Antithrombin III Doses Rounded to Available Vial Sizes in Critically Ill Pediatric Patients

Winifred M. Stockton, PharmD; Eimeira Padilla-Tolentino, PharmD, PhD; and Carolyn E. Ragsdale, PharmD

OBJECTIVES Children have decreased levels of antithrombin III (AT III) compared to adults. These levels may be further decreased during acute illness. Administration of exogenous AT III can increase anticoagulant efficacy. The objective of this study was to evaluate AT III doses rounded to available vial sizes compared to partial vial doses in critically ill pediatric patients, including patients receiving extracorporeal membrane oxygenation (ECMO) and continuous renal replacement therapy (CRRT).

METHOD This retrospective review evaluated pediatric patients 0-18 years of age admitted to a 24-bed medical/surgical pediatric intensive care unit between June 1, 2012, and December 31, 2014, who received plasma-derived AT III. Patients received unfractionated heparin, low-molecular-weight heparin, or no anticoagulation. This review included patients who received ECMO and CRRT.

RESULTS Eighty doses of AT III were administered to 24 patients (38 full vial size doses and 42 partial vial size doses). The AT III level following dose administration was $\geq 80\%$ for 26 full vial doses (70%) and 16 partial vial doses (41%; $p = 0.010$). For patients who received multiple doses of AT III, the median time between doses was 45 hours following full vial doses, and 23 hours following partial vial doses ($p = 0.011$). Seven patients (29%) had documentation of new or increased bleeding. The median waste prevented from rounding doses to full vial sizes was 363 units.

CONCLUSIONS After receiving AT III doses rounded to full vial sizes, patients were more likely to have a therapeutic AT III level and a longer interval between administrations. Rounding AT III doses to full vial sizes reduces waste and can result in cost savings.

ABBREVIATIONS AT III, antithrombin III; AWP, average wholesale price; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; PICU, pediatric intensive care unit

KEYWORDS antithrombin III; child; continuous renal replacement therapy; cost savings; extracorporeal membrane oxygenation; pediatrics; renal replacement therapy; standardized dosing; Thrombate III

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Introduction

Antithrombin III (AT III) is a naturally occurring inhibitor of clotting factors including factor Xa and thrombin.^{1,3} Thrombate III (Grifols, Research Triangle Park, NC) is a preparation of human AT III which is indicated in treating hereditary antithrombin deficiency.⁴ Although AT III is indicated only for hereditary antithrombin deficiency in adults, a recent review of AT III use in children less than 18 years of age found that 97% of patients received AT III for indications other than congenital antithrombin deficiency.¹ Acquired AT III deficiency is more common than congenital deficiency and results from decreased synthesis, accelerated consumption, increased excretion, or drug exposure. Causes of decreased synthesis include liver disease and prematurity. Accelerated consumption occurs in disease states such as disseminated intravascular coagulation or after surgery.^{1,2} Also, when a patient is treated with extracorporeal membrane oxygenation (ECMO), increased endog-

enous AT III consumption occurs from blood exposure to the ECMO circuit.⁵⁻⁷ Increased excretion may result from nephrotic syndrome, protein-losing enteropathy, inflammatory bowel disease, and chylothoraces. Drug-induced mechanisms that cause AT III consumption include L-asparaginase, estrogen, and heparin.^{1,2} Additionally, it has been shown that, compared with adults, children have decreased levels of factors XII, XI, X, IX, VII, and II, plasminogen and tissue plasminogen activator, and antithrombin. Thus, an inherently lower level of antithrombin in children may be further intensified by external factors.⁸

Heparin results in 1000-fold potentiation of the anticoagulant activity of antithrombin, and therefore, antithrombin deficiency affects physiologic response to anticoagulants.^{1,8} However, heparin administration also increases turnover of AT III, which may lead to an acquired deficiency in continuous or intermittent administration.² Continuous heparin infusion is a common method of anticoagulation in patients receiving ECMO

or continuous renal replacement therapy (CRRT).^{5-7,9} Patients treated with ECMO and CRRT have potential for developing antithrombin deficiency due to both heparin administration and blood exposure to the artificial surface of the ECMO circuit.⁵ Exogenous AT III is often administered to patients with AT III deficiency who are receiving heparin infusions in an effort to increase efficacy of heparin, thus lowering the heparin infusion rates required to achieve therapeutic partial thromboplastin time or activated clotting time.^{3,8} Additionally, higher AT III levels can result in more effective low-molecular-weight heparin doses.¹⁰

The formulary AT III product at this institution is Thrombate III (Grifols, Research Triangle Park, NC). According to the manufacturer, AT III doses are calculated by the equation [units required (IU) = (desired AT level % – baseline AT level %) × body weight (kg)/1.4]. Targeting a desired AT III level of 80% to 120% of normal activity is the recommended goal according to the manufacturer.⁴ Thrombate III is available in vials of approximately 500 units (exact potency is specified on individual vials). As of April 2016, the average wholesale price (AWP) was USD \$4.66 per unit.¹¹ Considering the high cost of AT III, rounding doses to available vial sizes may reduce waste and result in cost savings. Prescribing doses that match vial sizes can be difficult for providers, considering the exact potency of the product varies. Therefore, a protocol approved by the Pharmacy and Therapeutics Committee at this institution allows pharmacists to automatically round doses of AT III to full vial sizes if the vial size is within 10% of the originally prescribed dose. However, because the dose to administer is based on patient weight and AT III levels, young patients may require doses greater than 10% below commercially available vial sizes. The result is potential for a large amount of waste.³ Safely rounding doses in young patients to available vial sizes may lead to cost savings.

The primary objective of this study was to evaluate the increase in AT III levels following administration of AT III doses rounded to available vial sizes compared to partial vial doses, in critically ill pediatric patients. The secondary objectives were to evaluate documentation of bleeding events, a potential indicator of safety, and to evaluate the potential cost savings resulting from doses rounded to full vial sizes.

Materials and Methods

This study was a retrospective review performed to evaluate a cohort of pediatric patients admitted to a 24-bed medical/surgical pediatric intensive care unit (PICU) between June 1, 2012, and December 31, 2014. The study was approved by the Seton Healthcare Family Institutional Review Board and granted a waiver of the informed consent requirements. Patients were included in the study if they were less than or equal to 18 years of age and had received 1 or more doses of plasma-

derived AT III (Thrombate III; Grifols) while admitted to the PICU during the defined study period. Doses of AT III were ordered as single doses to be administered by intravenous infusion using a syringe pump with an infusion duration between 10 and 20 minutes according to the usual practice of the institution. A follow-up AT III level was often obtained within 24 hours to verify the target range had been achieved. After the target was achieved, additional levels were obtained at the discretion of the provider, if the suspected cause of AT III deficiency continued.

This review consisted of patients receiving unfractionated heparin continuous infusions, subcutaneous low-molecular-weight heparin, or no anticoagulation. Some of the patients in this review were receiving ECMO or CRRT at the time AT III was administered. Institution-specific ECMO equipment included Sorin SII roller pump (Sorin Group, Milan, Italy), Maquet Quadrox D with SOFTLINE Coating oxygenator (MAQUET Holding B.V. & Co. KG, Rastatt, Germany), and Terumo tubing pack with Xcoating (Terumo Corporation, Tokyo, Japan). Institution-specific CRRT equipment included Gambro Prismaflex system, HF1000 filter (Baxter, Deerfield, IL).

Demographic information documented for each patient included age, weight, ECMO status, and CRRT status. Data collected pertaining to the AT III dose included the dose ordered, the date and time the AT III dose was administered, and the exact vial size used to prepare the dose. Because the potency of vials varies, the specific vial sizes used for each dose were determined for this retrospective study by reviewing the pharmacy compounding logs, which contain the exact vial sizes for all doses of AT III prepared at this institution. The most recent AT III level prior to AT III dose administration and the first AT III level after dose administration were recorded. Finally, the medical record was reviewed for documentation of bleeding before and after AT III doses were given.

Medians were reported as a measure of central tendency. The Mann-Whitney *U* and chi-square tests were used to analyze time between repeat AT III doses and success in achieving AT III level $\geq 80\%$ after AT III dose administration, respectively. Fisher's exact test was used to analyze the incidence of new or increased bleeding. Data were analyzed using SPSS version 17.0 software (IBM, Armonk, NY).

Results

During the study period, 80 doses of AT III were administered to 24 patients as doses rounded to full vial sizes (38 doses) or partial vials (42 doses). Twelve patients received full vial doses, 8 patients received partial vial doses, and 4 patients received a combination of full and partial vial doses.

Table 1 describes patient demographics, clinical characteristics, prescribed anticoagulation, and indica-

Table 1. Patient Demographics

Characteristic	Full Vial Dose (n = 38)	Partial Vial Dose (n = 42)
Age on admission*	9.5 mo (5 days – 17 yr)	2 days (2 days – 2 mo)
Weight on admission, kg*	9.67 (3.2 – 94.3)	3.38 (2 – 6.9)
Indication		
ECMO ^{†‡}	17 (44.7%)	36 (85.7%)
CRRT ^{†‡}	21 (55.3%)	19 (45.2%)
Other ^{†‡}	15 (39.5%)	5 (11.9%)
Anticoagulation		
Continuous infusion heparin [†]	28 (73.7%)	42 (100%)
Subcutaneous enoxaparin [†]	3 (7.9%)	0 (0)
No anticoagulation [†]	7 (18.4%)	0 (0)

CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation

* Median (range)

[†] n (%)

[‡] Some patients received antithrombin III doses due to anticoagulation for both ECMO and CRRT

tion for AT III. Sixty doses of AT III (75%) were administered to patients due to anticoagulation for ECMO, CRRT, or both ECMO and CRRT. Twenty doses (25%) were administered to patients not receiving ECMO or CRRT; these patients had other indications for AT III administration including anticoagulation due to portal vein thrombosis, a Blalock-Taussig shunt, central sinus thrombosis, thrombosis of iliac vein, hypercoagulopathy risk due to malignancy, carotid dissection, and central sinus venous thrombosis. Two patients received AT III doses due to AT III levels obtained in preparation for ECMO or CRRT initiation. Additionally, 7 doses of AT III (9%) were administered to 2 patients who were not receiving anticoagulation; these patients received AT III replacement due to nephrotic syndrome and protein-losing enteropathy.

Following AT III administration, the AT III level was evaluated to determine the success in achieving a target level of $\geq 80\%$. Four doses did not have a follow-up ATIII level recorded (1 full vial dose and 3 partial vial doses) and were not included in the statistical analysis. The AT III level recorded after the dose was administered was $\geq 80\%$ for 70% (26 of 37 doses) of the full vial doses and 41% (16 of 39 doses) of the partial vial doses, χ^2 (1, n = 76) = 6.57; p = 0.01 (Figure 1). Due to uneven age distribution between patients receiving full vial doses and partial vial doses, a subgroup analysis was performed. The percentage of doses resulting in an AT III level $\geq 80\%$ was compared for patients < 1 year of age and ≥ 1 year of age. No patient ≥ 1 year of age received a partial vial dose. For patients < 1 year of age, the ATIII level recorded after the dose was administered was $\geq 80\%$ for 71% (15 of 21 doses) of the full vial doses and 41% (16 of 39 doses) of the partial vial doses, χ^2 (1, n = 60) = 5.05; p = 0.025 (Figure 1). A subgroup analysis was also performed for patients receiving ECMO and CRRT. Of those patients receiving ECMO, 94% (16 of 17 doses)

of the full vial doses and 40% (14 of 35 doses) of the partial vial doses had a corresponding AT III level $\geq 80\%$ after AT III dose administration, χ^2 (1, n = 52) = 13.73; p < 0.001 (Figure 2). Of those patients receiving CRRT, the AT III level was $\geq 80\%$ after AT III dose administration for 81% (17 of 21 doses) of full vial doses and 44% (8 of 18 doses) of partial vial doses, χ^2 (1, n = 39) = 5.61; p = 0.018 (Figure 3).

The median number of doses per patient was 2 doses (range, 1-14 doses). Fifteen of the 24 patients received multiples doses of AT III. Of the patients who received multiple doses, 6 patients received full vial doses (40%), 5 patients received partial vial doses (33%), and 4 patients received a combination of full vial and partial vial doses (27%). The time in hours before doses were repeated was greater after full vial doses (median = 45 hours) versus after partial vial doses (median = 23 hours) ($U = 232.5$; p = 0.011, r [effect size] = 0.34) (Figure 4).

In the 24 hours prior to the first AT III dose administration, 10 patients (42%) had documentation of bleeding. Seven patients (29%) had new or increased bleeding documented in progress notes or on imaging reports within 24 hours after administration of an AT III dose. New or increased bleeding was not significantly different between groups. One patient (4%) received full vial doses, 3 patients (13%) received partial vial doses, and 3 patients (13%) received a combination of full vial and partial vial doses. The patient who received only a full vial dose had reports of blood-tinged respiratory secretions. In the 3 patients who received only partial vial doses, there were reports of a scalp hematoma, bleeding from a wound vacuum, and an intracranial hemorrhage. The 3 patients who received a combination of full and partial vial doses had documentation of bleeding from the intrajugular catheter site; bleeding from the endotracheal tube; and bleeding from the mouth, nasogastric tube, Foley catheter, an intravenous

Figure 1. Antithrombin III level $\geq 80\%$ after antithrombin III dose administration by age.

■ Full vial dose; □ Partial vial dose

*There were no patients ≥ 1 year of age who received a partial vial dose.

site, and rectum. This institution has a protocol which allows pharmacists to round AT III doses up to a 10% deviation from the ordered dose in order to dispense a full vial and minimize waste. In this retrospective review, 10 patients received at least 1 full vial dose that was rounded up by more than 10%; of these 10 patients, 4 patients (40%) had new or increased bleeding (p value not significant).

Table 2 provides information about the doses rounded to full vial sizes. The median full vial dose administered was 559 units. Considering patient weight, the median full vial dose administered was 56 units/kg. At this institution, 120% is often the desired AT III level used to calculate AT III replacement doses. Assuming a desired AT III level of 120%, the “units required” was calculated for each full vial dose by using the manufacturer’s recommended equation. This calculated dose was dependent on both the patient weight and the AT III level. The median absolute difference between this calculated dose and the dose actually administered after rounding to a full vial size was 378 units. Considering patient weight, the median absolute difference was 19 units/kg.

Of the doses rounded to full vial sizes ($n = 38$), 11 were rounded by more than 500 units. It is assumed that these doses differed from the calculated dose for reasons other than rounding to available vial sizes. In order to evaluate the potential cost savings, additional analysis was performed considering only full vial doses rounded by less than 500 units ($n = 27$). Nineteen of these doses were rounded up (median increase of 332 units), and 8 were rounded down (median decrease of 97 units). Assuming a desired AT III level of 120%, the median absolute difference between the calculated dose required and the dose actually administered after rounding to a full vial size was 189 units. Considering patient weight, the median difference was 18 units/kg. Cost savings were calculated as AWP multiplied by units of waste prevented. In the event that a dose was rounded up, the waste prevented was equivalent

Figure 2. Antithrombin III level $\geq 80\%$ after antithrombin III dose administration by extracorporeal membrane oxygenation status.

ECMO, extracorporeal membrane oxygenation

■ Full vial dose; □ Partial vial dose

to the difference between the calculated dose and the dose administered. For example, if a calculated dose of 465 units is rounded up to 500-unit vial size, the 500 units administered minus the 465 units calculated = 35 units of waste prevented. In the event that the dose was rounded down, the waste prevented was 500 units minus the amount of units rounded down. For example, consider a 580-unit calculated dose that is rounded down to 500 units of vial size. The dose was rounded by 80 units. The waste prevented is the 500 units vial size minus 80 units rounded down = 420 units of waste prevented. The median units of waste prevented for a single dose was 363 units. Considering an AWP of USD \$4.66 per unit, this yields a median cost savings of USD \$1,692 for a single dose.

Discussion

This retrospective review of AT III doses administered in the PICU found that AT III replacement therapy administered as doses rounded to full vial sizes resulted in a significant improvement in achieving target AT III levels for patients receiving ECMO or CRRT compared to partial vial doses.

A recent study of AT III use found that from 2002 to 2011 there was a 5-fold increase in AT III use; ECMO was the most common procedure associated with AT III administration.¹ It is well documented in published reports that therapeutic drug monitoring is needed for patients on ECMO and/or CRRT due to drug interactions with the circuit but also due to changes in volume of distribution due to the blood volume of the circuit (especially for smaller patients).^{5,12} The prime volume (volume of blood needed to prime the circuit) at this institution for ECMO and CRRT for patients less than 10 kg are 425 mL and 165 mL, respectively. Considering a neonate has approximately 80 mL per kg of blood, the prime volumes of the neonatal ECMO and CRRT circuits are equivalent to the blood volumes of a 5.3-kg and a 2.1-kg

Figure 3. Antithrombin III level $\geq 80\%$ after antithrombin III dose administration by continuous renal replacement therapy status.

neonate, respectively, or the blood volume of a 7.4-kg neonate if both extracorporeal circuits are combined.^{13,14} The median weight in this study was 9.67 kg, therefore, circuit volumes greatly impact AT III by diluting the AT III replacement dose over a larger blood volume. This concept is what leads to subtherapeutic AT III levels in the partial vial group when using the manufacturer dosing equation based on body weight. At this institution some providers may use an adjusted patient weight to include the circuit volume to help achieve therapeutic AT III levels, as well as round to full vial size doses of AT III, which also has a cost savings benefit.

ECMO is associated with increased morbidity and mortality, and bleeding is the most common complication for patients receiving ECMO support. Heparin infusions, platelet dysfunction, and clotting factor hemodilution contribute to increased bleeding.¹⁵ The 2013 report of the Extracorporeal Life Support Organization (ELSO) registry showed that up to 11% of children have intracranial hemorrhage and 31% of children experience bleeding at the surgical or cannulation site. Bleeding events must also be balanced with the risk of thrombosis, as thromboses are also common, occurring most commonly in the oxygenator 17% of the time.¹⁶

Complications while receiving ECMO may be related to underlying pathology or to ECMO itself.¹⁵ Ryerson et al⁸ conducted a retrospective cohort study of AT III doses administered to infants and children. The practice at their institution was to prescribe a full vial of 1000 units in contrast to the manufacturer's calculated dose. The median dose reported by Ryerson et al⁸ was 311 units/kg for patients ≤ 3 months of age and 158 units/kg for patients > 3 months of age. The authors concluded that there were no clinically relevant acute major bleeding or clinically relevant bleeding episodes that were not related to the underlying condition.⁸ Niebler et al¹⁶ performed a retrospective review of AT III doses administered to infants and children receiving ECMO. The AT III doses administered were determined by the treating

Figure 4. Median time between antithrombin III dose administrations.

physician and, at times, were rounded to full vial sizes. Chest tube or measured dressing output and packed red blood cell transfusion volumes were compared to determine the effect of AT III doses on hemorrhagic complications. Comparing the entire cohort (median dose 82.8 units/kg) with a subgroup that received AT III doses greater than 100 units/kg (mean dose 177 units/kg), they also found no differences in measurements of bleeding. In this retrospective review, patients receiving full vial doses received a median dose of 559 units (range 532 - 4950 units) of AT III. Accounting for patient weight, the median dose was 56 units/kg (range 8 - 181 units/kg). There were reports of new and increased bleeding after AT III administration in this study; however, there were no significant differences found between the bleeding that occurred after full vial doses versus that after partial vial doses or after doses rounded by greater than 10% versus those rounded according to the institution's protocol.

Kozul et al³ performed a clinical audit of pediatric patients treated with AT III. They reported the median dose administered was 40 units/kg (range 11 - 200 units/kg). They evaluated achievement of goal AT III levels post antithrombin administration and found 50% of doses resulted in AT III levels within reference range, 30% of doses resulted in AT III levels outside of the reference range, and 20% did not have follow-up AT III levels. In this retrospective review, the median dose administered was 56 units/kg (range 8 - 111 units/kg) of AT III. A higher percentage of full vial doses in this study resulted in achievement of a target AT III level post antithrombin administration. The target AT III level was achieved after 70% of full vial dose administrations, and this percentage increased to 94% in the subgroup analysis of patients receiving ECMO and 81% in the subgroup analysis of patients receiving CRRT.

The brand of AT III used was different among these studies, limiting cross-comparison of AT III doses. The manufacturer-recommended calculation of units required for AT III replacement doses is unique to each product. The AT III product used by Ryerson et al⁸ was Antithrombin III Immuno (Baxter AG, Vienna, Austria). The manufacturer for that product recommends calculating dose units required by using the equation

Table 2. Characteristics of Doses Rounded to Full Vial Sizes

Characteristic	All Full Vial Doses (n = 38)	Full Vial Doses Rounded < 500 Units (n = 27)
Calculated dose, units* [†]	549 (104 – 4984)	392 (104 – 4850)
Calculated dose, units/kg* [†]	46 (29 – 79)	43 (29 – 79)
Dose administered, units*	559 (532 – 4950)	550 (532 – 4950)
Dose administered, units/kg*	56 (8 – 181)	63 (25 – 181)
Dose rounding, units* [‡]	378 (6 – 3364)	189 (6 – 431)
Dose rounding, units/kg* [‡]	19 (1 – 121)	18 (1 – 121)

* Median (range)

[†] Units required per the manufacturer-recommended equation based upon a desired antithrombin III level of 120%[‡] The absolute difference between the units administered (rounded to full vial sizes) and the units required

[dose (in IU) = (desired AT III activity (%) – baseline AT III activity (%) × body weight (in kg)/2%]; for disseminated intravascular coagulation, the equation is adjusted to divide by 1%.¹⁷ The AT III product used by Kozul et al³ was Thrombotrol (Commonwealth Serum Laboratories, Melbourne, Australia). The manufacturer-recommended equation for this product is [dose required (IU) = (desired – pretreatment AT III level) × weight (kg)/2.2], where the AT III level is expressed as a percentage of normal level based on functional AT III assay.¹⁸ The AT III product used in this retrospective review and that conducted by Niebler et al⁶ was Thrombate III (Grifols). According to the manufacturer, AT III doses are calculated by using the equation [units required (IU) = (desired AT level % – baseline AT level %) × body weight (kg)/1.4]. The differences in recommended dosing calculations make comparison across studies difficult.

Patients may require multiple doses of AT III. In a retrospective review of AT III use in pediatric patients, Ryerson et al⁸ found that the median number of AT III doses per patient was 2 doses (range 1 - 14 doses). Kozul et al³ evaluated 2 cohorts and reported the median number of doses to be 2 doses (range 1 - 8 doses) in the first cohort and 2 doses (range 1 - 15 doses) in the second cohort. The number of repeat doses in this study (median 2 doses, range 1-14 doses) was similar to those previous reports. Due to a short stability of 3 hours, each vial of AT III will most likely only be used to prepare a single dose.^{3,4} When administering doses of AT III, the manufacturer recommends monitoring plasma AT III levels in order to achieve a target between 80% and 120%.⁴ An AT III level < 80% after AT III dose administration often results in prescribing of additional doses at this institution. Patients in this study were more likely to have an AT III level ≥80% after a full vial dose was given. When multiple doses were needed, patients had a significantly longer interval between administrations after a full vial dose was administered. Therefore, patients receiving full vial doses may benefit from less frequent AT III dose administrations. Additionally, preventing waste from partial vials by rounding doses to full vial sizes may present a potential cost

savings. In this retrospective review, rounding doses to full vial sizes reduced waste by a median of 363 units per dose, which yields a median cost savings of USD \$1,692 per dose.

There were several limitations to this retrospective review of AT III doses rounded to available vial sizes. This study had a small sample size, and many patients received multiple doses. A total of 80 doses of AT III were administered during the review period, but due to multiple dose administrations to individual patients, there were only 24 patients evaluated in the study. This was not a randomized study. The decision to round AT III doses was dependent upon the preferences of staff at the time an AT III dose was indicated. This retrospective study was intended to determine whether the differences in prescribing at this institution affected the follow-up AT III level and to collect information regarding bleeding events. Additionally, there is a hospital policy for rounding doses of AT III to full vial sizes up to a 10% deviation from the original dose. As a result, most of the older children automatically received doses rounded to a full vial size. Only in younger children was the patient weight low enough such that rounding to a full vial would be greater than a 10% deviation from the original dose, resulting in a dose dispensed as a partial vial unless the provider manually rounded the dose to the vial size. Therefore, there was an uneven age distribution between the groups receiving full vial versus those receiving partial vial doses. In addition, a larger percentage of partial vial doses were administered to patients receiving ECMO than doses rounded to full vial sizes. This difference likely reflects the young age of many patients receiving ECMO and the higher distribution of partial vial doses in younger patients. Finally, bleeding assessment in this retrospective review was dependent on medical record documentation. The majority of the documentation of bleeding events was found in daily progress notes written by providers and reports from radiology procedures. As a result, the accuracy of evaluating safety based on bleeding events was heavily influenced by the thoroughness of documentation in provider progress notes.

Conclusions

AT III replacement therapy administered as doses rounded to full vial sizes resulted in increased achievement of target AT III levels in patients receiving ECMO or CRRT. AT III doses rounded to full vial sizes also resulted in longer time intervals before additional doses were needed. Furthermore, rounding AT III doses to full vial sizes reduced waste, providing an opportunity for cost savings. However, further studies are needed to improve understanding of the bleeding risks and ensure patient safety and to explore the dose response relationship in patients receiving ECMO and CRRT.

ARTICLE INFORMATION

Affiliations Department of Pharmacy, Children's Hospital of Orange County, Orange, California (WMS); Department of Pharmacy, Seton Healthcare Family, Austin, Texas (EPT); Department of Pharmacy, Dell Children's Medical Center of Central Texas, Seton Healthcare Family, Austin, Texas (CER)

Correspondence Carolyn E. Ragsdale, PharmD; carolynragsdale@gmail.com

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