develop a system of pharmacist-researchers and scientists and describe research as any research activity done by pharmacists, regardless of the topic. As health care professionals, pharmacists represent only one aspect of the complex and interdependent health care system. Focusing our energies and resources solely on studying the practice of pharmacy may or may not help in developing our practice, but it will likely add little to the entire health care system. Pharmacists must be involved in all aspects of health research, from basic laboratory investigations to population-based studies. Our unique set of skills and our focus will ensure that we have distinctive research topics. Limiting our contributions to the pillars of health services and clinical research represents a disservice to the advancement of pharmacy and to Canadians.

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Sheri L Koshman, BScPharm, PharmD, ACPR
Assistant Professor of Medicine
University of Alberta
Edmonton, Alberta
Joseph Blais, BScPharm
Pharmacy Resident
Pharmacy Services
Alberta Health Services
Edmonton, Alberta

Sheri Koshman is also a Clinical Pharmacotherapy Practitioner with Pharmacy Services, Alberta Health Services.

CURRENT-OASIS: A Potential Mirage of Numbers

CURRENT-OASIS 7, a 3-year randomized controlled trial, was designed to determine whether a doubling of the loading and initial maintenance doses of clopidogrel is superior to the standard-dose regimen for patients with acute coronary syndrome who have been referred for percutaneous coronary intervention.[1]

In this double-blinded trial, adult patients with non-ST-segment elevation acute coronary syndrome or ST-segment elevation myocardial infarction for whom percutaneous coronary intervention was to be performed within 72 h were randomly assigned to receive double the usual loading dose of clopidogrel (600 mg) or the standard loading dose (300 mg). For the 25 086 patients included in the study, the authors assessed the composite end point of cardiovascular death, myocardial infarction, and stroke as the primary outcome and found no significant difference between a 7-day double-dose regimen and the standard-dose regimen.[1]

Of the study group enrolled, 17 263 patients actually underwent the percutaneous coronary intervention, and the authors performed a subgroup analysis of these patients.[2] The report of this subgroup analysis is the focus of our letter. In our view, the abstract and conclusion of the study report[2] do not adequately represent the results of the study, instead leading the reader to believe that the results are more profound than they truly are.

Our first issue of concern is the unknown. No data are presented for serious adverse events, which would include any untoward medical occurrence that results in death, is life-threatening, necessitates admission to hospital or prolongs the hospital stay, or results in persistent or significant disability.[3] Documentation of serious adverse events should encompass all adverse events that occur during the trial, not only the serious events thought to be related to use of the drug. For example, if there had been fewer serious cardiovascular adverse events in the treatment arm than in the control (standard therapy) arm, but no change in total serious adverse events, then it could be concluded that serious *noncardiovascular* events were occurring more frequently and should be investigated. Information about all serious adverse events throughout the trial would also help to determine the "net effect" of the intervention. We have requested these data from the authors of the original study, but as of this writing (late 2010) had not received them.

Now, for argument's sake, let's say that the serious adverse events are not a factor in assessing the relative benefit of the doubled dose of clopidogrel. There are still some other considerations to be made.

Our second issue of concern is the following statement in the conclusion section of the abstract: "In patients undergoing PCI [percutaneous coronary intervention] for acute coronary syndromes, a 7-day double-dose clopidogrel regimen was associated with a reduction in cardiovascular events and stent thrombosis compared with the standard dose".[2] We think that this statement is misleading. The term "cardiovascular events" implies a much broader meaning than the results actually show. In fact, there were no significant reductions in stroke, ischemia,

or cardiovascular death, so it would have been more appropriate to refer to a reduction in the incidence of myocardial infarction, as opposed to cardiovascular events.

Our third issue of concern relates to the data for myocardial infarction, which was 1 of 3 outcomes measured in the study. The authors reported a 0.6% reduction in this outcome among patients assigned to receive double-dose clopidogrel, relative to those receiving the standard dose. There are 2 reasons why we question the clinical importance of this result. First, the effect size was small and of debatable clinical importance. Second, it is possible that this finding is a false positive (type 1 error), as no *p* value adjustment was made for the multiple comparisons performed in the trial.[4] The authors also used a postrandomization subgroup of the overall trial population, which leads to additional risk of a type 1 error.[5]

Our fourth issue of concern is the lack of reporting of harm in the conclusion statements of the abstract and the full article, which might lead a reader to believe that there are no risks associated with the double-dose regimen. In fact, the incidence of major bleeding (as defined by the CURRENT-OASIS 7 authors) was higher in the double-dose group than the standard-dose group (1.6% versus 1.1%, hazard ratio 1.41, 95% confidence interval 1.09–1.83, $p = 0.009$).[2] This represents a 0.5% absolute increase in the hazard of harm (major bleeding). The omission of this information from the concluding statements appears to be selective reporting, which is misleading.

Our final issue of concern relates to the overall assessment of harm versus benefit. Specifically, the 0.6% reduction in risk of myocardial infarction would seem to be nullified by the 0.5% increase in the risk of major bleeding. Although some would argue that the benefit of preventing myocardial infarction outweighs the risk of a major bleeding event, these 2 outcomes are only a subset of the possible effects of the double-dose regimen. Returning to our first issue of concern, described above, a full analysis of serious adverse events could help in determining the net effect of the double-dose regimen and provide more confidence in saying whether the benefit outweighs the risk.

Does this study provide enough information to support a double-dose regimen of clopidogrel? We're not convinced. Does something need to be done about the selective reporting of harm in conclusion statements? Absolutely.

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Tifaine Magnusson, BSc(Pharm)
Aaron M Tejani, BSc(Pharm), PharmD, ACPR
On behalf of the Therapeutics Initiative Drug Assessment Working Group
University of British Columbia
Vancouver, British Columbia

Pediatric Pharmacokinetics of Vancomycin: A Canadian Perspective

The practice of monitoring serum vancomycin concentrations in children remains controversial because of pharmacokinetic variability within and between patients and a lack of guidance from the literature.[1-8] Two questions remain unanswered: Should we be measuring the level of this drug in children, and what therapeutic ranges should be targeted?[1]

At the time of writing (late 2010), the initial vancomycin dosage at the Centre hospitalier universitaire (CHU) Sainte-Justine in Montréal, Quebec, ranged from 10 to 15 mg/kg per dose every 6 or 8 h, with each dose administered slowly by infusion over 1 h. For all patients, trough and peak vancomycin levels are usually measured in association with the third or fourth dose, with the trough being determined immediately before administration and the peak 1 h after infusion is complete. The dosage is then adjusted to achieve the target therapeutic ranges (i.e., 5–10 µg/mL for the trough and 20–40 µg/mL for the peak), according to the pharmacist's recommendations, which are based on a one-compartment model (Sawchuk–Zaske method) and calculated pharmacokinetic parameters. A local retrospective drug utilization review of vancomycin was conducted in 2010, using data for 30 patients with 5 days or more of therapy. Measured serum concentrations for trough and peak fell within the specified therapeutic ranges in 60% and 33% of the cases, respectively, up to the fifth day of vancomycin treatment (Delicourt A, Lavoie A, Touzin K, Therrien R, Lebel D. A retrospective study of vancomycin therapeutic drug monitoring in pediatrics. Manuscript submitted for publication).

To characterize therapeutic drug monitoring practices for vancomycin in pediatric patients across Canada, we surveyed 13 Canadian pediatric centres in May 2010 using SurveyMonkey. The questionnaire was to be completed by a single clinical pharmacist at each hospital, on the basis of the person's opinion and pursuant to the centre's usual practice. Data related to neonatology were excluded. Twelve of the 13 centres responded, for a response rate of 92%.

The initial vancomycin dosage used for children varied among the respondents, and the majority of children received the drug every 6 h (Table 1). Eight of the 12 respondents reported that their hospitals did not have a maximum initial dose. Among the remaining hospitals, the maximum dose was 60 mg/kg per day at 3 centres and 100 mg/kg per day at 1 centre.

After dose adjustment, a new target trough, with or without measurement of peak levels, was prescribed for a median of 80% (range 30% to 95%) of patients at each hospital ($n = 9$ respondents). Trough level was measured for a median of 100% (range