



ANESTHESIA & ANALGESIA®

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Editor-in-Chief

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To our readers:

Toho University today announced the retraction of eight manuscripts by Dr. Yoshitaka Fujii published under its auspices, as well as the dismissal of Dr. Fujii from Toho University. The manuscripts have been retracted for lack of proper ethics approval. Specific manuscripts that have been retracted are:

1. Fujii Y, Itakura M. Antiemetic efficacy of low-dose midazolam in patients undergoing thyroidectomy. *Otolaryngol Head Neck Surg.* 2011;144:206-9
2. Fujii Y, Itakura M. A prospective, randomized, double-blind, placebo-controlled study to assess the antiemetic effects of midazolam on postoperative nausea and vomiting in women undergoing laparoscopic gynecologic surgery. *Clin Ther.* 2010;32:1633-7
3. Fujii Y, Itakura M. Reduction of postoperative nausea, vomiting, and analgesic requirement with dexamethasone for patients undergoing laparoscopic cholecystectomy. *Surg Endosc.* 2010;24:692-6
4. Fujii Y, Itakura M. A comparison of pretreatment with fentanyl and lidocaine preceded by venous occlusion for reducing pain on injection of propofol: a prospective, randomized, double-blind, placebo-controlled study in adult Japanese surgical patients. *Clin Ther.* 2009;31:2107-12
5. Fujii Y, Itakura M. Low-dose propofol to prevent nausea and vomiting after laparoscopic surgery. *Int J Gynaecol Obstet.* 2009;106:50-2
6. Fujii Y, Itakura M. Pretreatment with flurbiprofen axetil, flurbiprofen axetil preceded by venous occlusion, and a mixture of flurbiprofen axetil and propofol in reducing pain on injection of propofol in adult Japanese surgical patients: a prospective, randomized, double-blind, placebo-controlled study. *Clin Ther.* 2009;31:721-7
7. Fujii Y, Itakura M. Comparison of propofol, droperidol, and metoclopramide for prophylaxis of postoperative nausea and vomiting after breast cancer surgery: a prospective, randomized, double-blind, placebo-controlled study in Japanese patients. *Clin Ther.* 2008;30:2024-9

8. Fujii Y, Itakura M. Comparison of lidocaine, metoclopramide, and flurbiprofen axetil for reducing pain on injection of propofol in Japanese adult surgical patients: a prospective, randomized, double-blind, parallel-group, placebo-controlled study. *Clin Ther.* 2008;30:280-6.

The announcement also identified a single manuscript for which there was evidence of appropriate IRB approval:

Fujii Y, Itakura M. Efficacy of the lidocaine/flurbiprofen axetil combination for reducing pain during the injection of propofol. *Minerva Anesthesiol.* 2011;77:693-7

The announcement by Toho University did not address 13 additional manuscripts by Dr. Fujii that list Toho University as the academic institution of record:

1. Fujii Y. Management of postoperative nausea and vomiting in women scheduled for breast cancer surgery. *J Anesth.* 2011;25:917-22
2. Fujii Y. Current review of ramosetron in the prevention of postoperative nausea and vomiting. *Curr Drug Saf.* 2011;6:122-7
3. Fujii Y. Management of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. *Surg Endosc.* 2011;25:691-5
4. Fujii Y. Prevention of nausea and vomiting during termination of pregnancy. *Int J Gynaecol Obstet.* 2010;111:3-7
5. Fujii Y. Clinical management of postoperative vomiting after strabismus surgery in children. *Curr Drug Saf.* 2010;5:132-48
6. Fujii Y. [Postoperative nausea and vomiting and their sex differences]. *Masui.* 2009;58:59-66
7. Fujii Y. Current management of vomiting after tonsillectomy in children. *Curr Drug Saf.* 2009;4:62-7
8. Fujii Y. Clinical strategies for preventing postoperative nausea and vomiting after middle ear surgery in adult patients. *Curr Drug Saf.* 2008;3:230-9
9. Fujii Y. The benefits and risks of different therapies in preventing postoperative nausea and vomiting in patients undergoing thyroid surgery. *Curr Drug Saf.* 2008;3:27-34
10. Fujii Y. Prevention of emetic episodes during cesarean delivery performed under regional anesthesia in parturients. *Curr Drug Saf.* 2007;2:25-32
11. Fujii Y, Nakayama M. Prevention of pain due to injection of propofol with IV administration of lidocaine 40 mg + metoclopramide 2.5, 5, or 10 mg or saline: a

randomized, double-blind study in Japanese adult surgical patients. *Clin Ther.* 2007;29:856-61

12. Fujii Y. Prophylaxis of postoperative nausea and vomiting in patients scheduled for breast surgery. *Clin Drug Investig.* 2006;26:427-37
13. Fujii Y, Nakayama M. Influence of age on flurbiprofen axetil requirements for preventing pain on injection of propofol in Japanese adult surgical patients: a prospective, randomized, double-blind, vehicle-controlled, parallel-group, dose-ranging study. *Clin Ther.* 2006;28:1116-22

These manuscripts were retracted because of lack of IRB approval. The announcement by Toho University did not address the possibility of fraud. However, the April 2000 issue of *Anesthesia & Analgesia* includes a disturbing Letter to the Editor by Kranke, Apfel, and Roewer alleging research fraud by Dr. Fujii¹ The title of the letter says everything you need to know: “Reported data on granisetron and postoperative nausea and vomiting by Fujii et al. are incredibly nice!” In 2001 Kranke and colleagues published a manuscript demonstrating consistent discrepancies between data published by Fujii supporting the efficacy of granisetron and data published by other investigators.²

The announcement by Toho University follows a joint effort over the past two years by multiple Editors-in-Chief to follow up on the Letter to the Editor in *Anesthesia & Analgesia* and lingering concerns about the integrity of Dr. Fujii’s published research. There will be further disclosure over the next few days by the involved editors. I want to explicitly thank Dr. Steve Yentis, Editor-in-Chief of *Anaesthesia*, who raised the question two years ago about the integrity of Dr. Fujii’s published studies and our responsibility to pursue allegations of misconduct more than 10 years old. I also want to thank Dr. Donald Miller, Editor-in-Chief of the *Canadian Journal of Anesthesia*, who is responsible for the inquiry conducted by Toho University that led to the public acknowledgment that Dr. Fujii’s work was compromised and his dismissal from Toho University.

These findings raise considerable concern about the integrity of the papers published by Dr. Fujii in *Anesthesia & Analgesia*. The following manuscripts in *Anesthesia & Analgesia* may represent fraudulent research:

1. Fujii Y, Uemura A. The effects of different dobutamine infusion rates on hypercapnic depression of diaphragmatic contractility in pentobarbital-anesthetized dogs. *Anesth Analg.* 2007;105:1379-84 (University of Tsukuba)
2. Fujii Y, Uemura A, Toyooka H. The recovery profile of reduced diaphragmatic contractility induced by propofol in dogs. *Anesth Analg.* 2004;99:113-6 (University of Tsukuba)
3. Fujii Y, Uemura A, Toyooka H. Midazolam-induced muscle dysfunction and its recovery in fatigued diaphragm in dogs. *Anesth Analg.* 2003;97:755-8 (University of Tsukuba)

4. Uemura A, Fujii Y, Toyooka H, Suzuki S, Sawada K, Adachi H. Olprinone for the treatment, but not prevention, of fatigue-induced changes in guinea-pig diaphragmatic contractility. *Anesth Analg.* 2003;96:1679-782 (University of Tsukuba)
5. Fujii Y, Uemura A, Toyooka H. The effect of inhaled colforsin daropate on contractility of fatigued diaphragm in dogs. *Anesth Analg.* 2003;96:1032-4 (University of Tsukuba)
6. Fujii Y, Uemura A, Toyooka H. Flumazenil recovers diaphragm muscle dysfunction caused by midazolam in dogs. *Anesth Analg.* 2002;95(4):944-7 (University of Tsukuba)
7. Fujii Y, Uemura A, Toyooka H. The dose-related efficacy of diltiazem for enhancing diaphragmatic fatigability in dogs. *Anesth Analg.* 2002;95:129-32 (University of Tsukuba)
8. Fujii Y, Uemura A, Toyooka H. The dose-range effects of propofol on the contractility of fatigued diaphragm in dogs. *Anesth Analg.* 2001;93:1194-8 (University of Tsukuba)
9. Fujii Y, Hoshi T, Uemura A, Toyooka H. Dose-response characteristics of midazolam for reducing diaphragmatic contractility. *Anesth Analg.* 2001;92:1590-3 (University of Tsukuba)
10. Fujii Y, Hoshi T, Toyooka H. Colforsin daropate improves contractility in fatigued canine diaphragm. *Anesth Analg.* 2001;92:762-6 (University of Tsukuba)
11. Fujii Y, Hoshi T, Takahashi S, Toyooka H. The effect of sedative drugs on diaphragmatic contractility in dogs: propofol versus midazolam. *Anesth Analg.* 2000;91:1035-7 (University of Tsukuba)
12. Fujii Y, Saitoh Y, Tanaka H, Toyooka H. Ramosetron for preventing postoperative nausea and vomiting in women undergoing gynecological surgery. *Anesth Analg.* 2000;90:472-5 (University of Tsukuba)
13. Saitoh Y, Fujii Y, Oshima T. The ulinastatin-induced effect on neuromuscular block caused by vecuronium. *Anesth Analg.* 1999;89:1565-9 (Toride Kyodo General Hospital)
14. Fujii Y, Hoshi T, Takahashi S, Toyooka H. Propofol decreases diaphragmatic contractility in dogs. *Anesth Analg.* 1999;89:1557-60 (University of Tsukuba)
15. Fujii Y, Takahashi S, Toyooka H. The effect of olprinone compared with milrinone on diaphragmatic muscle function in dogs. *Anesth Analg.* 1999;89:781-5 (University of Tsukuba)

16. Fujii Y, Saitoh Y, Tanaka H, Toyooka H. Comparison of ramosetron and granisetron for preventing postoperative nausea and vomiting after gynecologic surgery. *Anesth Analg.* 1999;89:476-9 (University of Tsukuba)
17. Fujii Y, Saitoh Y, Tanaka H, Toyooka H. Granisetron/dexamethasone combination for reducing nausea and vomiting during and after spinal anesthesia for cesarean section. *Anesth Analg.* 1999;88:1346-50 (University of Tsukuba)
18. Fujii Y, Saitoh Y, Tanaka H, Hidenori T. Preoperative oral antiemetics for reducing postoperative vomiting after tonsillectomy in children: granisetron versus perphenazine. *Anesth Analg.* 1999;88:1298-301 (University of Tsukuba)
19. Fujii Y, Saitoh Y, Tanaka H, Toyooka H. Prophylactic oral antiemetics for preventing postoperative nausea and vomiting: granisetron versus domperidone. *Anesth Analg.* 1998;87:1404-7 (University of Tsukuba)
20. Fujii Y, Takahashi S, Toyooka H. The effects of milrinone and its mechanism in the fatigued diaphragm in dogs. *Anesth Analg.* 1998;87:1077-82 (University of Tsukuba)
21. Fujii Y, Toyooka H, Tanaka H. A granisetron-droperidol combination prevents postoperative vomiting in children. *Anesth Analg.* 1998;87:761-5 (University of Tsukuba)
22. Fujii Y, Toyooka H, Tanaka H. Prevention of postoperative nausea and vomiting with a combination of granisetron and droperidol. *Anesth Analg.* 1998;86:613-6 (University of Tsukuba)
23. Fujii Y, Tanaka H, Toyooka H. The effects of dexamethasone on antiemetics in female patients undergoing gynecologic surgery. *Anesth Analg.* 1997;85:913-7 (Toride Kyodo General Hospital)
24. Fujii Y, Tanaka H, Tsuruoka S, Toyooka H, Amaha K. Middle cerebral arterial blood flow velocity increases during laparoscopic cholecystectomy. *Anesth Analg.* 1994;78:80-3 (Toride Kyodo General Hospital)

These manuscripts are from two institutions: the University of Tsukuba (21 papers) and Toride Kyodo General Hospital (3 papers). I will contact each institution requesting an inquiry into the integrity of these manuscripts. Although these manuscripts date back to 1994, we must make a determination what papers are valid, and what papers represent research fraud.

Following publication of the Letter to the Editor from Kranke and colleagues in April 2000, along with a non-specific response from Dr. Fujii, there was no follow-up on the allegation of data manipulation. There was no request for an institutional review of Dr. Fujii's research. Additionally, *Anesthesia & Analgesia* published 11 additional manuscripts by Dr. Fujii following the 2000 allegations of research fraud.

The Journal's response to the allegations of research fraud in the 2000 Letter to the Editor by Kranke and colleagues was inadequate. The subsequent submissions to the Journal by Dr. Fujii should not have been published without first vetting the allegations of fraud. I apologize to our readers, and the patients we serve, for the manner in which the allegations of fraud were handled by *Anesthesia & Analgesia*.

Sincerely,

A handwritten signature in black ink, appearing to read 'Steven L. Shafer'.

Steven L. Shafer, MD
Editor-in-Chief
Anesthesia & Analgesia

References:

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1. Kranke P, Apfel CC, Roewer N, Fujii Y. Reported data on granisetron and postoperative nausea and vomiting by Fujii et al. Are incredibly nice! *Anesth Analg*. 2000;90:1004-7
 2. Kranke P, Apfel CC, Eberhart LH, Georgieff M, Roewer N. The influence of a dominating centre on a quantitative systematic review of granisetron for preventing postoperative nausea and vomiting. *Acta Anaesthesiol Scand*. 2001;45:659-70