations of the gastrointestinal tract (365 endoscopies, 51 barium contrast radiography), anticholinergic agents were contraindicated in 35% of all subjects, and more than half (53%) of elderly subjects aged 65 years and older [22]. In the current large-scale study, we analyzed background factors using a questionnaire in 1480 subjects undergoing UGITE. The proportion of subjects in whom anticholinergic agents were contraindicated was significantly higher in subjects aged 65 years and older than in those under 65 years. In particular, more than half of elderly subjects had contraindications for anticholinergic agents, significantly higher than in subjects aged under 65 years. There was no significant difference between age groups in the proportion of subjects in whom glucagon was contraindicated.

From the point of view of risk management and prevention of complications associated with gastrointestinal endoscopy, our results show that taking a thorough history before the procedure will reveal important patient background factors, including underlying medical conditions and medications, thus facilitating selection of the appropriate premedication for that patient. In particular, in many elderly patients glucagon should be selected as the premedication for safer endoscopies because of its narrower range of complications and precautions for use in this population.

We analyzed risk groups for endoscopy using a question-

naire in 1480 subjects undergoing UGITE. Taking a detailed history before UGITE with the aid of a questionnaire at the same time as informed consent is obtained, is extremely useful in terms of risk management and selection of the appropriate premedication.

## References

- [1] Faigel, D.O., Eisen, G.M., Baron, T.H., Dominitz, J.A., Goldstein, J.L., Hirota, W.K., Jacobson, B.C., Johanson, J.F., Leighton, J.A., Mallery, J.S., Raddawi, H.M., Vargo, J.J. 2nd., Fanelli, R.D., and Wheeler-Harbough, J.: Preparation of patients for GI endoscopy. *Gastrointest. Endosc.*, **57**, 446–450, 2003.
- [2] Quine, M.A., Bell, G.D., McCloy, R.F., Charlton, J.E., Devlin, H.B., and Hopkins, A.: Prospective audit of upper gastrointestinal endoscopy in two regions of England: safety, staffing and sedation methods. *Gut*, **36**, 462–467, 1996.
- [3] Palmer, K.R.: Complications of gastrointestinal endoscopy. *Gut*, **56**, 456–457, 2007.
- [4] McLernon, D.J., Donnan, P.T., Crozier, A., Dillon, J., and Mowat, C.: A study of the safety of current gastrointestinal endoscopy (EGD). *Endoscopy*, **39**, 692–700, 2007.
- [5] Kaneko, E., Harada, H., Kasugai, T., Ogoshi, K., and Niwa, H.: The 4th report of national survey for incidence of gastroenterological endoscopy. *Gastroenterol. Endosc.*, **46**, 54–61, 2004 [in Japanese].
- [6] Okamura, T. and Miyano, N.: System for investigating drugs taken by outpatients prior to operations and its evaluation. *Jpn. J. Pharm. Health Care Sci.*, **31**, 892–899, 2005.
- [7] Cowie, M.R., Struthers, A.D., Wood, D.A., Coats, A.J., Thompson, S.G., Poole-Wilson, P.A., and Sutton, G.C.: Value of natriuretic peptides in assessment of patients with possible new heart failure in primary care. *Lancet*, **350**, 1349–1353, 1997.
- [8] Maisel, A.S., Krishnaswamy, P., Nowak, R.M., McCord, J., Hollander, J.E., Duc, P., Omland, T., Storrow, A.B., Abraham, W.T., Wu, A.H., Clopton, P., Steg, P.G., Westheim, A., Knudsen, C.W., Perez, A., Kazanegra, R., Herrmann, H.C., and McCullough, P.A.: Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N. Engl. J. Med.*, **347**, 161–167, 2002.
- [9] Population Estimates by Age (5-Year Group) and Sex. Data from Statistics Bureau, Director-General for Policy Planning (statistical standards) & Statistical Research and Training Institute, Ministry of Internal Affairs and Communications. Available from: <http://www.stat.go.jp/english/data/jinsui/tsuki/index.htm>. Accessed December 1, 2008.
- [10] Amornytin, S., Lertakayamee, N., Wongyingsinn, M., Pimukmanuskit, P., and Chalayonnavin, V.: The effectiveness of intravenous sedation in diagnostic upper gastrointestinal endoscopy. *J. Med. Assoc. Thai.*, **90**, 301–306, 2007.
- [11] Hui, A.J., Wong, R.M., Ching, J.Y., Hung, L.C., Chung, S.C., and Sung, J.J.: Risk of colonoscopic polypectomy bleeding with anticoagulants and antiplatelet agents; analysis of 1657 cases. *Gastrointest. Endosc.*, **59**, 44–48, 2004.

- [12] Brown, J.H.: The Pharmacological Basis of Therapeutics, 8th edn.: Atropine, scopolamine, and related antimuscarinic drugs, eds. By Gilman, A.G., Rall, T.W., Nies, A.S., and Taylor, P., Pergamon Press, New York, pp. 1560–1565, 1990.
- [13] Bough, E.W. and Meyers, S.: Cardiovascular responses to upper gastrointestinal endoscopy. *Am. J. Gastroenterol.*, **69**, 655–661, 1978.
- [14] Ogoshi, K., Kaneko, E., Tada, M., Mine, T., Yoshino, J., Yahagi, N., and Satho, N.: The management of anticoagulation and antiplatelet therapy for endoscopic procedures. *Gastroenterol. Endosc.*, **47**, 2682–2691, 2005, [in Japanese].
- [15] Mathew, P.K., Ona, F.V., Damevski, K., and Wallace, W.A.: Arrhythmias during upper gastrointestinal endoscopy. *Angiology*, **30**, 834–840, 1979.
- [16] Masunaga, T., Siozaki, K., Takayama, Y., and Takeda, R.: Clinical safety of glucagon for premedication of upper gastrointestinal endoscopy in patients with diabetes mellitus. *Gastroenterol. Endosc.*, **40**, 150–158, 1998, (in Japanese).
- [17] Stunkard, A.J., Van Itallie, T.B., and Reis, B.B.: The mechanism of satiety effect of glucagon on gastric hunger contractions in man. *Proc. Soc. Exp. Biol. Med.*, **89**, 258–261, 1955.
- [18] Dotevall, G. and Kock, N.G.: The effect of glucagon on intestinal motility in man. *Gastroenterology*, **45**, 664–667, 1963.
- [19] Miller, R.E., Chernish, S.M., Brunelle, R.L., and Rosenak, B.D.: Dose response to intramuscular glucagon during hypotonic radiography. *Radiology*, **127**, 49–53, 1978.
- [20] Umegaki, E., Abe, S., Tokioka, S., Takeuchi, N., Takeuchi, T., Shiraishi, N., Yoda, Y., and Higuchi, K.: Selection of premedication for gastrointestinal endoscopy from the risk management point of view. *Gastrointest. Endosc.*, **67**, AB66, 2008.
- [21] Standards of Practice Committee, Zuckerman, M.J., Shen, B., Harrison, M.E.3rd., Baron, T.H., Adler, D.G., Davila, R.E., Gan, S.I., Lichtenstein, D.R., Qureshi, W.A., Rajan, E., Fanelli, R.D., and Van Guilder, T.: Informed consent for GI endoscopy. *Gastrointest. Endosc.*, **66**, 213–218, 2007.
- [22] Saito, N., Honma, A., Sasaki, A., Kurokawa, I., Sakai, Y., Sirovani, N., and Kameoka, S.: Analysis of basal disease risk in gastrointestinal diagnosis receiver. *Jpn. J. Med. Pharm. Sci.*, **49**, 449–453, 2003, (in Japanese).