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Postoperative Acetaminophen and Warfarin. Undesirable Combination

To The Editor:—Warfarin anticoagulant used commonly; hence, the physician dealing with patients with chronic pain can expect to encounter patients taking these drugs and almost certainly will be involved in prescribing analgesic medications for such patients. Pain practitioners, therefore, should be particularly aware of the recent article published by Hylek *et al.*¹ and the accompanying editorial by Bell.² These articles showed that acetaminophen interacts with warfarin in an unknown fashion to substantially augment the degree of anticoagulation. This phenomena occurs gradually with long-term therapy. In this article, it has been shown that acetaminophen dosage from 2,275 mg to 4,549 mg per week (1 to 2 tablets of Vicodin [USP] or Lortab [UCB Pharma, Inc., Smyrna, GA] per day for 1 week) can increase the odds of having an international normalization ratio more than 6 from 3.5- to 6.5-fold. A further escalation of the dose to 9,100 mg acetaminophen or more per week (3-4 tablets of Vicodin or Lortab per day for 1 week) will increase this risk by 10-fold.

Acetaminophen intake in patients prescribed a stable warfarin dosage might increase the international normalization ratio within 18 to

48 h.² Hylek *et al.*² found that a potentiating effect was detected after 7 days and peaked by 12.5 days after acetaminophen intake.² Physicians should carefully consider prescribing acetaminophen-containing drugs in patients prescribed warfarin. It is especially important that physicians specializing in pain management be aware of this situation.

Mazin Elias, M.D., F.R.C.A.

Assistant Professor
The University Center for Pain Medicine
Houston, Texas

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Severe Anaphylactic Reaction Due to a Chlorhexidine-impregnated Central Venous Catheter

To the Editor:—We read with interest a case report by Oda *et al.*,¹ which appeared in a recent issue of ANESTHESIOLOGY. We also encountered a patient, a 28-yr-old man, in whom anaphylactic shock developed twice during anesthesia. He was scheduled to undergo surgery for traumatic brachial nerve palsy. Medical history was limited to allergic rhinitis. Atropine, hydroxyzine, and cefazopran hydrochloride were administered 1 h before the anesthesia. The induction of anesthesia and tracheal intubation was performed uneventfully using thiopental, fentanyl, and vecuronium, and maintained with nitric oxide (N₂O), oxygen (O₂) and isoflurane. A few minutes after the insertion of a central venous catheter impregnated with chlorhexidine and silver sulfadiazine (Arrow gard⁺ Blue, Arrow International Inc., Reading, PA), we noticed hypotension (from 115/45 mmHg to 72/28 mmHg), tachycardia (85 beats/min to 125 beats/min), fall of pulse oximetry (SpO₂)

(from 98% to 79%) and end-tidal pressure of carbon dioxide (PETCO₂) (from 55 to 6 mmHg), and skin erythema in his upper body. During resuscitation, his carotid artery pulse was palpable. With administration of ephedrine, lactated Ringer's solution and adrenaline, blood pressure was restored to 118/40 mmHg in 1 h. The surgery was postponed. The central venous catheter was withdrawn the next afternoon. Lymphocyte transformation test was performed for cefazopran hydrochloride, vecuronium, and thiopental. Only cefazopran hydrochloride appeared to be strong-positive (+++).

Four weeks later, his second surgery was scheduled. An arterial line was placed after lidocaine infiltrated locally. Induction of anesthesia and tracheal intubation were performed using midazolam, buprenorphine, ketamine, and vecuronium. Soon after the insertion of a chlorhexidine- and silver sulfadiazine-impregnated catheter (Arrow gard⁺

CORRESPONDENCE

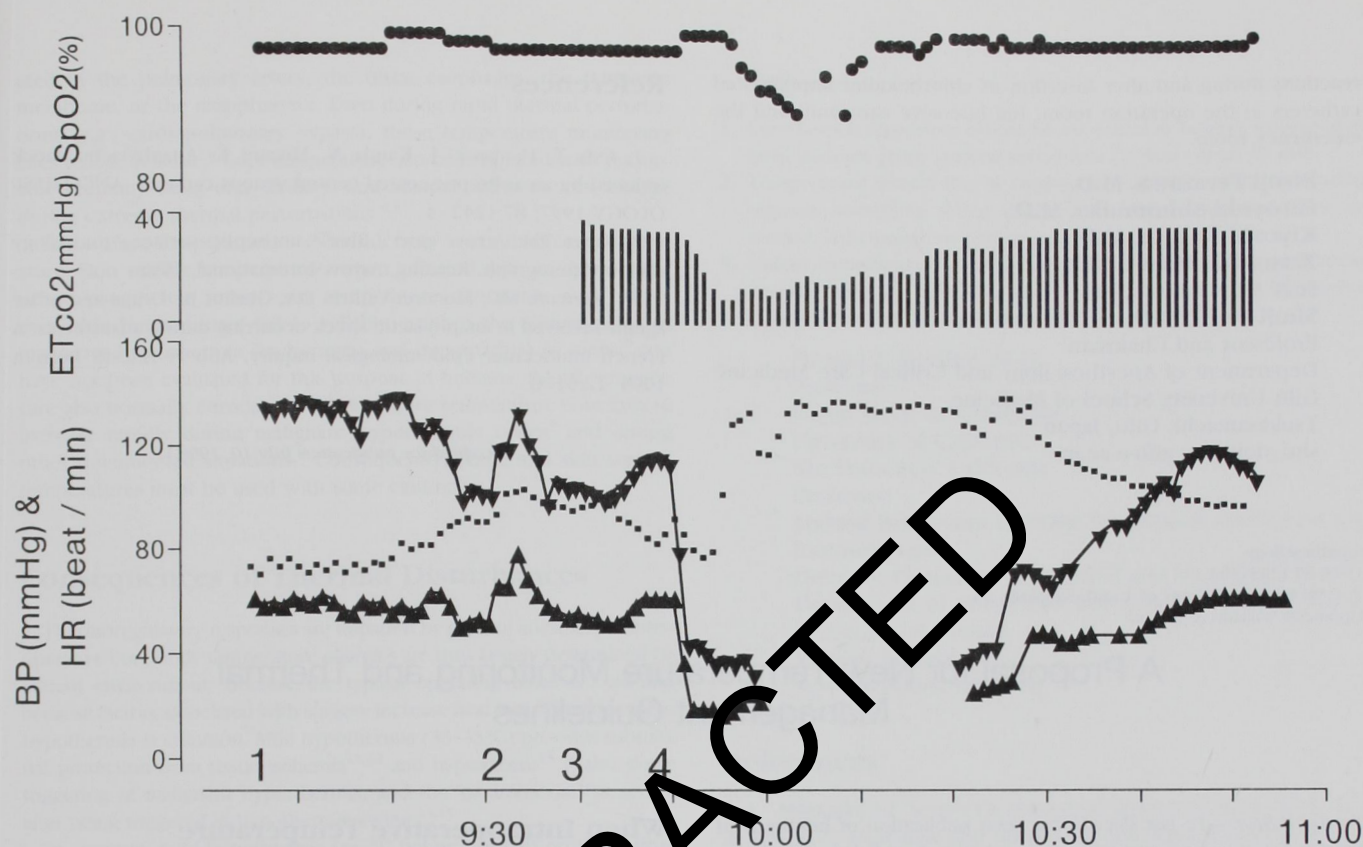


Fig. 1. Hemodynamic changes at the second episode: 1: arterial line under local anesthesia, 2: anesthesia start, 3: tracheal intubation and 4: insertion of CVP catheter

Blue), blood pressure decreased suddenly (fig. 1). Skin erythema with edema was manifest, and there was no arterial pulse wave. Reevaluated, although a carotid artery pulse was palpable, heart rate increased from 80 to 120 beat/min. Soon after we noticed this, we removed the central venous catheter and placed another catheter without impregnation using a guide wire. Blood pressure became measurable within 30 min after the patient received 3,000 ml lactated Ringer's solution and adrenaline, 200 μ g.

Anesthesia was discontinued and the patient regained consciousness with stable cardiorespiratory function. Then, operation was performed. Blood chemical analysis showed a basophil count decreased to zero and plasma histamine levels increased to 80 ng/ml soon after this event. Immunoglobulin E-specific antibody against Latex (Pharmacia & Upjohn, Uppsala, Sweden) was not detected. Six months later, skin testing showed a positive reaction only to 0.01% chlorhexidine (table 1) and a weak response to 0.001% chlorhexidine.

One yr later, the patient underwent arthrodesis of his shoulder during general anesthesia and had a central venous catheter placed without impregnation (Arrow) uneventfully.

We suspect chlorhexidine was the causative agent for the previous two events. Farber² reported that approximately 37% of chlorhexidine from the catheter was released into the blood on the first day of insertion (this level is at most 40 μ g/ml) and postulated that this blood level could not sensitize the patient. Because chlorhexidine is contained in various pharmaceutical products, it is possible that anaphylactic reactions could occur in such a sensitized patient. Although we know catheter-related anaphylactic reaction is very rare,³ we should be reminded of the possibility of anaphylactic

Table 1. Results of Skin Testing in the Patient after the Second Episode

| | % | Scratch | |
|---------------------------------------|------|----------------|-------------------|
| | | Wheal (mm) | Flare (mm) |
| Chlorhexidine (saline) | 0.01 | 3 × 4 4 × 5 | 10 × 11 7 × 10 |
| Sulfadiazine sodium (distilled water) | 1 | — | 3 × 4 3 × 4 |
| Silver sulfate (5% ethanol) | 1 | — | 2 × 3 1 × 2 |
| Silver benzoate (5% ethanol) | 1 | 2 × 3 5 × 5 | 6 × 7 6 × 8 |
| Vecuronium (saline) | 0.01 | — | 2 × 2 3 × 3 |
| Lidocaine (saline) | 0.01 | — | 3 × 3 3 × 3 |
| Povidone-iodine (saline) | 0.01 | — | 2 × 3 2 × 3 |
| Saline | — | — | 2 × 3 |
| Distilled water | — | — | 1 × 1 |
| 5% ethanol | — | — | 2 × 3 |

* The reaction was assessed after 15 min. Results were considered positive if the diameter of flare was 10 mm with wheal or more. Three control subjects had negative reactions to all tested substances. Because silver sulfadiazine was insoluble and chemical formula is monosilver 4-amino-N-(2-pyrimidinyl) benzenesulfonamide, we used silver sulfate, silver benzoate, and sulfadiazine sodium. All substances were dissolved in saline, distilled water, or 5% ethanol.

reactions during and after insertion of chlorhexidine-impregnated catheters in the operation room, the intensive care unit, and the emergency room.

Etsuji Terazawa, M.D.
Hiroyuki Shimonaka, M.D.
Kiyoshi Nagase, M.D.
Tatsuhiko Masue, M.D.

Staff Anesthesiologists

Shuji Dohi, M.D.

Professor and Chairman

Department of Anesthesiology and Critical Care Medicine

Gifu University School of Medicine

Tsukasamachi, Gifu, Japan

shu_dohi@cc.gifu-u.ac.jp

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A Proposal for New Temperature Monitoring and Thermal Management Guidelines

To the Editor:—The last decade has seen publication of hundreds of articles about perioperative thermoregulation, heat balance, and consequences of thermal disturbances. We thus know far more about control of body temperature and the effects of thermal perturbations than when the original Temperature Monitoring Standards of the American Society of Anesthesiologists were introduced. More importantly, four major outcome studies were published in recent years; these studies indicate that even small reductions in intraoperative body temperature produce substantial morbidity in selected patient populations.

We must therefore consider whether revision of the current Temperature Monitoring Standards might be appropriate. To that end, I would like to summarize major recent studies relevant to patient temperature monitoring and thermal management, and their clinical implications. I will then propose a revised set of guidelines based on our current understanding of perioperative temperature control.

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Address reprint requests to Dr. Sessler: Department of Anesthesia, University of California, San Francisco, 374 Parnassus Avenue, 3rd Floor, San Francisco, California 94143-0068.

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When Intraoperative Temperature Monitoring is Necessary

Normal core temperature varies between 36.5 and 37.5°C. Core temperature usually decreases 0.5-1.5°C in the first 30 min after induction of general anesthesia. Hypothermia results from internal redistribution of heat and various factors, the importance of which is hard to predict in individual patients.¹ As a result, core temperature perturbations during the first 30 min of anesthesia are difficult to interpret.

Significant subsequent decreases in core temperature are most likely in patients undergoing abdominal or thoracic surgery, but malignant hyperthermia—and hyperthermia from other causes—remains a risk in all patients. Consequently, body temperature should be monitored in most patients undergoing general anesthesia that exceeds 30 min. Body temperature ideally might be monitored continuously; however, 15-min intervals probably are sufficient in most patients.

The drugs used during intravenous sedation or regional anesthesia do not trigger malignant hyperthermia. However, core hypothermia occurs during conduction anesthesia,² especially when surgery involves major body cavities,³ and often is manifested as shivering. Core temperature should therefore be measured during spinal or epidural anesthesia in patients who clinicians believe are likely to become hypothermic.

Where to Monitor Body Temperature

The core thermal compartment is composed of highly perfused tissues, the temperature of which is uniform and high compared with the rest of the body. Temperature in this compartment can be evalu-