

# The Medical Letter®

## On Drugs and Therapeutics

---

Published by The Medical Letter, Inc. • 1000 Main Street, New Rochelle, NY 10801 • A Nonprofit Publication

---

**IN THIS ISSUE** (starts on next page)

**Glucose Control in the ICU** ..... p 6

## Important Copyright Message

The Medical Letter® publications are protected by US and international copyright laws. Forwarding, copying or any distribution of this material is prohibited.

Sharing a password with a non-subscriber or otherwise making the contents of this site available to third parties is strictly prohibited.

By accessing and reading the attached content I agree to comply with US and international copyright laws and these terms and conditions of The Medical Letter, Inc.

**For further information click: [Subscriptions](#), [Site Licenses](#), [Reprints](#)  
or call customer service at: 800-211-2769**

---

**FORWARDING OR COPYING IS A VIOLATION OF US AND INTERNATIONAL COPYRIGHT LAWS**

# The Medical Letter®

## On Drugs and Therapeutics

Published by The Medical Letter, Inc. • 1000 Main Street, New Rochelle, NY 10801 • A Nonprofit Publication

Volume 52 (Issue 1330)  
 January 25, 2010

www.medicalletter.org

### Glucose Control in the ICU

Once thought to be a beneficial response to critical illness, hyperglycemia is now recognized as independently associated with death and other adverse outcomes in various groups of critically ill patients. Whether normalization of blood glucose by insulin infusion is beneficial in such patients has been a subject of debate in the critical care community. Some new guidelines have been published.<sup>1</sup>

**CLINICAL STUDIES** — Among 1548 patients (about 60% post-cardiac surgery) in a surgical intensive care unit (SICU) randomized to receive intensive insulin therapy (IIT) to achieve a target glucose of 80-110 mg/dL (4.4-6.1 mmol/L) or to standard therapy with a conventional target of 180-200 mg/dL (10.0-11.1 mmol/L), in-ICU-mortality was 4.6% with IIT and 8.0% with the conventional target, a 42% decrease.<sup>2</sup> A similar study in 1,200 subjects in a medical intensive care unit (MICU) showed no significant difference in mortality between patients on the intensive protocol compared to those receiving conventional glucose control (37.3% with IIT versus 40.0% in the control group).<sup>3</sup> A combined analysis of these two studies found more hypoglycemic events in the IIT groups (11.3% vs. 1.8%), but with no serious consequences.<sup>4</sup>

Another study (n=523) confirmed the increased incidence of hypoglycemia with IIT – severe hypoglycemia (glucose  $\leq$ 40 mg/dL [ $\leq$ 2.2 mmol/L]) occurred in 28.6% of patients with IIT compared to 3.1% in conventionally treated patients – and found a 74% higher mortality (23.8% vs. 13.7%) in hypoglycemic patients, with no significant difference in mortality between IIT and conventionally treated patients.<sup>5</sup>

Among 537 patients in 18 ICUs with severe sepsis treated with IIT or conventionally, the rate of life-threatening hypoglycemia was significantly higher in the IIT group (5.3% versus 2.1%); there was no difference in mortality between the IIT and control groups, but the study was stopped early due to safety concerns.<sup>6</sup>

The Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial included 6104 medical and surgical patients in 42 hospitals. The target range glucose for the control group was 144-180 mg/dL and for the IIT group was 81-108 mg/dL. The results showed no significant difference in 28-day mortality (22.3% vs. 20.8%, P=0.17), but at 90 days the mortality rate was significantly higher in the IIT group (27.5% vs. 24.9%, P=0.02).<sup>7</sup>

A systematic review and meta-analysis of 26 randomized controlled studies of IIT in the ICU setting found

**Table 1. Some Studies of Insulin-Infusion Therapy in ICU Settings**

Study (N)	Design and Setting	Glucose Target mg/dL (mmol/L)	Achieved Mean Glucose	Mortality
Van den Berghe 2001 <sup>2</sup> N=1548	Randomized single center SICU	80-110 (4.4-6.1) 180-200 (10.0-11.1)	104 153	4.6% 8.0%*
Van den Berghe 2006 <sup>3</sup> N=1200	Randomized single center MICU	80-110 (4.4-6.1) 180-200 (10.0-11.1)	111 153	37.3% 40.0%
Arabi et al. <sup>5</sup> N=523	Randomized single center mixed ICU	80-110 (4.4-6.1) 180-200 (10.0-11.1)	115 171	13.5% 17.1%
WISEP <sup>6</sup> N=537	Randomized multicenter mixed ICUs	80-110 (4.4-6.1) 180-200 (10.0-11.1)	112 151	24.7% 26.0%
NICE-SUGAR <sup>8</sup> N=6104	Randomized multicenter mixed ICUs	81-108 (4.5-6.0) 144-180 (8.0-10.0)	115 144	27.5% 24.9%*

\* Statistically significant difference

no significant mortality benefit with use of IIT in the ICU (RR 0.93; CI 0.83-1.04).<sup>8</sup>

**CONCLUSION** — Clinical studies indicate that intensive insulin therapy with tight glycemic control (80-110 mg/dL [4.4-6.1 mmol/L]) is generally not beneficial for ICU patients, and may be harmful. Medical Letter consultants believe, however, that less intensive glucose control (140-180 mg/dL [7.8-10 mmol/L]) may prove to be beneficial. Whether some subgroups of ICU patients, such as diabetic patients post-cardiac surgery, would benefit from tighter control of blood glucose remains to be established. □

1. ES Moghissi et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. *Endoc Pract* 2009; 15:353.
2. G Van den Berghe et al. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001; 345:1359.
3. G Van den Berghe et al. Intensive insulin therapy in the medical ICU. *N Engl J Med* 2006; 354:449.
4. G Van den Berghe et al. Intensive insulin therapy in mixed medical/surgical intensive care units. *Diabetes* 2006; 55:3151
5. YM Arabi et al. Intensive versus conventional insulin therapy: a randomized controlled trial in medical and surgical critically ill patients. *Crit Care Med* 2008; 36:3190.
6. FM Brunkhorst et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. *N Engl J Med* 2008; 358:125.
7. The NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 2009; 360:1283.
8. DE Griesdale et al. Intensive insulin therapy and mortality among critically ill patients: a meta-analysis including NICE-SUGAR study data. *CMAJ* 2009; 180:821.

## The Medical Letter®

On Drugs and Therapeutics

**EDITOR IN CHIEF:** Mark Abramowicz, M.D.

**EXECUTIVE EDITOR:** Gianna Zuccotti, M.D., M.P.H., F.A.C.P., Harvard Medical School

**EDITOR:** Jean-Marie Pflomm, Pharm.D.

**ASSISTANT EDITORS, DRUG INFORMATION:** Susan M. Daron, Pharm.D., Blaine M. Houst, Pharm.D., Corinne E. Zanone, Pharm.D.

**CONSULTING EDITOR:** Brinda M. Shah, Pharm.D.

**ADVISORY BOARD:**

Jules Hirsch, M.D., Rockefeller University

Gerald L. Mandell, M.D., University of Virginia School of Medicine

Dan M. Roden, M.D., Vanderbilt University School of Medicine

**CONTRIBUTING EDITORS:**

Carl W. Bazil, M.D., Ph.D., Columbia University College of Physicians and Surgeons

Vanessa K. Dalton, M.D., M.P.H., University of Michigan Medical School

Eric J. Epstein, M.D., Albert Einstein College of Medicine

David N. Juurlink, BPhm, M.D., Ph.D., Sunnybrook Health Sciences Centre

Richard B. Kim, M.D., University of Western Ontario

Hans Meinertz, M.D., University Hospital, Copenhagen

Sandip K. Mukherjee, M.D., F.A.C.C., Yale School of Medicine

F. Estelle R. Simons, M.D., University of Manitoba

Jordan W. Smoller, M.D., Sc.D., Harvard Medical School

Neal H. Steigbigel, M.D., New York University School of Medicine

**SENIOR ASSOCIATE EDITORS:** Donna Goodstein, Amy Faucard

**ASSOCIATE EDITOR:** Cynthia Macapagal Covey

**EDITORIAL FELLOW:** Vincent Teo, B.Sc. Phm, Sunnybrook Health Sciences Centre

**MANAGING EDITOR:** Susie Wong

**ASSISTANT MANAGING EDITOR:** Liz Donohue

**PRODUCTION COORDINATOR:** Cheryl Brown

**EXECUTIVE DIRECTOR OF SALES:** Gene Carbona

**FULFILLMENT & SYSTEMS MANAGER:** Cristine Romatowski

**DIRECTOR OF MARKETING COMMUNICATIONS:** Joanne F. Valentino

**VICE PRESIDENT AND PUBLISHER:** Yosef Wissner-Levy

Founded in 1959 by

Arthur Kallet and Harold Aaron, M.D.

**Copyright and Disclaimer:** The Medical Letter is an independent nonprofit organization that provides health care professionals with unbiased drug prescribing recommendations. The editorial process used for its publications relies on a review of published and unpublished literature, with an emphasis on controlled clinical trials, and on the opinions of its consultants. The Medical Letter is supported solely by subscription fees and accepts no advertising, grants or donations.

No part of the material may be reproduced or transmitted by any process in whole or in part without prior permission in writing. The editors do not warrant that all the material in this publication is accurate and complete in every respect. The editors shall not be held responsible for any damage resulting from any error, inaccuracy or omission.

### Subscription Services

**Mailing Address:**

The Medical Letter, Inc.  
1000 Main Street  
New Rochelle, NY 10801-7537

**Customer Service:**

Call: 800-211-2769 or 914-235-0500  
Fax: 914-632-1733  
Web Site: [www.medicalletter.org](http://www.medicalletter.org)  
E-mail: [custserv@medicalletter.org](mailto:custserv@medicalletter.org)

**Permissions:**

To reproduce any portion of this issue, please e-mail your request to: [permissions@medicalletter.org](mailto:permissions@medicalletter.org)

**Subscriptions (US):**

1 year - \$98; 2 years - \$167;  
3 years - \$235. \$49.00 per year for students, interns, residents and fellows in the US and Canada.  
CME: \$70 for 26 credits.

**E-mail site license inquiries to:**

[info@medicalletter.org](mailto:info@medicalletter.org) or call 800-211-2769 x315.  
Special fees for bulk subscriptions. Special classroom rates are available. Back issues are \$12 each. Major credit cards accepted.

Copyright 2010. ISSN 1523-2859