

A multimodal strategy to improve health care for pediatric patients with cancer and fever in Peru

Ana Mendieta¹, Ligia Rios Lopez¹, Maria Vargas Arteaga¹, Essy Maradiegue², Walter Delgadillo Arone¹, Carlos Rueda Bazalar¹, Alexis Holguin², Carlos Santillan Salas³, Ivan Maza¹, Maysam Homsi⁴, Frankly Farias Barrios⁵, Claudia Assayag¹, Liliana Vásquez⁶, Claudia Pascual³, and Miguela Caniza⁴

Suggested citation Mendieta A, Rios Lopez L, Vargas Arteaga M, Maradiegue E, Delgadillo Arone W, Rueda Bazalar C, et al. A multimodal strategy to improve health care for pediatric patients with cancer and fever in Peru. Rev Panam Salud Publica. 2023;47:e140. https://doi.org/10.26633/RPSP.2023.140

ABSTRACT Objective. The DoTT (Decreasing Time to Therapy) project aimed to minimize the interval between fever onset and medical interventions for children with febrile neutropenia. The objective of this study was to determine the effect of implementing the DoTT project on the hospital time to antibiotic (TTA) and patient time to arrival (PTA) at the hospital in children with febrile neutropenia admitted to the emergency department.

> **Methods.** The DoTT project was implemented at a Peruvian hospital and followed the World Health Organization (WHO) multimodal improvement strategy model. Components included creating a healthcare delivery bundle and antibiotic selection pathways, training users of the bundle and pathways, monitoring patient outcomes and obtaining user feedback, encouraging use of the new system, and promoting the integration of DoTT into the institutional culture. Emergency room providers were trained in the care delivery for children with cancer and fever and taught to use the bundle and pathways. DoTT was promoted via pamphlets and posters, with a view to institutionalizing the concept and disseminating it to other hospital services.

> **Results.** Admission data for 129 eligible patients in our registry were analyzed. The TTA and PTA were compared before and after the DoTT intervention. The median TTA was 146 minutes (interquartile range [IQR] 97–265 minutes) before the intervention in 99 patients, and 69 minutes (IQR 50–120 minutes) afterwards in 30 patients (p < 0.01). The median PTA was reduced from 1483 minutes at baseline to 660 minutes after the intervention (p < 0.01).

Conclusions. Applying the WHO multimodal improvement strategy model to the care of children with febrile neutropenia arriving at the hospital had a positive impact on the PTA and TTA, thus potentially increasing the survival of these patients.

Keywords Oncology service, hospital; emergency service, hospital; febrile neutropenia; child health; patient care bundles; Peru.

Up to one-third of pediatric cancer patients develop fever during neutropenic episodes (1). Children with febrile neutropenia (FN) experience increased morbidity, prolonged hospitalization, and postponement of cancer treatment, and their risk of dying of sepsis is up to 1.6 times greater than that of children with other diseases (2, 3). Timely access to appropriate health care is essential for good outcomes of FN, which are accomplished by a joint effort by multidisciplinary health-care professionals (HCPs) and family members. However, in low- or middle-income countries (LMICs) (4, 5), multiple

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 IGO License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited. No modifications or commercial use of this article are permitted. In any reproduction of this article there should not be any suggestion that PAHO or this article endorse any specific organization or products. The use of the PAHO logo is not permitted. This notice should be preserved along with the article's original URL. Open access logo and text by PLoS, under the Creative Commons Attribution-Share Alike 3.0 Unported license.



Hospital Nacional Edgardo Rebagliati Martins, Lima, Peru

² Instituto Nacional de Enfermedades Neoplásicas, Lima, Peru

³ Pan American Health Organization, Lima, Peru

⁵ ESSALUD, Lima, Peru

⁶ Pan American Health Organization, Washington, D.C., United States of America

factors are associated with these delays, namely how families access healthcare resources, their environments, the quality of the available resources, and how processes are used (2, 5). Two studies (4, 5) exemplify the importance of reducing the time to initiate infection management in a patient with cancer survival. First, Kirby et al. (5) showed that the probability of intensive care unit admission and death increased by 20% with each one-day increase in antibiotic waiting time in a pediatric cancer center in the Philippines. Second, Gavidia et al. (4), in El Salvador, demonstrated that time delay in the administration of antibiotics after arriving at the hospital was a statistically significant factor (p = 0.04) associated with sepsis and infectious deaths among children with cancer.

Reducing the time to initiate management of infections in children with cancer can improve patient survival (6, 7). Decreasing Time to Therapy (DoTT) is a quality improvement (QI) project established to support the World Health Organization (WHO) Global Initiative for Childhood Cancer (GICC) in Peru (8). The goal of the GICC is to increase the survival of pediatric cancer by at least 60% by the end of the decade (9). The DoTT project represented a collaboration between the Hospital Nacional Edgardo Rebagliati Martins (Hospital Rebagliati) and the St. Jude Children's Research Hospital, department of Global Pediatric Medicine, and was based on the WHO multimodal improvement strategy (MMIS) that was originally designed to support better compliance of hand hygiene (10, 11). The MMIS is summarized as "Build it, teach it, check it, sell it, and live it" (11). The DoTT project targeted children with FN arriving at Hospital Rebagliati and used the MMIS to expedite access to appropriate therapy. The aim of this article is to report the effect of implementing the DoTT project on the patient time to arrival (PTA) at the hospital and the time to antibiotics (TTA) in children with FN admitted to the emergency department (ED) of Hospital Rebagliati.

MATERIALS AND METHODS

Setting

This study was conducted at the Hospital Rebagliati, a 1 600bed adult and pediatric tertiary care hospital in Lima, Peru. The pediatric oncohematology service has a 32-bed inpatient ward for children. The ED cares for an average of 45 000 children (600 with cancer) annually. Children with cancer needing hospitalization are admitted to the inpatient pediatric oncology wards from the oncology clinics during regular working hours and from the ED after hours. The ED staff comprises 116 individuals, including emergency physicians, pediatricians, physicians-in-training (fellows or residents), medical technologists, and nursing personnel. Specialists, including oncologists and infectious diseases specialists, are available on call if needed.

Definitions

PTA was defined as the time between the onset of fever and arrival in the pediatric ED, and TTA was defined as the time between the patient arriving in the ED and the administration of the first dose of the appropriate antibiotic. Fever was defined as a temperature of 38 °C obtained by any method, and neutropenia was defined as a blood absolute neutrophil count of 500 or less. A bundle was defined as a group of evidence-based

interventions that, when used together, can result in better outcomes than when these interventions are used individually (12). Clinical pathways are tools that contain clinical processes which have been derived from clinical practice guideline recommendations and are appropriate for providing care in a specific healthcare environment (13).

Intervention

In a pilot test at Hospital Rebagliati, we used the five following components of the WHO MMIS (11, 14) for prompt care delivery for children with cancer and fever.

System change ("Build it"). Adopting and adapting a care bundle and clinical pathways for antibiotic selection and using these in caring for children with cancer and fever. The interventions constituting the care bundle and the antibiotic selection pathways comprise routine evidence-based practices and parameters identified and assembled by the study team members (14-16). The DoTT care bundle (Table 1) interventions are based on pediatric practices used when evaluating and caring for children with cancer and suspected infection. The care bundle has four categories of essential interventions: (1) obtaining vital signs; (2) swift patient evaluation and interventions; (3) systematic patient evaluation and antibiotic administration; and (4) follow-up. Each category includes a set of actions. The antibiotic clinical pathways take the form of a decision flow diagram (Figure 1) of possible clinical and laboratory scenarios that will aid the selection of an appropriate antimicrobial when caring for children with fever in the ED and are illustrated in Spanish-language posters and pamphlets.

Teaching and training program ("Teach it"). The training program was delivered to a cohort of clinicians and nurses from the ED of Hospital Rebagliati and lasted eight weeks. The program was designed by an educational team comprising local physicians and St. Jude collaborators trained in pediatric oncology, pediatric emergency medicine, higher education, infectious diseases, teaching design, and global health. The team built an eight-week training program (1) to review essential topics about infections, risk factors, and the care required by children with cancer and fever; and (2) to teach the use of the DoTT care bundle and the antibiotic selection pathways. Five prerecorded lectures (155 minutes) in Spanish addressed fever in children with cancer, prevention of infections associated with central venous catheters, blood culture collection, diagnosis and treatment of infections, and the DoTT project. These lectures were uploaded on www.cure4kids.org, an educational website. A second segment of the training program had three synchronous live virtual workshops (60 minutes each) led by experts in pediatric infectious disease, and covered DoTT bundle tool use, risk categorization in FN, and antibiotic selection (Table 1, Figure 1). In the eight-week training, the students accessed the lectures asynchronously, but accessed the three live workshops synchronously (Figure 2). The minimum passing grade for the post-test exam was 80%. We used the reaction and learning domains of the Kirkpatrick evaluation model (17) to assess the efficacy of the training. A satisfaction survey, scored from 1 (worst) to 5 (best), applied at the end of each course, measured expectations, organization, methodology, applicability, and overall assessment of the course. A pre-test and post-test for learning assessment were also conducted to evaluate the knowledge gained from the course.

TABLE 1. DoTT care bundle interventions and actions

Category of intervention bundle – Fever in cancer	Actions
Step 1: Obtain vital signs	Temperature Blood pressure Heart rate Respiratory rate Capillary refill Oxygen saturation
Step 2: Swift patient evaluation and interventions	 Airway and respiration If there is respiratory distress, provide oxygen If no improvement or deterioration, be ready for ventilatory support Circulatory and mental status Poor capillary refill, 20 mL/kg fluids in bolus,^a repeat if patient tolerates up to 3 times If not improvement, consider vasopressors
Step 3: Systematic patient evaluation and antibiotic administration	 a. Evaluation of patient from head to toe Medical history and systematic patient evaluation from head to toe, including perianal and perineal mucosal and skin folds areas b. Laboratory studies and imaging Blood cultures (from peripheral puncture and every lumen of indwelling catheter) Complete blood cell count Urine analysis and culture Imaging if indicated c. Antibiotic selection and administration^b Broad spectrum antibacterial, provide additional antimicrobial if risk for multidrug-resistant organisms
Step 4: Follow-up	 Repeat evaluations of Step 3a daily until patient is stable Obtain additional studies based on findings and availability of resources Respiratory secretions (nasopharyngeal swabs, bronchoalveolar lavage) – viral, bacterial, fungal, and mycobacterial studies by cultures, PCR, antigen testing Chest X-ray imaging if respiratory symptoms or other indications Sinus evaluation if respiratory symptoms or other indications Diarrheic stools evaluation for gastrointestinal (GI) pathogens, including <i>C. difficile</i> toxins Abdominal imaging if GI symptoms

Note: ^a Perform blood cultures at initial peripheral venous access, and/or from each of the lumen of existing catheters; ^b Selection of antibiotics based on Figure 1. Source: Adapted from Caniza MA et al. (14).

Monitoring and feedback ("Check it"). We monitored how well the application of our DoTT bundle and antibiotic selection pathways addressed care delays and improved antibiotic selection. Eligible patients were children with hematologic neoplasms or solid tumors who had received chemotherapy in the last 15 days and who met the definitions of FN. We excluded patients whose medical records were unavailable for review or incomplete, patients receiving palliative treatment, and hematopoietic stem cell transplant recipients. We collected demographic, clinical, and laboratory data; the time the patient arrived in the clinical triage area; the initial patient evaluation; the laboratory report; and the medical consultation report. We also obtained the length of hospital stay in days, admission to the critical care unit, and mortality. The utility of the DoTT bundle and pathways (system change) and the training of the HCPs was assessed by observing the effect on the PTA and TTA for the patients enrolled in our study. We also monitored indicators of disease severity, indicators of care (including intensive care unit [ICU] admission), total length of hospital stay, and mortality. To monitor the frequency of use of the DoTT bundle, we reviewed the historical rates of children with FN and the number of children enrolled in our study during the study period.

Reminders and communications ("Sell it"). We distributed pamphlets, flyers, and posters as reminders of the DoTT bundle and the antibiotic clinical care pathways. Large reminders (posters) were placed on the ED walls, and small reminders (pamphlets) were provided to HCPs to use at the point of care.

Culture change ("Live it"). The DoTT project culture change required the ongoing participation of the hospital management and the pediatric ED director. This support facilitated the development and empowerment of an institutional multidisciplinary team of pediatricians, pediatric residents, pediatric emergency nurses, pediatric oncologists, and pediatric hematologists.

Data analysis

The PTA and TTA, as MMIS outcome indicators, were recorded for patients who received care in the ED of Hospital Rebagliati before and after the educational intervention for the ED HCPs, and the outcomes in the two patient cohorts were compared using the Fisher exact test and the Mann–Whitney U test. The Fisher exact test measured the association between the PTA and TTA, and the outcomes including sepsis, septic shock, and death. The Mann–Whitney U test measured PTA and TTA. Statistical significance was considered as p < 0.05. Descriptive statistics were used to report the frequency of degrees of infection severity and other healthcare indicator markers, including length of hospital stay, ICU admission, and mortality.

Ethical considerations

The project was reviewed and approved by the Hospital Rebagliati institutional ethics committee and by the Hospital Rebagliati Quality Management Office in October 2020. The

FIGURE 1. DoTT project antibiotic selection pathways



Note: AmB, amphotericin B; CVC, central venous catheter; DoTT, Decreasing Time to Therapy; ESBL, extended spectrum beta lactamase; MRSA, methicillin resistant Staphylococcus aureus; TMP/SMX, trimethoprim/ sulfamethoxazole; VRE, vancomycin resistant enterococcus. Source: Prepared by the authors.

FIGURE 2. DoTT training: timeline and components of distance and in-person learning



analyses used anonymized, secondary, and aggregated data, and because of the nature of the study, the retrospective review, and the minimal risk, no consent was obtained from the patients.

RESULTS

Teaching and training

We trained three consecutive student cohorts from 1 May 2021 to 30 May 2022. At that time, the ED of Hospital Rebagliati had 103 HCPs, and we trained 84 physicians, residents, and nurses, representing 82% of the ED staff. Of the 84 participants, 61 (72%) completed both the pre-test and the post-test. The overall satisfaction of participants at the end of the three sessions was 3.7/5. The average results of the pre-tests of the three courses were 59, 57, and 50 and the post-tests were 95, 90, and 81, which reflected a 61%, 58%, and 62% knowledge increase at the end of the training sessions, respectively.

Monitoring and feedback

We analyzed the patient outcomes before and after the MMIS intervention with regard to the PTA, the TTA, and the effect of the time difference on the outcomes of patient care, namely the length of hospital stay, ICU admission, and mortality. The findings are detailed below.

Pre-intervention and post-intervention patient characteristics. The pre-intervention patient cohort were children with FN episodes who presented to the ED of Hospital Rebagliati between January 2020 and September 2021. In this cohort there were 99 episodes of FN in 99 patients, of whom 47% were female

TABLE 2. Characteristics of pediatric patients, under 15 years of age, who attended the emergency department because of febrile neutropenia

Characteristics	Pre-intervention group (<i>N</i> = 99)	Post-intervention group (<i>N</i> = 30)	
Sex Male (%) Female (%)	52 (53) 47 (47)	15 (39) 15 (61)	
Diagnosis Leukemia (%) Solid tumor (%)	85 (86) 14 (14)	17 (57) 13 (43)	

Source: Prepared by the authors.

and 85% had a leukemia diagnosis. The post-intervention cohort included 30 patients with 38 episodes of FN who came to the ED between October 2021 and May 2022. The median age of these 30 patients was 5.5 years (interquartile range [IQR] 4–10 years); 50% were female, and 57% had a leukemia diagnosis. These two cohorts are compared in Table 2.

Time from onset of fever to arrival in the ED (PTA). For patients in the pre-intervention group, the median time between fever onset and arrival in the ED (PTA) was 1 483 minutes (IQR 1 445–2 938 minutes). In the post-intervention group, the median time between fever onset and arrival in the ED was 660 minutes (IQR 210–2 500 minutes). A two-sample Wilcoxon rank-sum (Mann–Whitney) test showed this time reduction to be statistically significant (p < 0.001) (Table 3).

Time from arrival in the ED to first dose of antibiotics (TTA). In the pre-intervention group, the median time from arrival in the ED to the first dose of antibiotics (TTA) was 146 minutes (IQR 97–265 minutes). Post intervention, the emergency physician evaluated 100% of the patients within 10 minutes of their arrival at the hospital, with the median time to evaluation being 3.3 minutes. After their initial medical evaluation, all patients had an indication for blood culture, and the median time from evaluation to blood culture was 29 minutes (IQR 6-65 minutes). In the post-intervention group, the median TTA was 69 minutes (IQR 50–120 minutes). A two-sample Mann–Whitney U test showed this time reduction to be statistically significant (p < 0.001). And the analysis of 38 episodes in the post-intervention group found that a TTA longer than 120 minutes, using a Fisher exact test, had a statistically significant increased risk of developing septic shock (p = 0.035), but not significant relation to the length of stay, ICU admission, sepsis, severe sepsis, or mortality (Table 3).

Differences of type of malignancies and PTA and clinical outcomes. We found that PTAs were longer for patients with hematologic neoplasms than for patients with solid tumors (p = 0.004), but for the subsets of patients with these two types of malignancy whose TTAs exceeded 120 minutes, there was no difference between the two groups regarding length of hospital stay, transfer to the pediatric ICU, sepsis, severe sepsis, or mortality.

Reminders and communications

As a result of the widely distributed reminders and posters, the DoTT project rapidly became widely recognized and appreciated at Hospital Rebagliati.

TABLE 3. Clinical outcomes by time from arrival at the emergency room to first dose of antibiotics or time to antibiotics (TTA)

Outcomes	Pre-intervention group			Post-intervention group		
	TTA <120 min (<i>n</i> = 42)	TTA >120 min (<i>n</i> = 54)	р	TTA <120 min (<i>n</i> = 29)	TTA >120 min (<i>n</i> = 9)	p
Days of hospital stay median (IQR)	93 (72–108)	225 (168–333)		9 (7–10)	6 (5–33)	
Transfer to pediatric ICU n (%)	0 (0)	0 (0)	0.28	0 (0)	1 (11)	0.28
Sepsis n (%)				5 (65)	3 (35)	
Severe sepsis n (%)				2 (7)	2 (22)	0.19
Septic shock n (%)				1 (3)	3 (33)	0.03
Death <i>n</i> (%)				1 (3)	3 (33)	0.84

Note: min, minutes; IQR, interquartile range; ICU, intensive care unit; [--], no data; TTA, time to antibiotics Source: Prepared by the authors.

Culture change

At the time of writing, the hospital leaders have embraced the DoTT project as a valuable institutional initiative. The educational director of the resident program supported the DoTT training for the ED HCPs. DoTT project progress reports were provided to institutional leaders and team members and were disseminated countrywide as a national demonstration project. To sustain the project, we plan to insert each DoTT project component into the routine and established activities of the institution. To date, the DoTT project has received institutional and national awards in the category of QI.

DISCUSSION

We identified an opportunity to apply an MMIS to improve the outcomes of care for children with FN. Implementing components of the MMIS enhanced the access to health care and the quality of health care for the patients studied. We reduced the PTA and TTA and demonstrated that prolonged waits for health care could be shortened by targeted training of HCPs and by providing tools to facilitate healthcare decisions and practices, resulting in improved, effective, and possibly lowcost interventions.

The TTA in the pre-intervention group was 146 minutes. In our prior study of TTA at Hospital Rebagliati (18), patients who did not undergo a medical evaluation had a median TTA of 119 minutes, and those who underwent an evaluation had a median TTA of 393 minutes. Other Latin American studies also found long TTAs (4, 19). For example, in Chile, the TTA was 200 minutes (19), and the delay was associated with the high patient load in the pediatric ED, the lack of supplies for blood culture and for vascular access, the long wait time to obtain cultures and imaging studies, and difficulties in procuring antibiotics from hospital pharmacies. In El Salvador (4), although the TTA was 210 minutes, the PTA was recognized as a greater problem contributing to the morbidity and mortality of children with FN. Causes of delays in the El Salvador study were illiteracy, poverty, and long travel times to reach a hospital. However, similar causes of long TTAs have been identified in other LMICs. In a study in the Philippines, the mean TTA was 900 minutes (5), and it was concluded that the TTA could be reduced by educating parents and care providers about better care for infections, risk factors, and how to improve the availability of antibiotics and supplies. Likewise, TTAs were also prolonged in African countries, being reported as 336 minutes in Ethiopia (20) and 1 380 minutes elsewhere (21). In contrast, the TTAs in high-income countries (HICs) were shorter than those in the aforementioned LMICs at less than 60 minutes (22–24). The heterogeneous delays across the world for evaluating children with FN by HCPs and the waiting to administer antibiotics are often related to the socioeconomic conditions of the patients and their families and to multiple institutional factors that affect the TTA, which reflects not only the number and quality of human resources at the institution but also available supplies and processes for healthcare delivery. Advancing HCPs' knowledge and encouraging the adoption of a risk stratification for clinical management (25, 26) of children with cancer and FN improved outcomes (27-29). Factors contributing to the shorter TTAs in HICs include the standardization of the evaluation and reevaluation process and the continuous improvement in the quality of care. However, reasons and results of TTAs might be more complex. In the United States of America, a study found no differences in outcomes when TTAs were shorter or longer than 60 minutes (30). The divergent findings of these studies might be related to the longer wait times, worse patient health conditions, and overall lower quality of healthcare delivery in LMICs, as compared to HICs.

In our study, education of ED HCPs and using clinical care decision tools decreased TTA by half, bringing it close to the time recommended in published studies (29, 31). Due to the intricate reasons for prolonged TTA and the consequences of delays (32, 33), we adopted the MMIS elements that have been used to improve complex healthcare practices (10). Studies have shown that implementing a QI project like ours can reduce TTA for pediatric oncology patients in HICs and improve the quality of care and patient survival (6, 7, 27). But there are only a few reports on implementing such projects to reduce TTA in LMICs (27). A recent QI project had used a previously established model to decrease TTA (27) that expanded its application by following principles of the Collaborative model of the Institute of Health Improvement (34). This project brought significant reductions in TTA at multiple pediatric oncology centers throughout Mexico (P. Friedrich, Personal Communication, May 2023). The application of our model as a pilot project at Hospital Rebagliati had similarly positive results. Subsequent phases of our project will concentrate on evaluating our clinical decision tools and user satisfaction, saturation training of HCPs in topics relevant to children with fever and cancer, providing periodic feedback of relevant project information to DoTT stakeholders, and promoting the institutional adoption of DoTT QI. The delays in administering appropriate antibiotics will be addressed by expediting patient evaluation and resuscitation measures, laboratory evaluation, and vascular access and by improving access to essential antimicrobials and supplies for administration at the point of care (35). However, these clinical care measures and interventions will require sustained institutional participation in training HCPs and in implementing and evaluating the performance of clinical care processes (6) of the DoTT project into the routine and established activities of the ED, and into the professional education at Hospital Rebagliati as a whole.

We observed that the PTA before the intervention was 24 hours and that the PTAs for patients with hematologic malignancies were longer than those for patients with solid tumors. This finding requires additional analysis, considering that, at Hospital Rebagliati, hematologic malignancies in children are treated in the Pediatric Hematology Service and solid tumors are treated in the Pediatric Oncology Service. Few studies of PTA have been conducted, and in those of HICs (22) the delays are less significant than in LMICs where the socioeconomic level of patients is the main associated factor. While the studies in LMICs have noticed that the PTA is longer than the TTA, which is even more important and requires intervention to reduce the wait time and associated outcomes (4). Our PTA findings are similar to those of studies in other LMICs (4, 19). Although our primary objective was to reduce TTA, we also observed a statistically significant decrease in PTA to 11 hours in the post-intervention group (p < 0.01). We attributed this to the counseling that the ED HCPs gave to the parents and caregivers of hospitalized children, encouraging them to go promptly to the pediatric ED when the child had their next episode of fever.

Our study has some limitations with respect to its wider applicability. One of these is that the DoTT project is a collaborative strategy implemented within the framework of the GICC. However, the next objective of the DoTT work team is to achieve the institutionalization of the educational intervention as part of the annual training plan for HCPs in the Pediatric ED of Hospital Rebagliati and to expand the project to other institutions in Peru to replicate and confirm the results. Another limitation is that we used our clinical decision tools only at Hospital Rebagliati, and they were not validated for other healthcare institutions. However, the health systems across Peru are similar, and we hope that the DoTT clinical decision tools will maintain their performance in other settings. This will be demonstrated when they are implemented in those settings.

Conclusion

Our study demonstrates that using elements of the MMIS reduced the TTA in pediatric patients with cancer and FN, and that PTA was also decreased, but further studies will be required to adopt elements impacting the PTA delays. The findings of this study are relevant to Hospital Rebagliati, and potentially as a national model to replicate at other institutions in Peru. To sustain the DoTT project, Hospital Rebagliati must incorporate this initiative within its established institutional format, assigning resources to use DoTT elements, and report periodically PTA and TTA as quality indicators along with other established practices for the care of children with cancer. The institutional leadership ownership and accountability for the health benefits of the DoTT project and the savings that it could generate is a model to be adopted by other institutions in Peru and the region.

Author contributions. MC conceived the original idea; MC, LV, EM, and CP designed the study; AM, LRL, MVA, EM, MH, WDA, and CRB collected the data and contributed data; EM, CP, and LV analyzed the data; EM, CSS, LV, CP, and MC interpreted the results; all authors wrote the paper. All authors reviewed and approved the final version.

Acknowledgments. We thank all the healthcare providers from the ED at Hospital Rebagliati and the patients and their parents for participating in the project. We also thank Keith A. Laycock for excellent scientific editing of the manuscript; and the <u>www.</u> <u>Cure4Kids.org</u> team of St. Jude Children's Research Hospital. This study was supported by ALSAC.

Disclaimer. Authors hold sole responsibility for the views expressed in the manuscript, which may not necessarily reflect the opinion or policy of the *RPSP/PAJPH* and/or the Pan American Health Organization (PAHO).

REFERENCES

- Castagnola E, Fontana V, Caviglia I, Caruso S, Faraci M, Fioredda F, et al. A prospective study on the epidemiology of febrile episodes during chemotherapy-induced neutropenia in children with cancer or after hemopoietic stem cell transplantation. Clin Infect Dis. 2007;45(10):1296–1304.
- Burry E, Punnett A, Mehta A, Thull-Freedman J, Robinson L, Gupta S. Identification of educational and infrastructural barriers to prompt antibiotic delivery in febrile neutropenia: a quality improvement initiative. Pediatr Blood Cancer. 2012;59(3):431–435.
- Fletcher M, Hodgkiss H, Zhang S, Browning R, Hadden C, Hoffman T, et al. Prompt administration of antibiotics is associated with improved outcomes in febrile neutropenia in children with cancer. Pediatr Blood Cancer. 2013;60(8):1299–1306.
- 4. Gavidia R, Fuentes SL, Vasquez R, Bonilla M, Ethier MC, Diorio C, et al. Low socioeconomic status is associated with prolonged times to assessment and treatment, sepsis and infectious death in pediatric fever in El Salvador. PLoS One. 2012;7(8):e43639.
- 5. Kirby J, Dolendo M, Guimera D, Castillo C, Johnson KM, Mzayek F, et al. Predictors of wait-time for antibiotic initiation and association of wait-time with hospital length of stay and ICU admission among children with cancer at the Southern Philippines Medical Center. Pediatr Blood Cancer. 2014;61(4):680–686.
- Dandoy CE, Hariharan S, Weiss B, Demmel K, Timm N, Chiarenzelli J, et al. Sustained reductions in time to antibiotic delivery in febrile immunocompromised children: results of a quality improvement collaborative. BMJ Qual Saf. 2016;25(2):100–109.
- Monroe K, Cohen CT, Whelan K, King A, Maloney L, Deason J, et al. Quality Initiative to Improve time to Antibiotics for Febrile Pediatric Patients with Potential Neutropenia. Pediatr Qual Saf. 2018;3(4):e095.
- 8. Peru, Ministerio de Salud. Informe de la II Reunión Nacional sobre Cáncer Infantil en Perú. Lima: Ministerio de Salud; 2020.
- 9. World Health Organization. Global initiative for childhood cancer. Geneva: WHO; 2020 [cited 24 June 2023]. Available from: https://www.who. int/publications/m/item/global-initiative-for-childhood-cancer.
- 10. Chen JK, Wu KS, Lee SS, Lin HS, Tsai HC, Li CH, et al. Impact of implementation of the World Health Organization multimodal

hand hygiene improvement strategy in a teaching hospital in Taiwan. Am J Infect Control. 2016;44(2):222–227.

- World Health Organization. WHO multimodal improvement strategy. Geneva: WHO; [date unknown] [cited 25 June 2023]. Available from: https://cdn.who.int/media/docs/default-source/ integrated-health-services-(ihs)/infection-prevention-and-control/ core-components/ipc-cc-mis.pdf.
- 12. Resar R, Griffin FA, Haraden C, Nolan TW. Using care bundles to improve health care quality: IHI innovation Series white paper. Cambridge, MA: Institute for Healthcare Improvement; 2012.
- Busse R, Klazinga N, Panteli D, Quentin, W. Improving healthcare quality in Europe. Characteristics, Effectiveness and Implementation of Different Strategies. Copenhagen: European Observatory on Health Systems and Policies; 2019.
- 14. Caniza MA, Odio C, Mukkada S, Gonzalez M, Ceppi F, Chaisavaneeyakorn S, et al. Infectious complications in children with acute lymphoblastic leukemia treated in low-middle-income countries. Expert Rev Hematol. 2015;8(5):627–645.
- Chameides L, Samson RA, Schexnayder SM, Hazinski MF (editors). American Heart Association. Pediatric Advanced Life Support Provider Manual. Dallas, TX: American Heart Association; 2012.
- 16. Robertson J, Shilkofski N. The Harriet Lane Handbook. Philadelphia, PA: Elsevier Mosby; 2005.
- Kirkpatrick JD, Kirkpatrick WK. Kirkpatrick's Four Levels of Training Evaluation. Alexandria, VA: ATD Press; 2016.
- Rios L, Vasquez L, Maza I, Oscanoa M, Paredes G, Tarrillo F, et al. Time to first dose of antibiotics in children with cancer and febrile neutropenia. A report from a Peruvian hospital. Ann Med Clin Oncol. 2021;4:133.
- 19. De la Maza V, Simian D, Castro M, Torres JP, Lucero Y, Sepulveda F, et al. Administration Time for the First Dose of Antimicrobials in Episodes of Fever and Neutropenia in Children With Cancer. Pediatr Infect Dis J. 2015;34(10):1069–1073.
- Abebe W, Bacha T, Shane AL, Berkowitz T. Triage guideline for immunocompromised children with fever in an emergency centre in Ethiopia. Afr J Emerg Med. 2021;11(1):20–25.

- 21. Israels T, Afungchwi GM, Klootwijk L, Njuguna F, Hesseling P, Kouya F, et al. Fever and neutropenia outcomes and areas for intervention: A report from SUCCOUR Supportive Care for Children with Cancer in Africa. Pediatr Blood Cancer. 2021;68(9):e29224.
- Anderson K, Bradford N, Edwards R, Nicholson J, Lockwood L, Clark JE. Improving management of fever in neutropenic children with cancer across multiple sites. Eur J Cancer Care (Engl). 2021;30(3):e13413.
- 23. Benner CA, Mora E, Mueller E, Seagull FJ, Walkovich K, Johnson K, et al. Making Improvements in the ED: Does ED busyness affect time to antibiotics in febrile pediatric oncology patients presenting to the emergency department? Pediatr Emerg Care. 2018;34(5):310–316.
- 24. Burns B, Hartenstein M, Lin A, Langley D, Burns E, Heilman J, et al. Optimizing time to antibiotic administration in children with possible febrile neutropenia through quality improvement methodologies. Pediatr Qual Saf. 2019;4(6):e236.
- 25. Klastersky J, de Naurois J, Rolston K, Rapoport B, Maschmeyer G, Aapro M, et al. Management of febrile neutropaenia: ESMO Clinical Practice Guidelines. Ann Oncol. 2016;27(suppl 5):v111–v118.
- 26. Lehrnbecher T, Robinson P, Fisher B, Alexander S, Ammann RA, Beauchemin M, et al. Guideline for the management of fever and neutropenia in children with cancer and hematopoietic stem-cell transplantation recipients: 2017 update. J Clin Oncol. 2017;35(18):2082–2094.
- 27. Gonzalez ML, Aristizabal P, Loera-Reyna A, Torres D, Ornelas-Sanchez M, Nuno-Vazquez L, et al. The Golden Hour: sustainability and clinical outcomes of adequate time to antibiotic administration in children with cancer and febrile neutropenia in northwestern Mexico. JCO Glob Oncol. 2021;7:659–670.
- Roman CP, Poole SG, Dooley MJ, Smit de V, Mitra B. Implementation of hospital-wide reform at improving access and flow: Impact on time to antibiotics in the emergency department. Emerg Med Australas. 2016;28(2):133–137.

- 29. Salstrom JL, Coughlin RL, Pool K, Bojan M, Mediavilla C, Schwent W, et al. Pediatric patients who receive antibiotics for fever and neutropenia in less than 60 min have decreased intensive care needs. Pediatr Blood Cancer. 2015;62(5):807–815.
- Wadhwa A, Oakley J, Richman J, Bhatia S, Kutny MA. Time to antibiotic for pediatric oncology patients with febrile neutropenia at regional emergency departments. Pediatr Emerg Care. 2022;38(1):e94–e99.
- Rosa RG, Goldani LZ. Cohort study of the impact of time to antibiotic administration on mortality in patients with febrile neutropenia. Antimicrob Agents Chemother. 2014;58(7):3799–3803.
- Evans IVR, Phillips GS, Alpern ER, Angus DC, Friedrich ME, Kissoon N, et al. Association between the New York sepsis care mandate and in-hospital mortality for pediatric sepsis. JAMA. 2018;320(4):358–367.
- 33. Weiss SL, Fitzgerald JC, Balamuth F, Alpern ER, Lavelle J, Chilutti M, et al. Delayed antimicrobial therapy increases mortality and organ dysfunction duration in pediatric sepsis. Crit Care Med. 2014;42(11):2409–2417.
- 34. Institute for Healthcare Improvement. The Breakthrough Series: IHI's Collaborative Model for Achieving Breakthrough Improvement. IHI Innovation Series white paper. Boston, MA: IHI; 2003.
- 35. Cohen C, King A, Lin CP, Friedman GK, Monroe K, Kutny M. Protocol for reducing time to antibiotics in pediatric patients presenting to an emergency department with fever and neutropenia: efficacy and barriers. Pediatr Emerg Care. 2016;32(11):739–745.

Manuscript received on 3 July 2023. Revised version accepted for publication on 14 August 2023.

Una estrategia multimodal para mejorar la atención médica de pacientes pediátricos con cáncer y fiebre en Perú

RESUMEN

Objetivo. El proyecto DoTT (Disminuyendo el tiempo a la terapia, sigla en inglés) busca minimizar el intervalo entre el inicio de la fiebre y las intervenciones médicas en la población infantil con neutropenia febril. El objetivo de este estudio fue determinar el efecto de la implementación del proyecto DoTT sobre el tiempo transcurrido desde el inicio de la fiebre hasta la llegada del paciente (TLP) al hospital y el tiempo transcurrido en el hospital hasta la administración del antibiótico (TAA) en niños con neutropenia febril ingresados en el servicio de urgencias.

Métodos. El proyecto DoTT se puso en marcha en un hospital peruano, según el modelo de estrategia multimodal de mejora de la Organización Mundial de la Salud (OMS). Entre sus componentes se encontraban crear un conjunto de servicios de atención de salud y de algoritmos para la selección de antibióticos; capacitar a los usuarios en la utilización del conjunto de servicios y de los algoritmos; realizar un seguimiento de los resultados de los pacientes y recabar la opinión de los usuarios; fomentar el uso del nuevo sistema; y promover la integración del proyecto en la cultura institucional. Se capacitó al personal de la sala de urgencias en la atención de pacientes pediátricos con cáncer y fiebre, y en el uso del conjunto de servicios y de los algoritmos. Se informó sobre el proyecto DoTT mediante folletos y carteles, con vistas a institucionalizar el concepto y difundirlo a otros servicios hospitalarios.

Resultados. Se analizaron los datos de ingreso de 129 pacientes de nuestro registro que cumplían con los requisitos. Se compararon el TAA y el TLP al hospital antes y después de la intervención con las pautas del proyecto DoTT. La mediana del TAA fue de 146 minutos (intervalo intercuartílico [II]: 97-265 minutos) en 99 pacientes antes de la intervención y de 69 minutos (II: 50-120 minutos) en 30 pacientes después de ella (p <0,01). La mediana del TLP disminuyó de 1 483 minutos en el momento de la evaluación inicial a 660 minutos después de la intervención (p <0,01).

Conclusiones. La aplicación del modelo de estrategia multimodal de mejora de la OMS a la atención de la población infantil con neutropenia febril que acude al hospital tuvo un efecto positivo sobre el TLP y el TAA, lo que podría aumentar la supervivencia de estos pacientes.

Palabras clave Servicio de oncología en hospital; servicio de urgencia en hospital; neutropenia febril; salud infantil; paquetes de atención al paciente; Perú.

Uma estratégia multimodal para melhorar a prestação de serviços de saúde para pacientes pediátricos com câncer e febre no Peru

RESUMO

Objetivo. O projeto DoTT (Redução do Tempo para o Tratamento, na sigla em inglês) tem como objetivo reduzir ao máximo o intervalo entre o início da febre e as intervenções médicas em crianças com neutropenia febril. O objetivo deste estudo foi determinar o efeito da implementação do projeto DoTT no tempo desde o início da febre até a chegada do paciente (TCP) ao hospital e no tempo no hospital até a administração de antibióticos (TAA) em crianças com neutropenia febril admitidas no departamento de emergência.

Métodos. O projeto DoTT foi implementado em um hospital do Peru e seguiu o modelo de estratégia de melhoria multimodal da Organização Mundial da Saúde (OMS). Os componentes incluíram a criação de um pacote de prestação de serviços de saúde e de protocolos de seleção de antibióticos, o treinamento de usuários no pacote e nos protocolos de seleção, o monitoramento da evolução dos pacientes e obtenção de feedback dos usuários, o incentivo ao uso do novo sistema e a promoção da integração do DoTT à cultura institucional. Os profissionais do pronto-socorro foram capacitados na prestação de cuidados a crianças com câncer e febre e no uso do pacote e dos protocolos de seleção. O DoTT foi divulgado por meio de panfletos e pôsteres, com o objetivo de institucionalizar o conceito e disseminá-lo para outros serviços hospitalares.

Resultados. Foram analisados os dados de internação de 129 pacientes elegíveis em nosso registro. O TAA e o TCP foram comparados antes e depois da intervenção DoTT. O TAA mediano era de 146 minutos (intervalo interquartil: 97-265 minutos) antes da intervenção em 99 pacientes e de 69 minutos (intervalo interquartil: 50-120 minutos) depois da intervenção em 30 pacientes (p < 0,01). O TCP mediano diminuiu de 1483 minutos na linha de base para 660 minutos após a intervenção (p < 0,01).

Conclusão. A aplicação do modelo de estratégia multimodal de melhoria da OMS ao atendimento de crianças com neutropenia febril que chegam ao hospital teve um impacto positivo no TCP e no TAA, potencialmente aumentando a sobrevida desses pacientes.

Palavras-chave Serviço hospitalar de oncologia; serviço hospitalar de emergência; neutropenia febril; saúde da criança; pacotes de assistência ao paciente; Peru.