ARTICLE

Accuracy of Weights Used to Determine Doses of Enoxaparin, Eptifibatide, Tirofiban, and Tenecteplase in the Regina Qu'Appelle Health Region: Impact on Therapy in Patients with Acute Coronary Syndromes

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ABSTRACT

Background: The evolution of drug therapy has resulted in the development of potent new agents with narrow therapeutic windows, including several antithrombotic agents. Clinical trials have demonstrated that the dose per kilogram of body weight is critical to the efficacy and safety of these drugs. It follows that the accuracy of the weight used to determine doses is also critical.

Objectives: To identify the source of body weights used for determining doses of enoxaparin, eptifibatide, tirofiban, and tenecteplase for patients with acute coronary syndrome admitted to hospitals in the Regina Qu'Appelle Health Region (RQHR) and to assess whether the weights were accurate enough for safe and effective dosing of these agents.

Methods: All patients who were admitted to an RQHR tertiary care hospital and who started therapy with enoxaparin, eptifibatide, tirofiban, or tenecteplase for an acute coronary syndrome during specified periods within the first quarter of 2003 were eligible for inclusion in the study. Within 48 h of drug initiation, eligible patients were approached for consent to participate in the study. Each patient was asked to state his or her body weight; the patient was then weighed. Serum creatinine, target drug, hospital, hospital ward, dose administered, dosing weight, and all body weights listed in the patient's chart were also recorded. Interventions were undertaken and documented as appropriate.

Results: For 12 (35%) of the 34 patients participating in the study, the actual weight (rather than an estimate) was recorded in the medical chart. Discrepancies between patients' stated and actual weights ranged from an underestimate of 19 kg to an overestimate of 8 kg. However, overall there was a strong correlation between stated and actual weights (r = 0.970, p < 0.001). For 20 patients (59%), the discrepancy between stated and actual weights was 0 to

RÉSUMÉ

Historique : L'évolution de la pharmacothérapie s'est traduite par la mise au point de nouveaux agents puissants ayant une marge thérapeutique étroite, notamment plusieurs antithrombotiques. Au cours d'essais cliniques, on a démontré que la dose par kilogramme de poids corporel constitue un facteur déterminant de l'efficacité et de l'innocuité de ces médicaments. Il s'ensuit que l'exactitude du poids qui sert à établir ces doses s'avère aussi un facteur déterminant.

Objectifs : Déterminer la source du poids corporel utilisé pour établir les doses d'énoxaparine, d'eptifibatide, de tenecteplase et de tirofiban chez les patients présentant un syndrome coronarien aigu et admis dans des hôpitaux de la Regina Qu'Appelle Health Region (RQHR), et évaluer si le poids utilisé était suffisamment précis pour établir une dose sûre et efficace de ces agents.

Méthodes : Tous les patients admis à un hôpital de soins tertiaires de la RQHR et ayant amorcé un traitement par l'énoxaparine, l'eptifibatide, la tenecteplase ou le tirofiban pour un syndrome coronarien aigu durant des périodes déterminées au cours du premier trimestre de 2003 étaient admissibles à l'étude. Dans les 48 heures suivant l'amorce du traitement, on a demandé aux patients admissibles leur consentement à participer à l'étude. On leur a demandé leur poids, puis on les a pesés. On a aussi recueilli de leur dossier médical les paramètres suivants : créatinine sérique, médicament cible, hôpital, service hospitalier, dose administrée, poids servant à établir la dose et tous les poids inscrits. Les interventions ont été réalisées et notées comme il se doit.

Résultats : Chez 12 (35 %) des 34 patients qui ont participé à l'étude, le poids réel (plutôt que le poids estimé) a été inscrit au dossier médical du patient. L'écart entre le poids déclaré par le patient et le poids réel variait d'une sous-estimation de 19 kg à une

2.4 kg, for 8 patients (24%) it was between 2.5 and 4.9 kg, for 5 patients (15%) it was between 5.0 and 9.9 kg, and for 1 patient (3%) it was between 17.5 and 20.0 kg. Dose changes were required for 10 patients (29%). For 3 of these patients (9% of the total sample), the wrong dose had been selected because of misreading of the preprinted order forms, and 7 (21%) required a dose change after actual body weight was determined. Because of time constraints it was not possible to track patient outcomes over the short or long term.

Conclusions: There was a wide range of discrepancies between patients' stated and actual weights for each of the study drugs, and interventions were needed in 21% of the patients because of weight inaccuracies. Therefore, it is recommended that actual body weight be determined for any patient receiving a prescription for enoxaparin, eptifibatide, tirofiban, or tenecteplase, to optimize therapeutic outcomes and minimize adverse effects. The scales used to determine body weight must be calibrated regularly to ensure accuracy of body weight and hence accuracy of doses. Considerations of patient safety during initial instability must be balanced with the potential for adverse outcomes caused by overdosing or underdosing of these drugs. The results of this study suggest that it is most critical to obtain actual body weight when it is most difficult to do so: in high-risk patients receiving eptifibatide. Thus, the challenge is to obtain accurate weights in the most efficient manner possible. If it is impossible to determine actual body weight, the patient's own estimate should be used for dosing purposes, since that information was strongly correlated with actual weight.

Key words: body weight, enoxaparin, eptifibatide, tirofiban, tenecteplase

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surestimation de 8 kg. Toutefois, il y avait globalement une étroite corrélation entre les poids déclarés et les poids réels (r = 0.970, p < 0.001). L'écart entre les poids déclarés et les poids réels variait de 0 à 2,4 kg chez 20 patients (59 %), de 2,5 à 4,9 kg chez 8 patients (24 %), de 5 à 9,9 kg chez 5 patients (15 %), et de 17,5 à 20 kg chez 1 patient (3 %). Une modification de la dose a été nécessaire chez 10 patients (29 %). Une mauvaise dose a été choisie chez 3 de ces patients (9 % de l'échantillon total), à cause d'une erreur de lecture des formulaires d'ordonnance préimprimés, et une modification de la dose a été nécessaire chez 7 patients (21 %) après que leur poids corporel réel a été mesuré. Vu le manque de temps, il n'a pas été possible de faire le suivi à court ou à long terme de l'issue du traitement.

Conclusions : On a observé un écart considérable entre le poids déclaré et le poids réel des patients pour chaque médicament à l'étude, et des interventions ont été nécessaires chez 21 % des patients à l'étude, à cause des poids inexacts. Par conséquent, on recommande de mesurer le poids réel de tout patient recevant une ordonnance d'énoxaparine, d'eptifibatide, de tirofiban ou de tenecteplase, afin d'optimiser les résultats thérapeutiques et de réduire au minimum les effets indésirables. Les pèse-personnes utilisés pour mesurer le poids corporel doivent être étalonnés régulièrement afin d'assurer l'exactitude du poids corporel et par conséquent celle des doses administrées. On doit tenir compte de la sécurité des patients au cours de la période initiale d'instabilité par rapport aux risques possibles de résultats indésirables causés par le sous- ou le surdosage de ces médicaments. Les résultats de l'étude suggèrent qu'il est essentiel d'obtenir le poids corporel réel dans les cas où cela est le plus difficile, c.-à-d. chez les patients à haut risque qui reçoivent l'eptifibatide. Par conséquent, le défi est d'obtenir le poids exact de la façon la plus efficace possible. Lorsqu'il est impossible de mesurer le poids corporel réel, il faut utiliser le poids déclaré par le patient pour déterminer la dose, puisqu'on a établi une forte corrélation entre le poids déclaré et le poids réel.

Mots clés : poids corporel, énoxaparine, eptifibatide, tirofiban, tenecteplase

INTRODUCTION

The evolution of drug therapy has resulted in the development of potent new agents with narrow therapeutic windows, including several antithrombotic agents; enoxaparin, eptifibatide, tirofiban, and tenecteplase.[1-8] Clinical trials have demonstrated that the dose per kilogram of body weight is critical to the efficacy and safety of these drugs. It follows that the accuracy of the weight used to determine the drug dose is also critical. However, the weight recorded in a hospital patient's chart may not be correct. Central to the accuracy of the recorded weight is the method by which it was obtained. Ideally, upon admission, the patient is weighed accurately. However, given time constraints and lack of scales in the patient care area, this does not always happen. In these cases the weight may be obtained by asking the patient or a family member for an estimate. In some cases it may be left to the health care providers to estimate the patient's weight. Body weight, once documented in the chart, provides the basis for drug dosing, calculation of nutritional requirements, and determinations of body surface area. Recent data from a chart review of patients with acute coronary syndromes in the Regina Qu'Appelle Health Region (RQHR) indicated that for some patients, 2 or 3 body weights were recorded in the same chart, resulting in different doses of drugs (Marcil A, Bowman J, Ricci P, Semchuk W, Poulin S, Kuntz D. A retrospective review of the pharmacological management of acute coronary syndromes in the RQHR. March 2003 [unpublished report]). Given the ever-increasing number of drugs that have a critically effective dosing range, it seemed prudent to assess the origin and accuracy

of the weights used for determining doses. This study examined the origin and accuracy of weights used for dosing 4 cardiac drugs in which small differences in the dose per kilogram may result in ineffectiveness or adverse events. Enoxaparin and tirofiban were chosen because small dose changes can result in marked increases in hemorrhage.[1,6] Eptifibatide was chosen because of the potential for increased bleeding at higher doses per kilogram, as well as a decrease in reperfusion rates with underdosing.[5] All of these problems may occur with tenecteplase.[2]

The purposes of this study were to identify the source of weights used for dosing the 4 drugs and to assess whether these weights were sufficiently accurate to safely and effectively determine doses for patients with acute coronary syndrome admitted to RQHR hospitals.

BACKGROUND

Determination of Body Weight

Several trials have attempted to determine how patients' weights (for drug dosing purposes) are obtained and whether this has an impact on therapeutic outcomes. Fernandes and others[9] examined the accuracy of patient weight estimations by 117 patients, 26 nurses, and 11 physicians in an emergency department. The study included only ambulatory patients over the age of 18 years. The patient, his or her attending physician, and a bedside nurse were independently asked to estimate the patient's weight while clothed and ambulatory. The patient was then weighed, and percentage error was calculated. The authors stated that weight estimates differing by more than 10% from actual weight could render the treatment life-threatening. Mean error estimates in the study were 3.1% (95% confidence interval [CI] 2.7% to 3.5%) for patient-estimated weights, 8.4% (CI 7.6% to 9.2%) for nurse-estimated weights, and 8.1% (CI 7.1% to 9.1%) for physician-estimated weights. Weight estimations were less than 10% different from actual weight for 97% of the patient-estimated weights (95% CI 94% to 100%) and for 66% of nurse- and physician-estimated weights combined (95% CI 58% to 74%). Weight was estimated at more than 15% above actual weight by 1% of patients (95% CI 0% to 3%), 11% of nurses (95% CI 5% to 17%), and 16% of physicians (95% CI 9% to 23%).

Coe and others[10] examined the accuracy of estimates of weight and height for 38 supine patients awaiting urologic or orthopedic surgery. The study, involving 3 physicians and 1 assistant in the anesthesia department, demonstrated marked variation in the ability to assess height and weight accurately. Although 2 of the observers were fairly accurate in their estimations, the other 2 consistently overestimated low weights and underestimated high weights. The study authors noted that a 20% error in weight would probably not produce significant clinical problems within their anesthesia department, but this statement has not been validated and could not be considered true for all agents, or agents in other settings, given that anesthesiologists often titrate medications to effect rather then relying on standard doses of drugs.

These 2 studies highlight the variety of weight inaccuracies that may result from estimation of patient weight by not only health care providers but also patients. No studies were found specifically addressing how weight inaccuracies affect the doses of drugs prescribed and administered, or how patient outcomes may be affected by these inaccuracies.

Therapeutic Dosing Ranges

Enoxaparin, a low-molecular-weight heparin, has demonstrated efficacy for intermediate-risk patients with acute coronary syndromes. In the Thrombolysis in Myocardial Infarction (TIMI) 11A trial, patients received a 30-mg IV bolus of enoxaparin followed by either 1.0 mg/kg or 1.25 mg/kg subcutaneously.[1] The major hemorrhage rate was 1.9% with the lower dose and 6.5% with the higher dose. Therefore, the rate of major bleeding increased to more than 3-fold with an increase in enoxaparin dose of 0.25 mg/kg (25%). The 14-day incidence of death, recurrent myocardial infarction, or myocardial ischemia requiring revascularization was 5.2% in the group that received 1.0 mg/kg and 5.6% in the group that received 1.25 mg/kg. In the TIMI 11A study the lower dose (1.0 mg/kg) was associated with a lower risk of hemorrhage with efficacy equivalent to that of the higher dose (1.25 mg/kg). The manufacturer recommends a dose of 1 mg/kg for patients with unstable angina and non-Q-wave myocardial infarction.[11] The preprinted order forms currently used in the RQHR allow for a dose between 0.9 mg/kg and 1.1 mg/kg depending on where the patient's weight falls in the dosing range. Given that the RQHR and other centres are already employing a range of doses for enoxaparin, it would be prudent to ensure that the weight used to determine the enoxaparin dose is accurate.

Eptifibatide, a glycoprotein IIB/IIIA receptor inhibitor, is indicated for high-risk patients with acute coronary syndromes. Eptifibatide dosing was studied in a randomized, placebo-controlled dose-ranging trial.[5] The incidence of death or reinfarction was similar: 7.3% in the placebo group and 7.8% for patients at the highest eptifibatide dose (180 μg/kg bolus followed by 0.75 $\mu g \cdot kg^{-1} \cdot min^{-1}$ infusion). However, reperfusion rates at 90-min angiography varied. In the group receiving the highest eptifibatide dose, 79% of patients achieved TIMI grade 3 flow; in the placebo group, this proportion was 62%. This study highlighted the importance of correct dosing of eptifibatide, as underdosing could severely affect the degree of reperfusion.

Tirofiban, another glycoprotein IIB/IIIA receptor inhibitor, is also indicated for high-risk patients with acute

coronary syndromes. Kereiakes and others[6] initially assessed the safety of tirofiban in a dose-ranging trial. Their results showed the potential for large increases in bleeding rates with increases in the infusion dose of as little as 0.05 μg/kg. However, because of small sample size this study lacked the power to detect a clinically meaningful difference in clinical events between the tirofiban and placebo groups. The manufacturer's current recommended dose ranges allow for a bolus dose of 0.37 to 0.44 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and maintenance infusion of 0.09 to 0.10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ depending on where the patient's weight falls within the range.[4] Half this dose is used in patients whose estimated creatinine clearance is less than 30 mL/min. Because the dose-ranging trial showed the potential for increased bleeding rates with overdosing, it follows that inaccuracies in weight could affect adverse events in patients receiving tirofiban.

Tenecteplase is a modified form of human tissue plasminogen activator that binds to fibrin and converts plasminogen to plasmin. Tenecteplase is indicated for lysis of suspected occlusive coronary artery thrombi associated with evolving transmural myocardial infarction. The TIMI 10B trial[2,7] examined the safety of bolus doses of 30 mg, 40 mg, and 50 mg of this drug. The rates of intracranial hemorrhage were 1.0% with the 30-mg dose, 1.9% with the 40-mg dose, and 3.8% with the 50-mg dose. Serious bleeding, defined according to US Food and Drug Administration criteria, occurred in 1.9%, 5.2%, and 11.5% of cases, respectively. The study initially included 886 patients, for 781 of whom actual weight had been determined.[8] More significant bleeding and intracranial hemorrhage occurred at the highest weight-corrected dose (0.55 mg/kg). In the TIMI 10B trial, TIMI grade 3 flow was achieved in 62% to 63% of patients at doses of approximately 0.5 mg/kg but in only 51% to 54% of patients at lower doses. The manufacturer's suggested weight range effectively means that a patient may receive less than 0.50 mg/kg up to 0.58 mg/kg depending on where his or her weight falls in the range.[3] Therefore, weight inaccuracies could significantly affect the dose received.

METHODS

All patients who were admitted to an RQHR tertiary care hospital and who started taking enoxaparin, eptifibatide, tirofiban, or tenecteplase for an acute coronary syndrome during the study period were eligible for inclusion. Patients who were unable or unwilling to provide consent and those with hemodynamic instability, as determined by the attending physician or nurse, were excluded. Data collection occurred at the Regina General Hospital from January 5 to 31, 2003, and at the Pasqua Hospital from February 2 to 22, 2003. These study dates were chosen on the basis of where the lead investigator (A.M.) was doing her residency rotation at the time. No sample size calculation was done; rather, all patients who met the inclusion criteria during the study period were eligible.

A computerized report was obtained daily from the pharmacy system identifying all patients who had started any of the 4 target drugs within the previous 24 h. Within 48 h of drug initiation, eligible patients were approached for consent to participate in the study. Patients were asked their weight and were then weighed (while wearing a standard-issue hospital gown) with a top-loading analogue scale (Seca, Hanover, Maryland) that was calibrated daily. Serum creatinine, target drug, hospital, hospital ward, dose administered, weight used to determine drug dose, and all weights listed in the patient's chart were also recorded.

Discrepancies between reported and observed weights were calculated; when indicated, interventions requiring a change in drug or dosage were recommended to the attending physician and documented on the data collection form.

For the purposes of this study, chart weight was defined as the weight found in the Nursing Database, a 4-page form that is completed by nursing staff upon a patient's admission to hospital; a copy of the form is placed in the front of the patient's chart. Dosing weight was defined as the weight written on the preprinted order form for each of the study drugs. The patient's stated weight was defined as the weight that was provided verbally by the patient to the investigator upon entry into the study. The patient's actual weight was defined as the weight obtained using the study scale. Chart weights that were described in the database as "actual weights" were coded as actual weights, but if there was no description of the source of the chart weight, every effort was made to determine if the patient had been weighed or if he or she had provided a weight estimate; if this could not be determined the weight source was coded as unknown. Weight estimates provided by health care providers were coded as such if this descriptor was included in the database.

The data were analyzed descriptively with the SPSS 10.0 for Windows package. Two-tailed *t* tests were employed to determine between-group differences in means. One-tailed *t* tests were employed to determine if the mean dose of each drug differed significantly from the gold standard dose. An a priori α value of 0.05 was chosen to establish statistical significance. Pearson's correlation coefficient was employed to examine the degree of correlation between the various weight data. Percentage dosing error for each drug was calculated by subtracting the ideal dose from the actual dose, dividing by the ideal dose, and multiplying by 100. The same calculation was used to calculate percentage error for patient-stated and dosing weights.

This study protocol was reviewed and approved by the Regina Qu'Appelle Research Ethics Board.

RESULTS

A total of 44 patients met the inclusion criteria during the 2 data collection periods. Ten patients were subsequently excluded; 4 were identified more than 48 h after drug initiation, and 6 did not wish to participate. Data were available for 38 drug exposures in these 34 patients; 4 patients received a second study drug when their risk stratification changed (enoxaparin followed by eptifibatide in 2 patients, enoxaparin followed by tirofiban in 1 patient, and enoxaparin followed by tenecteplase in 1 patient). Nineteen (56%) of the 34 patients received enoxaparin, 14 (41%) received eptifibatide, 4 (12%) received tirofiban, and 1 (3%) received tenecteplase (Tables 1 and 2).

Sources of Weights

For 10 (29%) of the 34 patients, more than one weight was listed in the medical chart. In the Nursing Database form, actual weight was recorded for 12 patients (35%), a patient estimate was recorded for 9 (26%), an estimate made by a health care provider was recorded for 1 (3%), and the source was unknown in 12 cases (35%). For each of 2 patients, the chart listed 2 actual weights that differed because they had been determined on different wards with different scales; the difference was 3 kg for one patient (receiving eptifibatide) and 5 kg for the other (receiving enoxaparin). The 3-kg discrepancy would not have affected the first patient's eptifibatide dose, but the 5-kg discrepancy would have affected the dose of enoxaparin received by the second patient.

Accuracy of Weights

Discrepancies between patients' stated and actual weights ranged from an underestimation of 19 kg to an overestimation of 8 kg. Overall, however, there was a strong correlation between patients' stated and actual weights (r = 0.970, $p < 0.001$). For 20 patients (59%), the discrepancy between stated and actual weights was 0 to 2.4 kg, for 8 patients (24%) it was between 2.5 and 4.9 kg, for 5 patients (15%) it was between 5.0 and 9.9 kg, and for 1 patient (3%) it was between 17.5 and 20.0 kg (Figure 1).

Weight Differences

This study examined the differences between the weights used for drug dosing and patients' actual weights, as well as the difference between patients' estimates of their own weight and actual weight. These differences are expressed as percent error in Figure 2. The percent error in dosing weight and the percent error in stated weight were strongly correlated (r = 0.77, $p < 0.001$). For only 1 patient were these errors greater than 10%. This patient was obese and had provided a weight estimate at the time of admission.

Table 1. Characteristics of 34 Patients Who Received Cardiac Drugs with Weight-Based Dosing*

Variable	Mean (and SD) or No. (and %)	
Mean drug dose		
Enoxaparin (*n* = 19)	0.99 mg/kg	(7.60)
Eptifibatide (*n* = 14)	178.40 µg/kg	(7.29)
Tirofiban (*n* = 4)	0.31 µg/kg	(0.11)
Tenecteplase (*n* = 1)	0.36 mg/kg	NA
Hospital (no. and % of 38 drug exposures)		
General	33	(87)
Pasqua	5	(13)
Ward (no. and % of 38 drug exposures)		
Cardiac Care Unit	7	(18)
Cardiac Surveillance Unit	17	(45)
Emergency Department	14	(37)
Source of chart weight (no. and % of 34 patients)		
Actual weight	12	(35)
Estimate by patient	9	(26)
Estimate by health care provider	1	(3)
Unknown	12	(35)
Mean weight (kg) (*n* = 34 patients)		
Chart weight	85	(15)
Dosing weight	85	(15)
Stated weight	85	(15)
Actual weight	86	(17)
Mean % error in weight		
In dosing weight	–0.95	(5.09)
In stated weight	–0.79	(4.76)
Mean % dosing error		
All drugs	1.65	(10.74)
Enoxaparin	4.42	(6.23)
Eptifibatide	3.16	(2.54)
Tirofiban	–9.37	(25.44)
Tenecteplase	28.00	NA

NA = not applicable.
*There were a total of 38 drug exposures for the 34 patients.

Accuracy of Dosing

Dose changes related to weight were indicated for 10 of the 34 patients (29%). For 3 patients (9% of the entire sample) the wrong dose had been chosen from the preprinted order forms on the basis of weight used. Two of these patients received tirofiban, and the third received eptifibatide. A dose change was required for 7 patients (21%) after an actual weight was obtained. Four of these patients had provided an estimate of their own weight, and 3 had a chart weight from an unknown source. For 5 of these 7 patients, the initial drug order had been written in the emergency department, and for 2 patients the drug had been initiated in the Cardiac Care Unit; none of these incorrect drug dosages were initiated in the Cardiac Surveillance Unit. None of the patients who had an actual weight recorded in the database required dose changes.

Table 2. Weights, Drug Doses, and Calculated Dosing Errors

		Patient's Weight (kg)				Initial Dose†				
Code*	Drug	Recorded in Chart (and Source)	Used for Dosing	Stated by Patient	Actual	Total	Per kg	% Dosing Error‡	% Error in Dosing Weight§	% Error in Stated Weight‖
1	Enoxaparin	92.3 (unknown)	92.3	92	92.5	90	0.97	3.00	–0.22	–0.54
2	Enoxaparin	97.7 (actual)	97.7	97	97.5	100	1.03	3.00	0.21	–0.51
3	Eptifibatide	76.0 (patient)	76.0	77	75.0	13 600	181.30	0.72	1.33	2.67
4	Tirofiban	56.0 (actual)	56.0	54	55.0	700	0.21	5.00	1.82	–1.82
5	Enoxaparin	97.0 (actual)	97.0	99	100.5	100	0.99	1.00	–3.48	–1.49
6	Enoxaparin	66.0 (actual)	66.0	73	68.0	70	1.02	2.00	–2.94	7.35
7	Enoxaparin	97.0 (HCP)	92.25	97	97.0	100	1.03	3.00	–4.90	0.00
8	Eptifibatide	97.0 (HCP)	97.0	97	97.0	18 000	185.00	2.78	0.00	0.00
9	Enoxaparin	78.0 (actual)	78.0	79	80.5	80	0.99	1.00	–3.11	–1.86
10	Enoxaparin	88.0 (unknown)	88.0	91	94.0	90	0.96	4.00	–6.38	–3.19
11	Eptifibatide	113.0 (unknown)	109.0	109	112.0	19 000	169.64	5.76	–2.68	–2.68
12	Eptifibatide	67.0 (actual)	70.0	70	70.0	12 400	177.14	1.59	0.00	0.00
13	Enoxaparin	70.0 (actual)	70.0	70	70.0	70	1.00	0.00	0.00	0.00
14	Enoxaparin	65.0 (actual)	65.0	69	69.0	70	1.01	1.00	–5.80	0.00
15	Enoxaparin	99.0 (actual)	99.0	96	97.5	100	1.03	3.00	1.54	–1.54
16	Enoxaparin	93.0 (patient)	93.0	93	85.0	90	1.06	6.00	9.41	9.41
17	Tirofiban	64.0 (unknown)	64.0	64	65.0	400	0.21	–47.50	–1.54	–1.54
18	Enoxaparin	90.0 (unknown)	90.0	90	88.0	90	1.02	2.00	2.27	2.27
19	Tirofiban	90.0 (unknown)	90.0	90	88.0	1 100	0.41	2.50	2.27	2.27
20	Enoxaparin	70.5 (unknown)	70.5	73	72.5	70	0.97	3.00	–2.76	0.69
21	Eptifibatide	85.0 (patient)	85.0	84	81.0	15 800	195.06	8.36	4.94	3.70
22	Eptifibatide	74.0 (unknown)	74.0	75	78.0	13 600	174.00	3.33	–5.13	–3.85
23	Eptifibatide	102.0 (patient)	102.0	102	101.5	18 000	177.34	1.48	0.49	0.49
24	Eptifibatide	88.8 (actual)	88.8	87	88.0	15 800	179.55	0.25	0.91	–1.14
25	Eptifibatide	79.0 (unknown)	79.0	80	80.5	14 600	181.37	0.76	–1.86	–0.62
26	Eptifibatide	85.0 (unknown)	85.0	84	86.0	15 800	183.70	2.06	–1.16	–2.33
27	Enoxaparin	78.0 (unknown)	78.0	76	72.5	80	1.10	10.00	7.59	4.83
28	Enoxaparin	107.9 (actual)	107.9	105	107.0	100	0.93	7.00	0.84	–1.87
29	Eptifibatide	80.0 (unknown)	80.0	77	79.0	14 400	182.28	1.27	1.27	–2.53
30	Enoxaparin	57.0 (actual)	59.0	57	57.0	60	1.05	5.00	3.51	0.00
31	Eptifibatide	97.5 (unknown)	97.5	98	104.0	18 000	173.00	3.89	–6.25	–5.77
32	Enoxaparin	84.0 (patient)	84.0	84	81.5	80	0.98	2.00	3.07	3.07
33	Tirofiban	79.5 (patient)	79.5	80	73.0	900	0.41	2.50	8.90	9.59
34	Eptifibatide	78.0 (patient)	78.0	78	81.5	13 600	166.87	7.29	–4.29	–4.29
35	Enoxaparin	118.0 (patient)	118.0	120	139.0	100	0.72	28.00	–15.11	–13.67
36	Tenecteplase	118.0 (patient)	118.0	120	139.0	50	0.36	–28.00	–15.11	–13.67
37	Eptifibatide	102.0 (patient)	102.0	102	105.0	18 000	171.43	4.76	–2.86	–2.86
38	Enoxaparin	89.0 (actual)	89.0	82	90.0	90	1.00	0.00	–1.11	–8.89

Note: HCP = estimate by health care provider.
*Codes 7 and 8 apply to the same patient, as do codes 12 and 13, codes 18 and 19, and codes 35 and 36.
†Enoxaparin and tenecteplase doses are in milligrams; eptifibatide and tirofiban doses are in micrograms.
‡Dosing error = [(actual dose – ideal dose)/ideal dose] x 100.
§Error in dosing weight = [(dosing weight – actual weight)/actual weight] x 100.
‖Error in stated weight = [(patient's stated weight – actual weight)/actual weight] x 100.

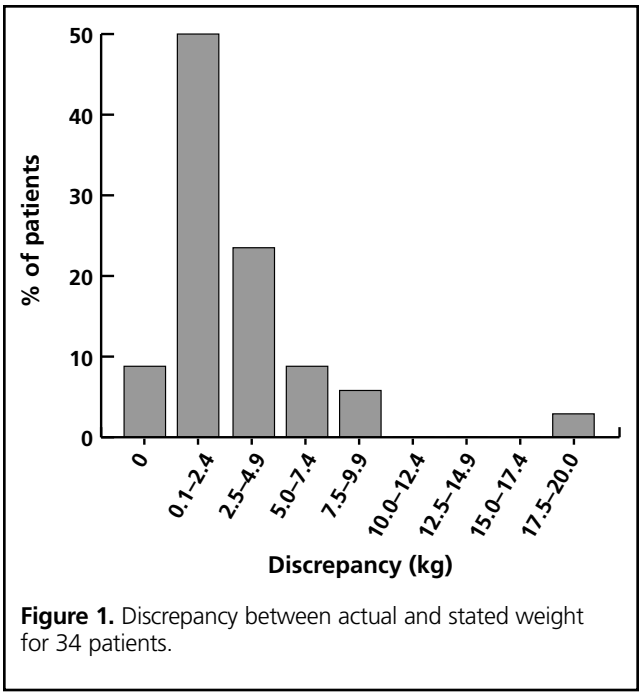

Figure 1. Discrepancy between actual and stated weight for 34 patients.

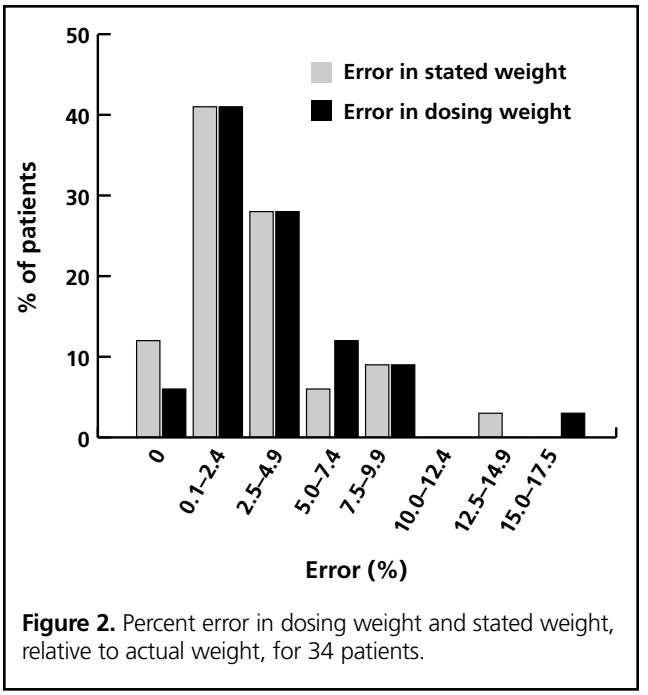

Figure 2. Percent error in dosing weight and stated weight, relative to actual weight, for 34 patients.

Dosing Outcomes

Enoxaparin

Enoxaparin doses of 1 mg/kg are associated with a lower risk of major hemorrhage than doses of 1.25 mg/kg, and a range of 0.9 to 1.1 mg/kg has been determined as acceptable at the RQHR. The enoxaparin doses in this study ranged from 0.72 to 1.10 mg/kg (mean 0.99, standard deviation [SD] 7.67). This value was not significantly different from the literature standard of 1 mg/kg (p = 0.68). The percent dosing error ranged from 0 to 2.4% (in 8 of 19 patients) up to greater than 15% (in 1 of 19 patients) (Figure 3). Enoxaparin dosing errors of greater than 25% lead to poorer patient outcomes including major hemorrhage[1]; however, it is not known if this risk increases linearly over the range of error.

Of the 19 patients who received enoxaparin, 1 (5%) required an intervention: the enoxaparin dose had to be reduced because of a weight discrepancy of 4 kg. The origin of the weight used for enoxaparin dosing in this patient was unknown.

Another patient overestimated his weight by 8 kg but no change in dose was required, because of the dose ranges employed on the preprinted order forms. One morbidly obese patient received a dose of 0.72 mg/kg; however, current guidelines recommend a dose of 100 mg every 12 h for all patients over 95 kg, so no intervention was required. Of note are recent studies indicating that weight, body mass index, and body surface area may affect the anti-Xa levels of obese patients treated with low-molecular-weight-heparins,[12,13] and it has been suggested that weight-based regimens with no ceiling dose be used for obese patients.[12,13] The dosing of low-molecular-weight heparin in this population continues to be studied and debated, and hopefully a definitive answer will be available soon.

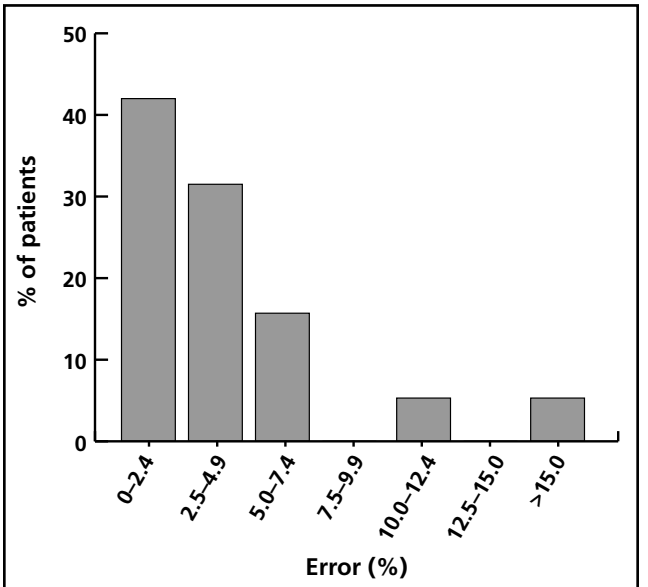

Figure 3. Percent error in dosing weight for enoxaparin for 19 patients.

Eptifibatide

In the dose-ranging trial,[5] the dose of eptifibatide was increased as safety endpoints were met. A bolus dose of 135 $\mu g \cdot kg^{-1} \cdot min^{-1}$ was associated with TIMI grade 3 scores

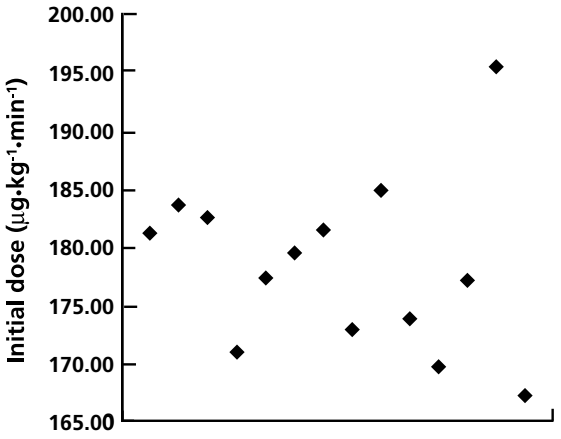

Figure 4. Initial dose of eptifibatide received by 14 patients.

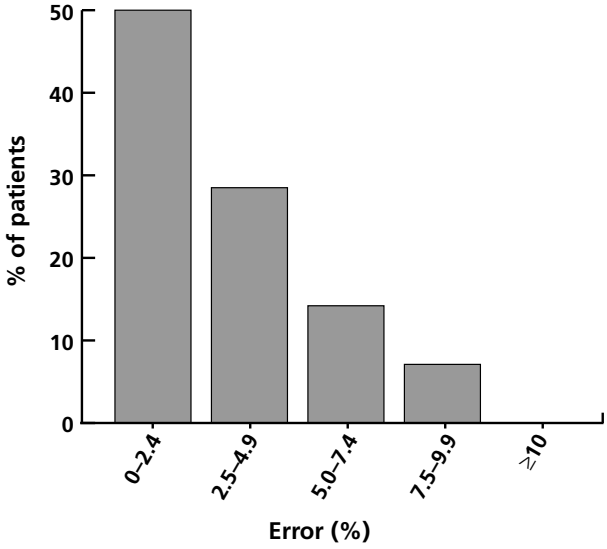

Figure 5. Percent error in dosing weight for eptifibatide for 14 patients.

in 43% and 57% of patients in each of 2 arms of the trial. A bolus dose of 180 µg·kg^{-1}·min^{-1} was associated with TIMI grade 3 flow reperfusion in 71% of patients. The overall dose range observed in the current study was 167 to 195 µg·kg^{-1}·min^{-1} (mean 178.30, SD 7.29) (Figure 4). These doses were not statistically different from the gold standard of 180 µg·kg^{-1}·min^{-1} (p = 0.43).

Of the 14 patients who received eptifibatide, 9 (64%) received an accurate dose. The other 5 patients (36%) required a dose change once actual weight was determined. For one patient the dose was too high because of a 4-kg weight discrepancy; he required a reduction in his maintenance infusion dose. Three patients were being underdosed because of discrepancies of 3 kg, 3.5 kg, and 6 kg, respectively, and required an increase in the maintenance infusion rate. The fifth patient would have required a dosage increase because of a weight difference of 3 kg, but no intervention was performed because the infusion had already been discontinued.

Three patients (21%) had a dosing error of at least 5% on the basis of actual weight (Figure 5). For eptifibatide the range of error at which patient outcomes will be most affected is not clear. The dose-ranging trial[5] examined doses that differed from the gold standard of 180 µg·kg^{-1}·min^{-1} by a range of 25% to 80% (i.e., 36 to 135 µg·kg^{-1}·min^{-1}). Of the patients who received 135 µg·kg^{-1}·min^{-1} (25% dosing difference), 57% achieved TIMI grade 3 flow, whereas 71% of patients who received 180 µg·kg^{-1}·min^{-1} achieved this flow. It is not known if reperfusion decreases linearly with a decrease in eptifibatide dose.

Among the patients in the current study who had dosing errors, only one chart weight was of unknown origin; the remainder of errors occurred in patients who had provided estimates of their own weight.

Tirofiban

On the basis of manufacturer recommendations, bolus doses of tirofiban should be 0.4 µg·kg^{-1}·min^{-1} in patients with estimated creatinine clearances greater than 30 mL/min and 0.2 µg·kg^{-1}·min^{-1} in patients with estimated creatinine clearances less than 30 mL/min. Three of the four patients who received tirofiban in this study received the correct dose. However, one patient with an estimated creatinine clearance greater than 30 mL/min received only 0.2 µg·kg^{-1}·min^{-1} (rather than 0.4 µg·kg^{-1}·min^{-1}) (Figure 6), a dosing error of 50%. This error was a result of misreading and incorrect completion of the preprinted order form, rather than use of an inaccurate weight. A second patient would have received the wrong dose for his weight, but because the preprinted order form was misread and filled in incorrectly, the correct dose for his body weight was actually received.

Dose increases of 50% correlated with increased bleeding in the dose-ranging trial[6]; however, that study was underpowered to detect differences in clinical outcome. The range in percent error at which adverse clinical outcomes can be expected remains unknown.

Of the 4 patients receiving this drug, only 1 had an actual weight recorded; 2 weights were of unknown origin and 1 was a patient estimate.

Tenecteplase

Only one patient in this study received tenecteplase. Doses of 0.5 mg/kg of tenecteplase achieve TIMI grade 3 flow.[2] However, current manufacturer recommendations suggest that all patients over 90 kg should receive a fixed dose of 50 mg.[3] This 50-mg dose translated to only

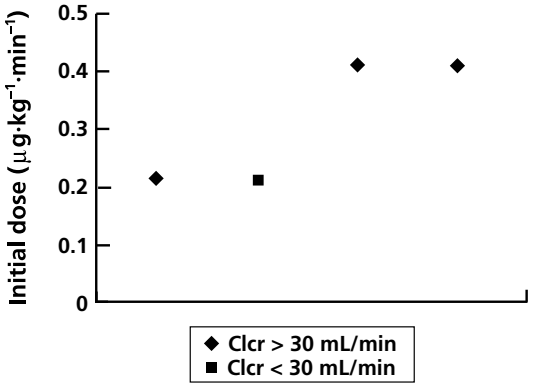

Figure 6. Initial dose of tirofiban received by 4 patients.

0.36 mg/kg in the single patient receiving tenecteplase in this study, who was obese, a 28% dosing error relative to the ideal of 0.5 mg/kg. However, this would not be considered an error given the manufacturer's current dose recommendations.

DISCUSSION

In this study fewer than half of the patients were weighed before their medication was prescribed and administered. None of the patients who had been weighed required dose changes. Three patients who provided estimates of their own weight required dose changes, and 4 of those with a recorded weight from an unknown source required dose changes. Given the need for interventions in 21% of the patients (none of whom were actually weighed), it seems prudent to obtain actual weights for patients who are receiving enoxaparin, eptifibatide, tirofiban, or tenecteplase. However, discussions with nursing staff have suggested that patients who present with an acute coronary syndrome may not be weighed, because of chest pain or hemodynamic instability. These are valid concerns, and alternative measures, such as sling scales or bed scales, may have to be employed in these cases. Education of nursing and medical staff as to the importance of accurate weights for the provision of optimal medication therapy should be undertaken regularly. The extra time required to use a sling or bed scale should be put into the context of patient safety and the potential for improved outcomes. Patients' stated weights demonstrated the strongest correlation with their actual weights; therefore, when a patient absolutely cannot be weighed, asking the patient for a weight estimate is the best option.

During the study, 2 charts were found in which actual weights for a given patient, measured on 2 different wards with different scales, differed from one another (a 3-kg difference for one patient and a 5-kg difference for the other). These discrepancies would have affected the dose of drug in one patient but not the other. Scales should be calibrated regularly to prevent dosing errors that may result from inaccurate weights. It may be necessary to mandate scale calibration through risk-management efforts, as inaccurate weights can lead to adverse effects and the potential for poorer outcomes.

Misreading of preprinted order forms contributed to medication errors in 3 of the 34 patients. Doses were chosen incorrectly on the basis of the weight used for dosing. It is suggested that new forms for complex dosing regimens be subject to an in-service education process for physicians and nurses before being circulated throughout the hospitals, to ensure readability and lessen the chance for dosing errors.

Eptifibatide was the drug most sensitive to weight-based dosing errors; 5 (36%) of the 14 patients taking this drug required a dose change, whereas only 1 (5%) of the 19 patients receiving enoxaparin needed a dose change. Eptifibatide may have been most affected for a number of reasons. Only high-risk patients receive eptifibatide; these patients are more likely to be unstable and, therefore, to not be weighed. The weight ranges for eptifibatide dosing are tighter than those for enoxaparin, so small differences in weight estimates or between scales may be more noticeable with eptifibatide. Finally, because of small sample size, dosing errors that might have occurred with tirofiban and tenecteplase would not necessarily have been identified.

Patients with dosing errors were more likely to come from the emergency department or the Cardiac Care Unit. Again, these are often the patients at highest risk and their condition may be unstable. Whether these patients are not being weighed because of their instability or because of time constraints remains to be determined.

Further research is necessary to clarify dosing in patients with extremes of body weight in the dosing of these and other drugs. Recommended doses of these drugs are the same for all patients over 90–95 kg. Obese patients whose drug doses were based on current guidelines would appear to be underdosed per kilogram of body weight. Reperfusion did not occur in the patient who received a dose of only 0.36 mg/kg of tenecteplase, and he required coronary artery bypass graft surgery. Although causality cannot be established, it is possible that the current recommendations for tenecteplase dosing in obese patients may be inadequate. Larger studies are required to examine this issue.

Limitations

There was only one weight determination by a health care provider, so no conclusions can be drawn about the

accuracy of health care provider estimates. This study was confined to examining weight accuracies as they related to the dosing of 4 critical drugs. Time constraints prevented the tracking of patient outcomes. It is not known how the accuracy of weights affected the patients in either the short term or the long term.

CONCLUSIONS

Given the vast range of discrepancies in patients' estimated and actual weights across the therapeutic spectrum of each study drug and the need for interventions (because of weight inaccuracies) in 21% of the patients, it would seem prudent to obtain actual weights in patients for whom enoxaparin, eptifibatide, tirofiban, or tenecteplase is prescribed. It is imperative that the scales used to obtain these weights be calibrated regularly to ensure accurate weights and accurate doses. A balance is needed between patient safety during initial instability and the potential for adverse outcomes due to overdosing or underdosing of these drugs. These results suggest that it is most critical to obtain a weight when it is hardest to do so, in high-risk patients receiving eptifibatide. Thus, the challenge is to obtain accurate weights, when required, in the most efficient manner possible. If it is impossible to obtain the actual weight, the patient's own weight estimate should be used, as such estimates were strongly correlated with actual weights in this study.

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