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About the cover:

From acting as a bridge for home-based patients completing their daily infusions of remdesivir during the COVID-19 pandemic to therapeutic monitoring and interventions for outpatient parenteral anti-infective therapy, home infusion pharmacists answer “yes” to the question “Who wants to be responsible for the infusion medication plan of care and the collaborative communication the plan of care requires?”

A Retrospective Quality Improvement Study of Pharmacist-Directed Vancomycin Dosing Among Adult Home Infusion Patients

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Shelby George, PharmD; Megan K. Zielke, PharmD, BCCCP

A Retrospective Descriptive Study of Remdesivir Treatment in the Home or Outpatient Setting Among Adult Patients Diagnosed with Coronavirus Disease 2019 (COVID-19)

Julia K. Nguyen, PharmD; Rulin Hechter, MD, PhD, MS;
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Acquired Immunodeficiency Syndrome in Hemophilia A: A Case Report and Literature Review

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From the Editor

Pharmacist Service at the Center of Care

Michelle C. Simpson, PharmD, BCSCP

Editor-in-Chief, *Infusion Journal*

This issue of *Infusion Journal* brings you 3 articles highlighting diverse ways pharmacist professional services have been applied in home infusion and it continues a pattern of publishing research articles studying the value pharmacists have on patient outcomes. Pharmacists can be found at the center of the prescription process collaborating and adapting to a seemingly infinite number of individual patient scenarios and clinical task workflows.



Research published in the article, A Retrospective Quality Improvement Study of Pharmacist-Directed Vancomycin Dosing Among Adult Home Infusion Patients, demonstrated the value pharmacists provide through therapeutic monitoring and interventions. Pharmacists were central to the study variables. They were a direct connection point for organizing medication treatment for home infusion patients prescribed outpatient parenteral anti-infective therapy.

Home infusion pharmacist professional services related to the research published in the article, A Retrospective Descriptive Study of Remdesivir Treatment in the Home or Outpatient Setting Among Adult Patients Diagnosed with Coronavirus Disease 2019 (COVID-19), noted a benefit of home infusion pharmacists' ability to procure remdesivir in conjunction with the health system pharmacy. The home infusion pharmacists were the bridge for patients completing their daily infusions at home for 1,776 patients from 5 medical centers during the pandemic when diverting as many appropriate patients as possible from acute care settings was critical.

These 2 articles exemplify the necessity of the pharmacist remaining centrally involved despite differences in professional pharmacy services task categories. Home infusion pharmacists answer yes to the question of who wants to be responsible for the infusion medication plan of care and the collaborative communication the plan of care requires. Putting clinical tasks into standard categories was a first step in moving this type of research forward. A prior issue of *Infusion Journal* featured an article covering home infusion pharmacist professional services studied through time motion reports of clinical tasks in standardized categories. The authors described professional pharmacy services as being organized by a pharmacy and delivered by a pharmacist who applies their specialized knowledge to optimize patient care with the goal to improve health outcomes.^{1,2} After reading the studies here and others, we are able to compare results because the tasks are similarly defined and measured. The therapeutic monitoring and interventions collected by the authors studying pharmacist-driven vancomycin dosing were defined by the same terms as those in prior studies.

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Being a central point of contact and responsibility for pharmacy services leads pharmacists to being involved in a large volume of daily tasks and workflows. This can look like web of communication and documentation between pharmacists, providers, patients, and differing technologies. When measured in terms of individual tasks divided into categories, the amount of pharmacist professional time spent for each task was small, but the number of tasks was enormous. By separating out and analyzing pharmacist time devoted to assessments and interventions in managing medications with clinical monitoring, researchers can determine these task activities averaged 8:16 min/sec in one study and 6:82 min/sec in another.^{1,3} What happens when individual tasks occur concurrently with other tasks is what becomes the framework of keeping the pharmacist centrally located and the organizer of professional pharmacy services.

How pharmacists spend their time and resources makes a big impact and *Infusion Journal* proudly publishes research where the results provide evidence to support the value of pharmacist professional services. This issue even includes a case report where the author described a patient diagnosed with hemophilia A who contracted HIV from contaminated plasma more than 40 years ago and continues to live independently with the support of pharmacist professional services from their home infusion provider.

Infusion Journal's mission is to share original research in infusion therapy conducted by a broad range of infusion specialists that will advance evidence-based practice and shape industry standards. We are dedicated to publishing content that reflects the interest and needs of all professions and represents infusion research. *Infusion Journal* welcomes submissions from authors on topics relevant to infusion therapy administered in the home, clinic, suite, or other outpatient setting.

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A Retrospective Quality Improvement Study of Pharmacist-Directed Vancomycin Dosing Among Adult Home Infusion Patients

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ABSTRACT

Background

Vancomycin is widely used to treat gram-positive infections. Vancomycin therapy is accompanied by the clinical monitoring of trough levels in order to maintain therapeutic efficacy and patient safety. The home infusion patients receiving vancomycin therapy may undergo physiologic changes from inpatient care to home infusion that could affect their response to therapy. Home infusion pharmacists are uniquely positioned to facilitate continued acute monitoring, assess pharmacokinetic changes, and further support the patient transitioning to the post-acute care setting. There is insufficient data regarding the impact of pharmacist-directed vancomycin dosing and utilizing a standardized protocol within the home infusion setting. Using results from this study, this institution intends to demonstrate the value that pharmacists have in recommending therapeutic adjustments, developing a formal pharmacist-directed dosing protocol, and providing education to clinical pharmacists about the use of that protocol.

Methods

This retrospective, quality improvement study characterized data from patients receiving pharmacist-directed vancomycin dosing. This study included patients ≥ 18 years of age who received vancomycin dosed to a goal trough of 15-20 mg/L and were on service between January 1, 2021, and December 31, 2021. The primary objective of this study was to evaluate the efficacy of pharmacist-directed vancomycin therapy in a home infusion setting by analyzing rates of therapeutic trough levels, duration of therapy, and resolution of infection. The secondary objective of this study was to evaluate safety outcomes in patients receiving vancomycin in a home infusion setting by analyzing the incidence of acute kidney injury (AKI).

Results

Thirty-one patients met the inclusion criteria for retrospective analysis. Eighteen patients (58.06%) experienced resolution of infection. Of the patients who did not meet the criteria for resolution of infection, 11 (78.6%) had therapeutic extensions. The median duration for therapeutic extensions was 12 days. The average trough with pharmacist-directed dosing was 16.71 ± 4.84 mg/mL. When assessing the secondary outcomes of patients with supratherapeutic troughs, it was reported that 4 patients (13%) experienced adverse safety events. Two patients (6.5%) experienced AKI secondary to vancomycin therapy. Both patients had supratherapeutic vancomycin troughs at the time of AKI appearance.

Conclusion

Pharmacist-directed dosing led to sustained improvements in therapeutic troughs and maintained a low incidence of AKI.

Keywords: Vancomycin, pharmacokinetic dosing, clinical monitoring, antibiotic, infectious disease, home infusion

Background

Vancomycin, a glycopeptide antibiotic, is widely used to treat various gram-positive infections in inpatient, outpatient, and home infusion health care settings. Vancomycin therapy is accompanied by the clinical monitoring of trough levels in order to maintain therapeutic efficacy and patient safety. Therapeutic efficacy is frequently described as achieving and maintaining vancomycin troughs within goal ranges. Maintenance of therapeutic safety involves the prevention of adverse drug reactions (ADRs), including acute kidney injury (AKI). Vancomycin is associated with a broad incidence of AKI dependent on the study referenced (0-40%).¹ The patients at the greatest risk of experiencing adverse safety outcomes are those who reach supratherapeutic trough levels.¹ Patients more susceptible to reaching supratherapeutic trough levels are those treated to higher goal troughs of 15-20 mg/L.²

Pharmacokinetic vancomycin dosing protocols are widely developed and utilized in inpatient health care settings as they generally have been proven to improve efficacy and safety outcomes associated with patient care. Marquis et al. completed a pre-post study to evaluate the impact and utility of implementing a pharmacist-driven protocol in an inpatient setting.³ The pre-implementation phase involved retrospective audits of medical records for patients receiving vancomycin therapy during a defined time range, and the post-implementation phase involved the utilization of a pharmacist-driven vancomycin protocol, which employed traditional, trough-based, and area under the curve (AUC) pharmacokinetic dosing strategies.³ Data analyses from this study showed improved patient outcomes, including increases in optimal dosing, decreases in nephrotoxicity, and reduced duration of vancomycin therapy after implementation.³ Analyses from this study and studies with similar designs in the inpatient setting also allow institutions to see a pharmacist-driven impact on patient outcomes as they refine vancomycin dosing practices.³⁻⁷ Unfortunately, there is currently insufficient data regarding the impact of pharmacist-directed vancomycin dosing and utilizing a standardized protocol within the home infusion setting.

Patients receiving prolonged courses of vancomycin in the home not only require assessment of therapy-specific parameters on a clinically appropriate schedule, but also, these lab assessments need to be

coordinated with the individual patient's vancomycin administration time. Additionally, patients discharged from the hospital to the home after an acute hospital stay may undergo physiologic changes, including hydration status, from inpatient care to home infusion that could affect their response to vancomycin therapy. Home infusion pharmacists are uniquely positioned to facilitate continued acute monitoring, assess pharmacokinetic changes, and further support patients transitioning to the post-acute care setting. Using results from this study, this institution intends to demonstrate the value that pharmacists have on recommending therapeutic adjustments, develop a formal pharmacist-directed dosing protocol, and provide education to clinical pharmacists about the use of that protocol.

Methods

Study Design

This was a retrospective, quality improvement study, which characterized data from a 12-month sample of patients receiving pharmacist-directed vancomycin dosing. Pharmacist-directed dosing is defined as pharmacist-recommended dose changes provided to and accepted by the prescribing/ managing provider. This study included patients ≥ 18 years of age who received vancomycin dosed to a goal trough of 15-20 mg/L and on service with a home infusion provider servicing Pennsylvania, northeastern West Virginia, eastern Ohio, and western New York between January 1, 2021, and December 31, 2021. The goal trough range was chosen to evaluate outcomes in patients at a higher risk of negative safety outcomes, including AKI. Patients must also have received initial vancomycin therapy or loading doses in the inpatient setting, before transitioning to therapeutic continuation in the home infusion setting. Patients receiving vancomycin for surgical prophylaxis were excluded.

The study received approval from the institution's Quality Review Board (QRB) and was exempt from Institutional Review Board (IRB) approval. Data was de-identified and maintained confidentially. Data was collected via retrospective electronic health record (EHR) review.

The primary objective of this study was to evaluate the efficacy of pharmacist-directed vancomycin therapy in a home infusion setting by analyzing

rates of therapeutic trough levels, duration of therapy, and resolution of infection. Therapeutic trough levels included troughs that were collected at appropriate intervals relative to dosing and were within the goal range of 15-20 mg/L. Duration of therapy was analyzed to determine whether therapeutic extensions were required to resolve infection. Resolution of infection was defined as completion of vancomycin therapy for expected duration (without extension) and without therapeutic change to an alternative antibiotic. Data collected to assess the primary objective included vancomycin troughs, vancomycin regimens and changes, and intended (as originally ordered) and actual therapy duration.

The secondary objective of this study was to evaluate safety outcomes in patients receiving vancomycin in a home infusion setting by analyzing the incidence of AKI defined by KDIGO guidelines (1.5 times increase in serum creatinine from baseline within the last 7 days), non-AKI ADRs, and premature discontinuation of therapy.⁸ The specific definition for AKI from KDIGO guidelines was selected due to the weekly frequency with which labs are typically collected for home health patients. Premature discontinuation of therapy was defined as discontinuation secondary to safety reasons (AKI, non-AKI ADRs, and patient death). Data collected to assess the secondary objectives included laboratory markers of renal function (BUN, SCr), supratherapeutic trough values (troughs >20 mg/L), concomitant nephrotoxic therapies associated with acute tubular injury (antimicrobials, chemotherapeutic agents, calcineurin inhibitors, diuretics), concomitant disease states considered susceptibilities for AKI (chronic kidney disease, congestive heart failure, hypertension, diabetes mellitus, malignancy, anemia), and therapeutic discontinuation secondary to AKI and non-AKI ADRs.^{3-6, 9}

Statistical Analysis

Data was analyzed and tabulated using descriptive statistics to identify central tendency. Statistical means were used to characterize continuous data sets with normal distributions. Standard deviations (SD) were used to represent the spread of data sets with calculated means. Statistical medians were

used to characterize continuous data sets with skewed distributions. Interquartile ranges (IQR) were used to represent the spread of data sets with calculated medians.

Results

Patients with vancomycin therapy in their institutional profile were screened for inclusion in the study. Thirty-one patients ultimately met inclusion criteria for retrospective analysis. Most patient exclusions occurred due to the following reasons: physician-directed vancomycin dosing was used, patients had goal troughs outside of the study range, and patients did not ultimately receive vancomycin after they were referred for onboarding (due to change in antibiotic therapy after initial referral or decision for patients to complete vancomycin courses in the hospital). The baseline characteristics represented a relatively uniform patient population. There were more males than females with the majority of patients being white males without underlying renal insufficiency (Table 1). Osteomyelitis was the most common indication for vancomycin therapy, occurring in 14 patients (45.16%). Methicillin-

TABLE 1 | Baseline Characteristics of Home Infusion Patients Receiving Vancomycin

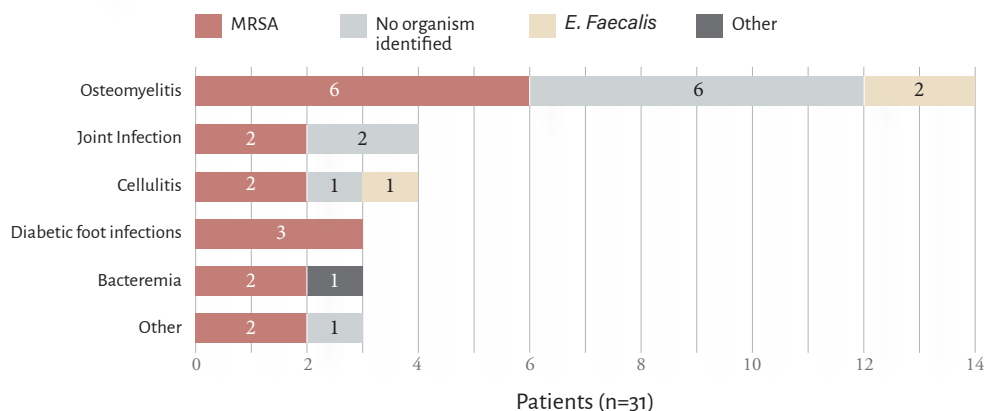
Patient Characteristics (n = 31)	
Age, years ^a	61.29 ± 14.13
Male sex assigned at birth, n (%)	21 (67.74)
Race (non-Hispanic/white), n (%)	31 (100)
Height, inches ^a	68.6 ± 4.81
Ideal body weight, kg ^{a,b}	68.32 ± 12.64
Adjusted body weight, kg ^{a,b}	79.98 ± 11.05
Total body weight, kg ^{a,b}	97.47 ± 22.65
Renal Function (n = 31)	
SCr, mg/dL ^{a,b}	1.05 ± 0.58
BUN, mg/dL ^{a,b}	19.58 ± 11.90
CrCl, mL/min ^{a,b}	93.37 ± 43.39
Concomitant Nephrotoxic Therapy (n = 31)	
Loop diuretics, n (%)	9 (29.03)

Abbreviations: SCr, serum creatinine; BUN, blood urea nitrogen; CrCl, creatinine clearance

a. Data presented as mean ± SD.

b. Values at the time of outpatient onboarding

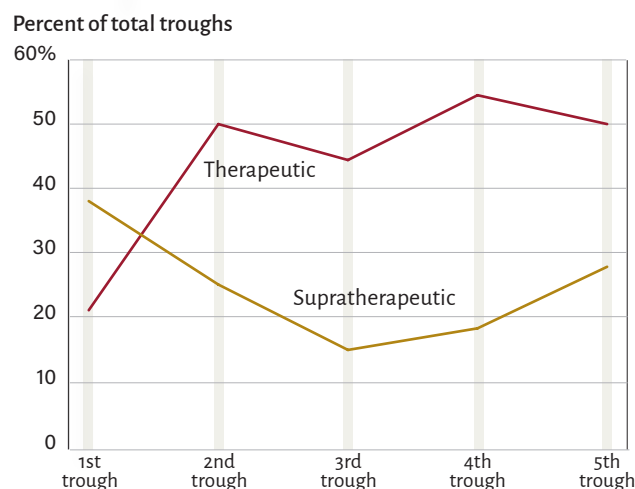
FIGURE 1 | Infection Characteristics of Vancomycin Patients



resistant *Staphylococcus aureus* (MRSA) was the most frequently identified organism among available cultures (17 patients, 51.61%) (Figure 1).

Eighteen patients (58.06%) experienced a resolution of infection as defined in the study design (Table 2). Of the patients who did not meet the criteria for resolution of infection, 11 (78.6%) had therapeutic extensions. The median duration for therapeutic extensions was 12 days. Of the 11 patients with therapeutic extensions, 9 (81.8%) had at least 1 subtherapeutic trough throughout therapy. The average trough with pharmacist-directed dosing was 16.71 ± 4.84 mg/mL (Table 2). All trough values after the first outpatient trough reflected pharmacist-directed vancomycin dosing. The first outpatient troughs reflected the initial outpatient dosing regimen provided at the time of inpatient discharge and home infusion onboarding. Six (20.7%) patients with detectable first outpatient troughs had therapeutic troughs prior to pharmacist-directed dosing, while 14 (50%) patients had therapeutic second troughs after initiating pharmacist-directed dosing (Figure 2). The authors suspect that the achievement of therapeutic troughs after initiation of pharmacist-directed dosing

FIGURE 2 | Characteristics of Detectable Outpatient Troughs



was directly related to pharmacist interventions; however, this finding should be further evaluated with correlative objective data in future studies. The trend line in Figure 2 also reflects the maintenance of therapeutic drug levels through the fifth trough measurement. Analyzed data did not expand past the fifth trough due to a median duration of therapy of 38 days (Figure 2).

TABLE 2 | Primary Outcomes and Evidence of Efficacy

Efficacy Outcomes	
Patients with resolution of infection ^a , n (%)	18 (58.06)
Average trough with pharmacist-directed dosing, mg/L ^b	16.71 ± 4.84
Actual duration of therapy, days ^c	38 [25-42]

a. Defined as completion of vancomycin therapy for expected duration (without extension) and without therapeutic change to another antibiotic.
 b. Data presented as mean \pm SD.
 c. Data presented as median [IQR].

Safety data regarding suprathreshold troughs is reported in Table 3. Four patients (13%) experienced adverse safety events (Figure 3). Two patients (6.5%) experienced AKI secondary to vancomycin therapy. Both patients had suprathreshold vancomycin troughs at the time of AKI appearance. The first patient met KDIGO criteria for AKI at the second trough draw (day 11 of home infusion vancomycin therapy), and the second met these criteria at the fifth trough draw (day 26 of home infusion vancomycin therapy). Additionally, both had pauses in therapy after experiencing AKI. The first patient with AKI

TABLE 3 | Secondary Outcomes and Evidence of Safety

Safety Outcomes	
Total number of supratherapeutic troughs, n(%) ^a	32 (21.77)
Total daily dose associated with supratherapeutic troughs, gram ^{a,b}	2.5 [1.5-2.88]
Total daily weight-based dose for supratherapeutic troughs, mg/kg (mean) ^a	31.29

a. Troughs > 20 mg/L

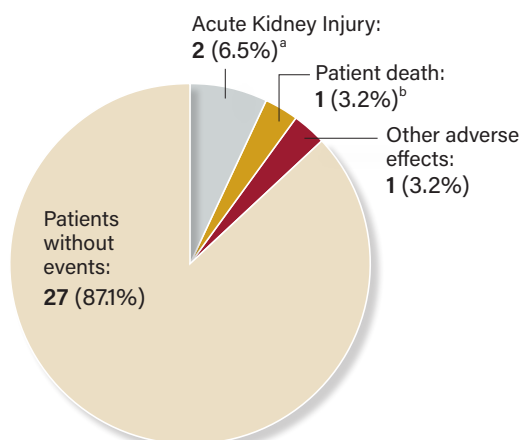
b. Data presented as median [IQR].

did not resume dosing after an initial pause in therapy, and the second resumed therapy at a lower dose. One patient (3%) reported a non-AKI ADR, characterized as nausea and vomiting. One patient death (3%) was reported while on vancomycin therapy; however, this was found to be unrelated to vancomycin. Overall, safety results represent tolerability of vancomycin, made evident by the low incidence of adverse safety outcomes attributed to vancomycin itself (3 patients, 9.7%) and an even lower incidence of vancomycin discontinuation due to adverse outcomes (2 patients, 6.5%).

Discussion

The results of this study show an increase in the number of therapeutic troughs and a decrease in the number of supratherapeutic troughs after the initiation of pharmacist-directed dosing in the home infusion setting. Subsequent troughs reflected similar trends. This indicates that most pharmacist-directed interventions led to the successful achievement of therapeutic goals in the absence of regularly scheduled inpatient care and daily lab monitoring.

FIGURE 3 | Secondary Outcomes – Adverse Events Reported, n (%)



a. Defined by KDIGO guidelines as an increase in serum creatinine ≥ 1.5 times baseline within 7 days

b. Death determined as not vancomycin-related

The incidence of vancomycin-related ADRs remained low with home infusion vancomycin therapy and pharmacist-directed dosing. Although the exact incidence of AKI and additional vancomycin-related ADRs are unknown, there is evidence that patients receiving vancomycin have an increased risk of AKI (relative risk of 2.45).¹¹ In a pre-post study from Philips, et al., researchers examined the outcomes of a clinical practice guideline for pharmacist-led vancomycin dosing, and 6 patients (11.32%) developed nephrotoxicity pre-protocol.⁴ In a similar study from the Marquis, et al., 14 patients (8.7%) developed nephrotoxicity pre-protocol.³ These results closely reflect this study's findings for the incidence of AKI.

The average creatinine clearance for the study population upon onboarding may have been contributory to observed lower risks of AKI. The authors suspect the baseline renal function may have been affected by the hydration status of patients while in the hospital. Altered hydration status is common after hospital discharge due to the reduction or elimination of supplemental IV hydrations. Expansion of the study population may demonstrate how dynamic changes in hydration status may affect rates of AKI. Furthermore, minimized rates of AKI may partially be attributed to the reduced presence of concomitant nephrotoxic therapy in the study population. Loop diuretics were the only identified drug class from the list of screened medications that could potentiate AKI.

Although the preferred method of therapeutic drug monitoring (TDM) for vancomycin involves ratios of the area under the curve (AUC) compared to the minimum inhibitory concentration (MIC), the home infusion setting is unique because most patients receive labs on a weekly basis due to factors that affect patients and home health nursing agencies.² Because there is minimal existing data for trough-based protocolized dosing in the home infusion setting, there is a similar deficiency of information for AUC:MIC protocolized dosing in this setting. Additionally, Bayesian software used for recommendations to vancomycin dosing may prove cost-prohibitive to institutions, and it is more accurate when using both peaks and troughs instead of troughs only.^{2,10} Resultantly, trough-based dosing continues to be the mainstay of vancomycin management in a home infusion setting and is the most appropriate method for protocol development based on current home health practices.

Limitations from this study resulted from the small sample size, the limited number of prescribers that employed pharmacist-directed dosing, and the retrospective study design. Although there were initially 1,208 patients with vancomycin in their institutional profiles during the study's timeframe, these patients had to be evaluated individually for adherence to inclusion criteria due to the institution's lack of therapy-specific search criteria during the data-collection process. The limited search criteria contributed to a large population of excluded patients. This study did not require a large sample size to be adequately powered since it was observational in nature and no comparator group was utilized. The small sample size, however, represented a narrow demographic of patients receiving vancomycin from this institution, thereby limiting the external validity of findings. The low sample size also indicates that a small portion of this institution's collaborating prescribing physicians currently utilize pharmacists for the purpose of TDM and dose adjustments for vancomycin. The retrospective study design limited data collection to information obtained from onboarding documentation and patient EHRs. Furthermore, limited access to many of the patients' EHRs restricted thorough analysis of the collected data

points. For example, the rationale for therapeutic extensions could not be investigated secondary to a lack of EHR accessibility.

In order to address the limitations of this study for future investigations, this institution can market the ability of the clinical pharmacists to monitor and make recommendations for patients on vancomycin therapy to providers' offices. Additionally, following implementation of a standardized pharmacokinetic dosing model, this institution plans to expand our study population to further explore the impact of pharmacist-directed vancomycin dosing in the home infusion setting. This would increase the potential sample size and create a population more reflective of the patients serviced with this institution.

Conclusion

Overall, the results indicate that pharmacist-directed dosing led to sustained improvements in therapeutic troughs. Additionally, low incidences of ADRs, including AKI, occurred following pharmacist-directed dosing. Results from this study will be considered to establish educational modules for the clinical pharmacist staff, develop an institutional pharmacist-directed vancomycin dosing protocol, and assess efficacy of this protocol once implemented.

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A Retrospective Descriptive Study of Remdesivir Treatment in the Home or Outpatient Setting Among Adult Patients Diagnosed with Coronavirus Disease 2019 (COVID-19)

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ABSTRACT

Background

At the onset of the COVID-19 pandemic, early conflicting evidence complicated implementation of therapy. Despite this dilemma, comprehensive outpatient care including integration of remdesivir treatment was scaled up in a multi-center, integrated health care system. This retrospective descriptive report describes program characteristics and learnings from the frontline.

Methods

Treatment guidelines, medical center policies, implementation checklists, and workflow diagrams were evaluated for cohesion. From a pool of eligible patients with COVID-19 enrolled in remote patient monitoring (RPM), a sub-cohort of patients 18-75 years of age who had received remdesivir between December 15, 2020 and August 31, 2022, either in tents/infusion center staffed with nurses proximate to hospitals or via home infusion was identified via prescription dispensing database.

Results

Among 21,766 patients who enrolled in a COVID-19 pandemic RPM, >95% had positive COVID-19 evaluation and 80% entered the program from the emergency room or hospital. A subset of 1,776 patients was treated with remdesivir of which 1,427 (80%) received treatment before the FDA expanded indication. Highest outpatient remdesivir quantity dispensed occurred between July 2022 and December 2022 associated with prevalence of the highly transmissible Omicron and subvariants. Average outpatient remdesivir treatment duration was 2.59 days.

Conclusions

Rapid implementation of comprehensive outpatient care of COVID-19 was facilitated by multiple factors including expeditious adoption of RPM and telehealth to support traditional home health and advanced medical care at home. While patients treated with remdesivir comprised a small percentage of all RPM patients, this critically timed option during recurrent surges helped to relieve strained hospital resources.

Keywords: COVID-19, remdesivir, home infusion, outpatient, implementation

Introduction

Early in the coronavirus disease (COVID-19) pandemic, only intravenous biologics and remdesivir (RDV) a potent antiviral, were available under Emergency Use Authorization. Subsequently in October 2020, remdesivir emerged as the first Food and Drug Administration-approved drug for treating COVID-19. Initial use was intended for a hospital or health care setting capable of providing acute care comparable to inpatient hospital care.¹⁻²

Despite these developments, implementation of therapy was delayed. Among contributing factors were fluctuating evidence and authoritative treatment guidelines while already strained hospitals struggled to withstand repeated COVID-19 surges.³⁻⁹ Against this background, patients with lower oxygenation and severe clinical status who previously would have been admitted had to be diverted to the outpatient setting.¹⁰⁻¹²

Concurrently, hospitals that had previously applied to participate in the Centers for Medicare & Medicaid Services “Hospital without Walls” program were galvanized to participate in the expanded initiative to include acute hospital care at home. Targeting patients who require acute inpatient admission to a hospital with daily rounding by a physician and a medical team monitoring care needs on an ongoing basis, acute care is provided by a hybrid of telehealth, remote monitoring, and regular in-person visits by nurses. It differs from traditional home health which provides skilled nursing and other skilled care services in the home.¹³

Such delivery systems of care were sporadic during COVID-19 surges resulting in limited research on implementation. This report overcomes this gap by describing program characteristics and facilitators of large-scale comprehensive outpatient care, including integration of remdesivir treatment in a multi-center, integrated health care system.

Methods

Setting

Kaiser Permanente Southern California (KPSC) is a non-profit integrated health system with 15 medical centers and provides comprehensive preventive and medical care to approximately 4.7 million members who are demographically similar to the diverse socioeconomic, ethnic California population at large.¹⁴ Treatment guidelines, medical center policies,

implementation checklists, and workflow diagrams were evaluated in a crosswalk for cohesion and COVID-19 outpatient care program components identified.

The KPSC Institutional Review Board (IRB) reviewed and approved all study activities with waiver of written informed consent. All methods were conducted in accordance with relevant guidelines and regulations in accordance with the Declaration of Helsinki. This descriptive report followed the relevant elements of the Standards for Reporting Qualitative Research guidelines for retrospective observational data.

Components

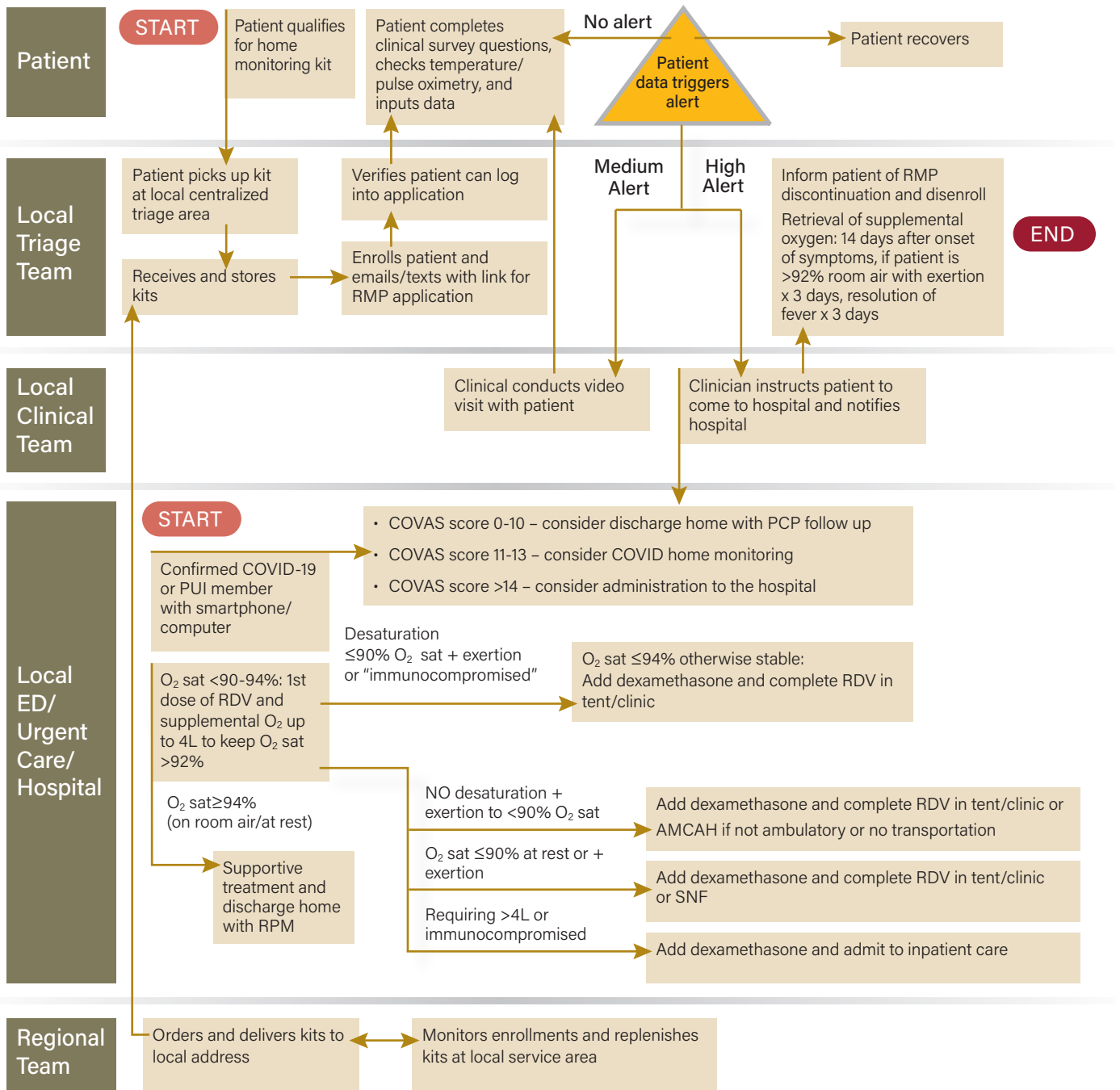
Remote patient monitoring (RPM)

The KPSC COVID-19 remote patient monitoring (RPM) initiative was launched on April 13, 2020, and completed region roll-out on August 3, 2020. The COVID-19 Outpatient Monitoring & Treatment Workflow Process is depicted in Figure 1. Participation required patients to be alert and oriented to self-report symptoms and have a smart phone/computer.

Patients enrolled in RPM were sent home with a remote monitoring kit that included a thermometer, pulse oximeter, and a software platform that enabled video capability and daily patient surveys. Patient education initiated in the hospital or emergency room was reinforced by the home visiting nurse. Patients were notified to take daily up to every 8-hour measurements including temperature, oxygen saturation, and to complete a symptom check survey. Links to up-to-date COVID-19 information and meditation/relaxation application were also included. RPM oversight was provided by clinical support teams of local providers, virtual medical center, or on-call continuing care physicians. Redeployed providers including social workers, pharmacists, physical, and respiratory therapists were engaged to support lab and vital signs monitoring.

If patient measurements were out of range for defined parameters, medium to high alerts were sent to clinicians. A medium alert was generated for oxygen reading <92% or 3% lower than previous entry, which prompted a physician video visit. A high alert was generated for oxygen saturation reading <90% or 4% lower than previous entry, and patients were automatically alerted to seek immediate medical attention. High alerts also prompted physicians to arrange for hospital admission.

FIGURE 1 | Covid-19 Outpatient Monitoring & Treatment Workflow Process



Legend
 RPM – remote patient monitoring
 RDV – remdesivir
 SNF – skilled nursing facility
 PUI – person under investigation
 AMCAH – acute medical care at home
 PCP - primary care provider
 COVAS - risk score
 HH - home health

All enrolled RPM patients were visible to clinicians within their medical center through a COVID-19 clinical dashboard in the electronic medical record. On-demand, live reports through the vendor platform could be generated by both the regional command center and local administrators, providing useful metrics on:

- Total volumes
- Enrollments
- Patient adherence
- Patient satisfaction
- Length of stay
- Patient end points
- Home oxygen orders
- COVID status for persons under investigation
- Demographics
- Patient entry points
- Task response time
- Alert volumes
- Times

Disenrollment from RPM occurred when one of the following criteria was met: 14 days since symptom onset, 3 days since last fever, or 3 days of respiratory improvement. Early detection of patient deterioration expedited hospital admission or treatment with medications. A detailed description of the KPSC RPM initiative and preliminary results have been previously reported.¹⁵

Risk Assessment

Initial eligibility criteria for RPM enrollment were health system members with confirmed COVID-19 or person under investigation (PUI) identified in the emergency room, urgent care, or hospital setting with oxygen saturation >92%, heart rate <100 bpm, respiratory rate <20 breaths/min, mild symptoms, low disease burden, age <60 years, and body mass index <40. These criteria were later replaced in May 2020 by a validated predictive COVID risk score, COVAS, which assessed comorbidities, obesity/BMI ≥40, vital signs, age, and sex for patient risk stratification.¹⁶

Depending upon entry point, patients from the emergency room or urgent care were stratified into 3 risk categories based on COVAS score.

- For COVAS score of 0-10, discharge home with primary care provider with follow up was recommended.

- For those with a COVAS score of 11-13, enrollment in RPM was recommended.
- For COVAS score >14, hospitalization was considered.

Patients discharged from the hospital were further risk stratified based on required supplemental oxygen 2-5 L/min.

Remdesivir Treatment

Remdesivir infusions required COVID-19 baseline laboratory results to be available prior to administration. All first doses were administered in a controlled setting and continuous monitoring for adverse drug events was performed.

Linkage with the medical center allowed the home infusion pharmacy to procure remdesivir during initial shortages for outpatient reallocation while it was still indicated for acute use. Initial 5-day treatment with remdesivir 200 mg loading dose on the first day and 100 mg daily for 4 additional days was the standard regimen. This outpatient regimen was later updated to an early 3-day course of remdesivir validated by a recent study, where an early 3-day course of remdesivir among non-hospitalized patients who were at elevated risk for COVID-19 progression demonstrated benefit with significant risk reduction of COVID-19-related hospitalizations and all-cause death.¹⁷

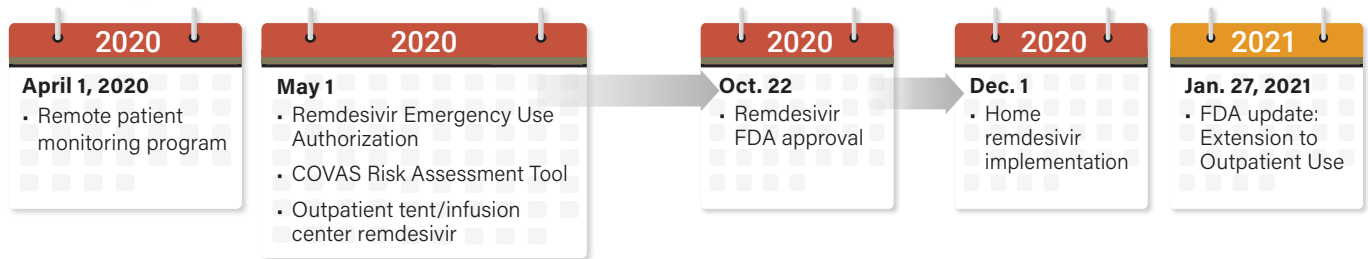
Outpatient/Home Infusion

Pulse oximetry oxygen saturation (SpO₂) ≥94% on room air with symptoms and SpO₂ <94% on room air and/or requiring low-flow supplemental oxygen (<6 L/minute) was used as the threshold value for primary triage stratification. To be eligible for home health, symptomatic patients with SpO₂ <90% had to be medically stable during observation in the ER or hospital. If symptoms had not progressed in 24 hours, they were treated similarly to symptomatic patients with SpO₂ 90-94% who were otherwise stable. After the first dose of remdesivir administration was confirmed, they were enrolled in RPM and referred for home infusion to complete the regimen.

Nurses initiated a virtual video follow-up visit with the physician while at the home for the next day infusion of remdesivir and daily as needed. Patients could be discharged from home health or AMCAH after completion of remdesivir and continue with the RPM until disenrollment.

Daily or every other day labs included complete blood cell count with differential, basic metabolic panel, liver function tests, and protime/INR that were obtained by an external contracted independent phlebotomy

FIGURE 2 | Timeline of Remdesivir Use



provider group. Daily point of care test glucose monitoring for patients with diabetes or elevated daily glucose while on a corticosteroid was considered on a case-by-case basis for patients without diabetes.

Early remdesivir discontinuation was considered for adverse effects: ALT 5-10 times the upper limit of normal with signs of liver inflammation occurring by the third day of remdesivir. Escalation to re-hospitalization was considered for patients with worsening prognosis, increasing oxygen requirement, confusion, and critical laboratory results.

Telehealth

Simultaneous integration of multiple technology vendors and point product applications were utilized to streamline care coordination and transform the patient telehealth experience. They encompassed live video, asynchronous patient data sharing, and mobile health applications. A hallmark feature was real-time, HIPAA-compliant secure communication to expand access to providers in the field and remotely. Additional features included linkage to the electronic medical record care management workbench to transmit instantaneous information, 24/7 back to the care team, and a billing mechanism for Medicare and Medicaid reimbursements. Virtual physician follow-up was available 7 days a week and after hours.

Results

RPM was implemented at 12 of 15 medical centers by August 3, 2020. Among 21,766 patients who enrolled in COVID-19 pandemic RPM, all completed by meeting disenrollment criteria. More than 95% tested positive for COVID-19 and 80% entered from the emergency room or hospital. Enrollment duration in RPM was 11 days (mean) ranging 1-14 days with high adherence to daily monitoring of temperature, oxygen

saturation, and symptoms (92%). Approximately 11% were hospitalized while enrolled in RPM. Figure 2 depicts timeline of outpatient care.

Local virtual clinical teams supporting RPM ranged in size from 7 to 165 and were comprised of nurses (171) and physicians from the hospital, emergency room, and urgent care (219). Other specialties supporting this core team were internal medicine/family medicine (12), and geriatrics/continuing care/emeritus (53). A total of 284 physicians not including rotation physician coverage were trained. Volume of COVID-19 patients by medical center who completed RPM ranged from 298 to 4,237. Traditional home health agencies performed monitoring for 2,316 patients until discontinuation of the RPM initiative on May 2, 2022. An additional 181 COVID-19 patients were monitored by the AMCAH model until August 31, 2022, for a total of 2,497 patients.

A subset of 1,776 patients was treated with remdesivir of which 1,427 (80%) received treatment before the FDA expanded indication on January 27, 2022 for outpatient treatment of mild-moderate COVID-19 and at elevated risk for progression to severe COVID-19, including hospitalization or death. The majority of patients (93%, n=1,659) was referred by 3 of 5 medical centers which implemented outpatient remdesivir treatment. Infectious disease physicians were actively involved with planning and implementation at 2 medical centers. Average outpatient treatment duration was 2.59 days. Highest outpatient remdesivir utilization occurred between July and December 2022 associated with prevalence of the highly transmissible SARS-CoV-2 variant Omicron and subvariants.

Discussion

This report retrospectively describes multiple seamless facilitators of outpatient COVID-19 care including expeditious adoption of an RPM initiative leveraging

diverse health care workers that allowed detection of patients in early stages of deterioration. Use of the COVAS risk score efficiently standardized stratification of patients who would most benefit from treatment intervention with critically timed remdesivir during surges. Telehealth further allowed scaling up while reducing COVID-19 exposure for other patients and health care workers.¹⁸ These findings support similar previously reported strategies to increase acute health service capacity.¹⁹⁻²¹

Limitations

The descriptive design of this report did not evaluate remdesivir treatment effectiveness or value of outcomes to patients, providers, and health care organizations.²²⁻²³ One such outcome is provider and patient satisfaction with massive technology upgrades to enable RPM and telehealth with the trade-off in lack of a single interface and end-user application in one universal platform. Furthermore, we did not assess why some medical centers opted to participate in AMCAH vs traditional home health and outpatient remdesivir and others did not.

Scaling up of this care model would be incomplete without mention of treatment cost, a potential barrier to integration of outpatient remdesivir. The Institute for Clinical and Economic Review (ICER) preliminary cost recovery pricing for a 10-day course of remdesivir

was estimated at \$10. An estimated ceiling of \$4,500 threshold for cost-effectiveness pricing was used for treatment of large patient populations.²⁴ Until Medicare Part B updated its reimbursement policy, inability to link billable telehealth services with outpatient remdesivir and its administration limited generalizability to a fee-for-service setting. In an updated ICER report, a health-benefit price benchmark of \$2,470 for hospitalized patients with moderate-to-severe disease and \$70 for patients hospitalized with milder disease was used to reflect less severely ill patients.²⁵

Conclusion

RPM and telehealth that maintained standard of care, privacy, and real-time patient data exchange buttressed the framework for delivery of care in the home. While patients treated with remdesivir comprised a small percentage of all RPM patients, this critically timed option during recurrent surges relieved strained hospital resources by enabling early discharges or avoiding admission. These findings demonstrate the feasibility of an expanded comprehensive outpatient care model and provide learnings for future application to a large-scale emergency response.

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Acquired Immunodeficiency Syndrome in Hemophilia A: A Case Report and Literature Review

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ABSTRACT

Background

Hemophilia is an X-linked recessive coagulation disorder which is characterized by factor VIII deficiency. Hemophilia A is the most common inherited bleeding disorder, accounting for up to 85% of the hemophilia population worldwide. The association between hemophilia A and acquired HIV/AIDS is infrequently seen in practice nowadays. We present a rare case of congenital hemophilia A with acquired HIV/AIDS due to contaminated plasma products during the HIV epidemic between the 1980s and 1990s.

Case Presentation

We report a case of a 50-year-old male with a complicated medical history of moderate to severe congenital hemophilia A, immune thrombocytopenia, multiple episodes of upper gastrointestinal (GI) bleeding, target joint bleeding, arthritis, and acquired HIV/AIDS. The prolonged partial thromboplastin time (PTT) of 32.5 secs and baseline FVIII of 0-3% confirmed the diagnosis of hemophilia A. Medical records revealed the patient was treated with cryoprecipitate and factor concentrates for hemophilia in early childhood. Aggressive HIV/AIDS regimens were given along with long-term antibiotics for opportunistic infections. A literature review was performed to identify similar unique cases of this rare association.

Conclusion

Acquired HIV/AIDS present in hemophilia A patients is not commonly seen in practice. The plasma contamination tragedy enforced stringent regulations and guidelines on the manufacturing industry. Remarkably, hemophilia patients can now achieve a longer lifespan and quality of life through novel hemophilia treatment.

Keywords: Hemophilia A, AIDS/HIV, Factor VIII activity, Contaminated plasma products.

Introduction

Hemophilia A is an X-linked recessive coagulation disorder characterized by factor VIII deficiency. Hemophilia A is the most common bleeding disorder, accounting for 80-85% of the hemophilia population, with an occurrence rate of ~1 in 10,000 live births.¹ Carrier mothers often have a 50% chance of passing the mutated F8 gene to the male child. The spontaneous mutation of the F8 gene leads to abnormal production of factor VIII, which disrupts downstream regulation of the clotting cascade.

Hemostasis is important to maintaining hemodynamic stability and circulation. The 2 components of hemostasis are primary and secondary hemostasis. Primary hemostasis consists of platelet aggregation and platelet plug formation at the injury site. During an injury, platelets are exposed to the subendothelial space, where they aggregate and adhere to stop the bleeding. Fibrin can also activate platelets. Secondary hemostasis consists of the clotting cascade, which stabilizes the platelet plug and further repairs the site. The clotting cascade has 3 main pathways: extrinsic, intrinsic, and common pathway. The common pathway can be achieved by both the extrinsic and intrinsic pathways via activation of factor X to Xa. The final step of the clotting cascade occurs when fibrin and factor VIIIa stabilize the clot at the injury site by forming a cross-linked fibrin mesh.

Genomic studies suggest that mutations in F8 genes result in hemophilia A. F8 gene is a large structural complex with 26 exons, and it is located at the end of gene Xq28.² Various mutations of this gene, including inversion, insertion, missense, and deletion, cause hemophilia, but 50% of the cases are attributed to inversion mutations.³ Factor activity (FA) level is used to classify patients into 3 severity scales: mild >5-40%, moderate 1-5%, and severe <1%. Target joint hemorrhage is the most common complication in hemophilia A, often recurrent and localized to 1 joint. A meta-analysis study by Soucie et al. with 7,914 hemophilia patients noted that hemophilia A patients have a 30% higher risk of undergoing invasive orthopedic procedures than those with hemophilia B ($p = 0.4$). The study further demonstrated that an FA level of approximately 20% is required to prevent target joint hemorrhages, and the risk of orthopedic procedures is reduced by 40% for every 10% increase in FA.⁴ This data shows the vast difference in clinical severity between hemophilia A and B.

For decades, clotting factors remained the therapy of choice, given their known safety and efficacy. Currently marketed products are either derived from human plasma donors or created by using DNA recombinant technology.

Case Report

A 50-year-old male with moderate to severe congenital hemophilia A presented to the hemophilia treatment center with chief complaints of bilateral knee and right shoulder pain. The patient denied gastrointestinal (GI) bleeding, fever, night sweats, weight loss, chest pain, and dyspnea. The patient had a baseline factor VIII level of 0-3% and an inhibitor titer of 0 Bethesda units (BU). His right knee was a target joint with additional hemophilic arthropathy issues in his right wrist and right shoulder. Complicated medical history included HIV, hepatitis C, immune thrombocytopenia (s/p splenectomy in 1/1985), *mycobacterium avium intracellular infection* (MAI), upper GI bleeding, arthritis secondary to hemophilic arthropathy, and chronic back pain due to a fall.

During his infancy, the patient had a prolonged bleeding post-circumcision. The extensive bruising was noted at his 6-month-old checkup, which led to further testing and diagnosis of hemophilia A. His bleeding disorder was initially treated with cryoprecipitate until he was 8 years old. Afterward, the treatment was replaced by on-demand FVIII replacement regimen, which consisted of 3,000 units for mild bleeding and 7,000 units for severe bleeding. In 2013, the patient was switched to prophylaxis therapy due to recurrent hospitalizations from gastrointestinal (GI) bleeding. The admission laboratory tests revealed a significantly low level of factor VIII activity, 22.4%, unremarkable inhibitor assay of 0 titers, and PTT of 32.5 seconds (H). His bleeding history prior to starting prophylaxis FVIII therapy included right iliopsoas hematomas, right elbow and right knee hemarthrosis, GI bleeding, right wrist hemophilic arthropathy/hemarthrosis, right shoulder pain with bicipital tendinopathy, and right hip pain related to iliopsoas bleeding. Upon multiple hospitalizations due to unrevoked GI bleeding, the patient was placed on an escalated prophylaxis dosing of FVIII replacement therapy with Kogenate 3,100 units 3 times weekly.

Status post splenectomy due to chronic ITP in 1984, he was diagnosed with acquired HIV and hepatitis C. The patient was treated with Zidovudine (Retrovir)

for 9 years, then therapy was discontinued, assumingly due to noncompliance. Ten years later, the patient was re-hospitalized due to MAI in the form of a neck mass; he was treated with clarithromycin, ethambutol, and rifabutin. Other readmission complications included candidal esophagitis and AIDS status. Diagnostic laboratory tests showed a critically low CD4/CD8 lymph ratio of 0.65 (L) and a CD4 count of 612/ μ L. HIV/AIDS treatment was reinitiated with Atripla (efavirenz, emtricitabine, tenofovir) and later changed to Odefsey (emtricitabine, rilpivirine, tenofovir) (serum creatinine 0.84mg/dL, eGFR >60 mL/min/1.73m², ALT/AST 15 and 23U/L, respectively). His HIV viral load of 3970/mL had been intermittently detectable since 2012, while his hepatitis C viral load had been undetectable since his hospitalization in 2013.

Discussion

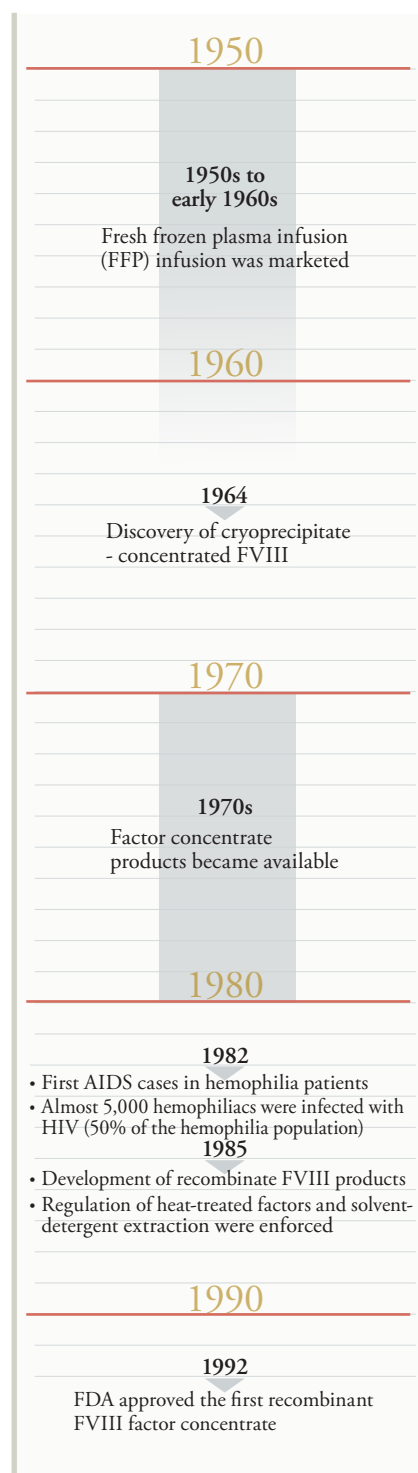
Between the late 1950s and early 1960s, fresh frozen plasma (FFP) first became available for hemophilia patients in hospital settings. Infusion of FFP faced the challenge of volume overload to obtain the necessary amount of clotting factor at the plasma level. This led to another breakthrough when cryoprecipitate, a concentrated factor VIII, was developed in 1965. Since cryoprecipitate provided concentrated amounts of factor VIII in a smaller volume than fresh frozen plasma (FFP), it became the most popular therapy of choice to control bleeding at that time. By the 1970s, powdered factor VIII concentrates were widely marketed, and self-infusion and home treatment became manageable for hemophiliacs.

However, the revolution of plasma concentrates soon recorded the first transmission of HIV/AIDS cases through contaminated products in 1982. Since then, reportedly, about 5,000 patients with hemophilia have been infected with HIV due to the contamination in the United States. In 1992, the Food and Drug Administration (FDA) approved the first recombinant factor VIII (Figure 1).^{5,6}

Remarkably, life expectancy for patients with severe hemophilia rose significantly due to the robust development of plasma infusions. Tragically, a vast population of hemophilia patients were unknowingly infected with human immunodeficiency virus (HIV) from contaminated plasma-derived clotting factors. Soon after, an acquired immunodeficiency syndrome (AIDS) became the leading cause of death for Americans in the 1990s.⁷

In 1982, while HIV/AIDS mortality reached its peak, the Centers for Disease Control and Prevention (CDC) reported several cases of hemophilia A patients with acquired HIV/AIDS who received clotting factors. **Patient 1** started

FIGURE 1
The Evolution of Hemophilia Products



experiencing weight loss, fever, and chest x-ray showed interstitial infiltration, which was associated with pneumonia. A lung biopsy was conducted and revealed *Pneumocystis carinii* (*P. carinii*). Unfortunately, patient 1 died after he was treated with sulfamethoxazole and trimethoprim (Bactrim) for 2 weeks. **Patient 2** was noted with fever, oropharyngeal candidiasis, recurrent fever, and dysphagia. He was also diagnosed with *P. carinii* pneumonia and *cytomegalovirus* (CMV). He was given a month-long course of pentamidine and Bactrim until his death. **Patient 3** was diagnosed with *P. carinii* pneumonia, oral candidiasis, and *Mycobacterium avium* (MAC) bacteremia. Fortunately, the patient survived after extensive courses of antibiotics (SMZ/TMP) and antifungal treatment (Ketoconazole).⁸

From late-1982 to early-1983, additional cases of acquired HIV/AIDS in hemophilia A were further recorded. **Patient 4** developed anorexia and progressive weight loss. Hospital readmission revealed transient thrombocytopenia and persistent inversion of the T-helper/T-suppressor ratio (TH/TS=0.2). On his third admission, sputum culture showed *P. carinii*, and the patient survived after a long course of SMZ/TMP. **Patient 5** was noted with 101.2°F fever, thrombocytopenia, elevated serum IgG, IgM, and IgA. Chest x-ray revealed *P. carinii* and rare *Cryptococcus neoformans* pneumonia. Remarkably, the patient clinically improved after an extended treatment of Bactrim and amphotericin B.

Patient 6 had mild hemophilia with relatively infrequent factor VIII concentrate treatment. His admission recorded dysphagia, diaphoresis, and weight loss. The TH/TS ratio was 0.25. A lung biopsy confirmed *P. carinii* pneumonia. The patient died after showing no improvement while on treatment with SMZ/TMP and pentamidine. Lastly, **Patient 7** was recorded with persistent lymphopenia, leukopenia, oral candidiasis, and bone marrow granuloma with rare *Histoplasma capsulatum*. The patient initially improved after being given amphotericin B. Several months later, the patient was re-hospitalized with leukopenia, lymphopenia, and pulmonary infiltration. Biopsies were collected and revealed disseminated *H. capsulatum*. Further results showed that the white cell count was 400 cells/μL, and lymphocytes were absent. Unfortunately, the patient died after treatments failed.⁹ (Table 1)

Following the HIV/AIDS epidemic, hemophiliacs who were unknowingly infected with HIV/AIDS filed lawsuits against several pharmaceutical companies over their contaminated factor products. The action accused these companies of lacking safety and screening processes for bloodborne pathogens. The lawsuits asserted that these pharmaceutical companies acquired their plasma pool from high-risk donors such as drug users and prisoners. Unfortunately, the epidemic continued spreading through Latin America, Asia, and Europe in the mid-1990s. Consequently, these companies agreed to pay \$640 million as a settlement.¹⁰ Furthermore, Americans demanded a safer system in the manufacturing process for the plasma supply. As a result, this tragedy immediately prompted manufacturers to implement stricter policies and develop another alternative technology, DNA recombinant.

Editor's Note: According to the U.S. Centers for Disease Control and Prevention (CDC), scientists have changed both the classification and the name of *Pneumocystis carinii* since it first appeared in patients with HIV in the 1980s. *P. carinii* was previously classified as a protozoan; *Pneumocystis jirovecii* is now considered a fungus.

Conclusion

We reviewed 7 cases of hemophilia A patients with HIV/AIDS during the early 1980s when AIDS was not yet well understood. Most of these patients received treatment with antibiotics and antifungals for opportunistic infections, but unfortunately, not all of them survived. Since 1985, no new cases of acquired HIV/AIDS in patients with hemophilia A have been reported. The tragic loss of many hemophiliac patients prompted the manufacturing industry to comply with stringent regulations and develop further novel therapies, including recombinant FVIII products.

Literature also reported 2 brothers cases of hemophilia A who acquired HIV/AIDS due to the contamination.^{11,12} Before 1985, 2 older brothers were treated with tainted factor VIII products and unknowingly got infected with HIV. Their young brothers had severe hemophilia A with HIV negative at the time of the older brothers' diagnostic period. Unexpectedly, the set of 2 younger brothers were both found HIV positive in 1991 and 1992, respectively. In these 2 cases, medical records revealed that the 2 younger brothers were contaminated with HIV from

TABLE 1 | HIV Infection in Hemophilia A Patients – Literature Review

Patient No.	1	2	3	4	5	6	7
Sex	M	M	M	M	M	M	M
Age	62	59	27	55	10	49	52
Severity of hemophilia	Severe	Severe	Severe	Severe	Severe	Mild	Severe
Hemophilia treatment	Factor VIII concentrate	Factor VIII concentrate	Factor VIII concentrate	Factor VIII concentrate	Factor VIII concentrate	Intermittent factor VIII concentrate	Factor VIII concentrate
Other medical history	Chronic hepatitis	NA	NA	Diabetes mellitus, hepatosplenomegaly	Healthy	NA	NA
Onset of AIDS	Feb 1981	Oct 1980	Jul 1981	Sep 1981	Sep 1982	1982	Apr 1982
AIDS diagnosis date	Jan 1982	Feb 1982	Oct 1981	Jun 1982	Oct 1982	Nov 1982	Nov 1982
Symptoms	Weight loss, abdominal pain, severe respiratory distress	Weight loss, dysphagia, ulcers, anterior cervical adenopathy	Fever, urinary urgency, extreme lassitude, splenomegaly, anemia, lymphopenia	Anorexia, weight loss	Fever, vomiting, anorexia, fatigue, sore throat, nonproductive cough	Dysphagia, weight loss, cellulitis, dyspnea, diaphoresis	Fever, lymphadenopathy, abdominal pain, lymphadenopathy, abdominal pain, weight loss
Opportunistic infection	<i>P. carinii</i>	<i>P. carinii</i> CMV Oropharyngeal candidiasis	<i>P. carinii</i> CMV Oropharyngeal candidiasis	<i>P. carinii</i> Herpes zoster	<i>P. carinii</i> C. neoformans	<i>P. carinii</i> HSV	Esophageal candidiasis
Labs	NA	NA	NA	Absolute lymphocyte 450/mm ³ , elevated LFT, thrombocytopenia 63,000/mm ³	Lymphocyte 580/mm ³ , platelet 171,000/mm ³ , elevated IgG, IgA and IgM	WBC 11,000/mm ³ , absolute lymphocyte 990/mm ³	Lymphocyte 480/mm ³ , WBC 400/mm ³ , granulomata
CXR/sputum culture	NA	NA	NA	Bilateral PNA	Bilateral PNA	Diffuse PNA Sputum HSV	Infiltration <i>H. capsulatum</i>
TH/TS ratio	NA	Inverted ratio	Inverted ratio	0.2	0.1	0.25	0.1
AIDS treatment	SMZ/TMP	SMZ/TMP Pentamidine	SMZ/TMP Ketoconazole	SMZ/TMP Adenosine arabinoside	SMZ/TMP Amphotericin B	SMZ/TMP Pentamidine	SMZ/TMP Amphotericin B
Outcome	Patient expired after 2 weeks of treatment	Patient expired 7/5/1982	Alive	Alive	Alive	Expired 11/22/1982	Expired 1982

See Editor's Note on page 24.

their older siblings rather than directly from contaminated blood products. As a result, it highlighted the importance of taking necessary precautions to prevent cross-contamination of bloodborne diseases in health care and home settings.

We report a rare case of hemophilia A patient with acquired HIV/AIDS who also suffered from multiple opportunistic infections, consequently followed by the contaminated plasma product tragedy in the 1990s. Our patient further presented hemophilic complications such as GI bleeding, hemophilic arthropathy, and target joint bleeding throughout his life. However, novel therapies and advanced medical technologies continue to evolve and improve their quality of life. Thus, gene therapy is expected to be the new groundbreaking management for hemophilia. Additionally, other innovative treatments, including anti-tissue factor pathway inhibitors and RNA interference therapy targeting antithrombin, are being explored as potential futuristic treatments.¹³

Abbreviation Key

PNA	pneumonia
CXR	chest x-ray
TH/TS	T-helper/T-suppressor lymphocyte
<i>P. carinii</i>	<i>Pneumocystis carinii</i>
<i>C. neoformans</i>	<i>Cryptococcus neoformans</i>
<i>H. capsulatum</i>	<i>Histoplasma capsulatum</i>
HSV	herpes simplex virus
CMV	cytomegalovirus
SMZ/TMP	sulfamethoxazole and trimethoprim

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