Outcome and complications of outpatient parenteral therapy in pediatric emergency utilizing only peripheral vascular access

A retrospective descriptive study

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ABSTRACT

الأهداف: لوصف معدلات الشفاء والمضاعفات للعلاج الوريدي للمرضى الخارجيين (OPT) باستخدام الوصول إلى الأوعية الدموية الطرفية فقط.

المنهجية: باستخدام تصميم دراسة وصفية بأثر رجعي، قمنا بمراجعة المخططات الطبية للأطفال حتى عمر 15 عامًا والذين خرجوا من قسم الطوارئ إلى وحدة رعاية OPT من يناير 2018 إلى أبريل 2019. وكانت النتائج الأولية هي معدلات الشفاء والمضاعفات.

النتائج: من أصل 814150 زيارة، تمت معالجة 2788 زيارة (0.34%) في وحدة OPT، وهو ما يمثل 2126 مريضًا. كان لدى الأغلبية أعراض لمدة يومين، وكان 26.4٪ يعانون من أمراض مصاحبة. بدأ معظم المرضى بعلاج حالات الإنتان المشتبه بها والتهابات المسالك البولية المشتبه بها أو المؤكدة. بلغ إجمالي أيام العلاج لجميع المرضى 3663 يوم. تم استخدام cephalosporins بنسبة 75٪، ومعظمها ceftriaxone. أكمل معظم المرضى العلاج الوريدي خلال يومين، وتطلبت 2.8٪ من الحالات تغيير المضادات الحيوية. وتم تحقيق تجنب إعادة الدخول للمستشفى والتعافي الكامل في 99.3٪، وكان 0.7٪ بحاجة إلى إعادة الدخول للمستشفى. كان لدى جميع المرضى إمكانية الوصول إلى الأوعية الدموية الطرفية. حدثت مضاعفات في 21٪ من الحالات وكان معظمها مرتبطًا بالوصول إلى الأوعية الدموية، ولكن تمت إدارة أكثر من 80٪ من الحالات عن طريق إعادة إدخال المغذي الوريدي لمرة واحدة، ولم يتم تعديل العلاج إلا في 0.5٪ بسبب هذه المضاعفات.

الخلاصة: بالنسبة للمرضى المختارين بعناية في طوارئ الأطفال، يبدو العلاج الوريدي في العيادات الخارجية فعالاً وآمنًا مع حدوث مضاعفات يمكن التحكم فيها، وقد يؤدي إلى تقليل القلق العائلي مقارنة بالدخول للمستشفى.

Objectives: To describe the cure and complication rates of outpatient parenteral therapy (OPT) utilizing only peripheral vascular access.

Methods: Using a retrospective descriptive study design, we reviewed the medical charts for children aged up to 15 years old who had been discharged from the emergency department into the care of the OPT unit from January 2018 to April 2019. The primary outcomes were cure and complication rates.

Results: Out of 814,150 visits, 2,788 (0.34%), accounting for 2,126 patients, were managed in the OPT unit. The majority had 2 days of symptoms, and 26.4% had comorbidities. Most patients started the treatment for suspected sepsis and suspected or confirmed urinary tract infections. The total days of therapy for all patients were 3,663. Cephalosporins were used for 75%, mostly ceftriaxone. Most patients completed the IV therapy within 2 days, 2.8% of cases required a change of antibiotics. Readmission avoidance and full recovery were achieved in 99.3%, and 0.7% needed readmission. All patients had peripheral vascular access. Complications occurred in 21%. Most were related to vascular access, but more than 80% were managed by one-time IV cannula re-insertion, and only 0.5% had treatment modification because of these complications.

Conclusion: For carefully selected patients in the pediatric emergency, outpatient parenteral therapy seems effective, safe with manageable complications, and may result in less family disturbance than hospital admission.

Keywords: outpatient, parenteral, therapy, pediatric, emergency, cannula

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In 1974, for the first time outside of hospitals, patients with cystic fibrosis were given intravenous (IV) medicines.[1] Since then, it has been used more and more. This practice is possible in areas where supportive elements exist and replace the need for multiple intramuscular injections.[2,3] Home health care services made it easier for the families by administering the IV medications at home not only for chronic conditions, such as immunodeficiency and cystic fibrosis but also for cellulitis, respiratory, urinary, and other infections in children and adults.[4-7] Such "hospitals at home" have lower mortality, readmission rates, and costs.[8] According to the user's view of such a service in acute childhood illness, 90% had a clear preference for the hospital-at-home service, which is not widely available.[9] Many places do not offer short courses of IV injections for patients who do not have long-term conditions.

A child's hospitalization can be hard on the family, there are risks of getting an infection in the hospital, and healthcare costs are rising.[10-15] Therefore, there is a growing trend toward setting up outpatient parenteral therapy (OPT). By providing the first IV dose in the pediatric emergency department, then discharging patients with a "capped" IV catheter to come back to a specific area in the emergency department for the subsequent doses of IV antibiotic and reassessment, it was found to be a safe and effective alternative to hospitalization.[16,17] It was also less expensive, and 94% of the parents preferred it.[18]

Aside from home health care, out-patient IV antibiotics have been used for several illnesses in children, such as low-risk febrile neutropenia in oncology patients, moderate to severe skin infections, pre-septal cellulitis, urinary tract infections, and mastoiditis.[13,19-26]

Central vascular catheters (CVC) and peripherally inserted central catheters (PICC) have been successfully used in patients discharged from inpatient care to home health services.[2-8]

The objective of this study was to describe our experience in the administration of outpatient IV therapy focusing on the cure rate and safety by utilizing only peripheral intravenous cannulations for patients discharged from pediatric emergency centers (PECs).

Methods. This is a retrospective descriptive study of patients treated in the OPT unit in an academic tertiary healthcare facility in Doha, Qatar, between January 2018 and April 2019. All patients below 15 years of age accepted for continuation of IV treatment in the OPT unit were included. Patients who were discharged from the emergency department (ED) but did not attend for at least one day were excluded from the analysis.

Prior to discharge from the ED, a parent was asked to sign an acceptance and commitment form stating that he/she will bring the child back to the medical staff for making a reasonable decision.

Patient selection for treatment in the OPT unit was based on the joint assessment and agreement by the senior consultant or consultant level supervising the observation areas in the PEC and the consultant in charge of the OPT unit.

The decision for IV therapy is carried out after a period of close observation and monitoring in the ED observation area to ensure patient stability.

The capped IV cannula was checked and flushed with saline to ensure its functionality before discharge from the ED or during the OPT unit follow-up, with family instructions to apply pressure if the cannula accidentally dislodged. In each OPT unit follow-up visit, the IV cannula was rechecked with a saline flush prior to medication administration. Then, if not functioning or there was a need to make a needle prick for aminoglycoside trough level with a better vein, the IV cannula was changed. The OPT unit is managed by senior pediatric emergency physicians and senior nurses with several years of experience in pediatric emergency.

Patients were identified by a medical record number in the OPT unit census record. A data collection sheets were designed to standardize the data extraction by different senior PEC physicians who worked in the OPT unit. This sheet contained information on demographics; clinical features; diagnosis; laboratory workup; type of vascular access; type of treatment in the ED observation areas; type and frequency of treatment during OPT unit follow-up, duration of therapy; ID consultations; continuation of OPT as planned; follow-up visits after discharge from the OPT unit; and success rate. The cure rate was defined as the resolution of the clinical signs and symptoms and, if available, supported by laboratory workup, including cultures. Safety was defined as the rate of vascular or drug-related complications. This study was approved by the institutional review board committee of Hamad General Hospital, Doha, Qatar (MRC-01-20-1062).

Statistical analysis. The Statistical Package for the Social Sciences, version 27.0 (IBM Corp, Armonk, NY, USA) software was used for analyses. A *p*-value of <0.05 was considered significant. Descriptive statistics were used to summarize and determine patients'

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characteristics. Categorical data were summarized using absolute numbers and percentages.

Results. From January 2018 to April 2019, 814,150 patients visited the main PEC and 3 PEC satellites, among others within the organization. During the same period, 2,788 (0.34%) visits for 2126 patients were referred to the OPT unit. The majority were referred from the main PEC (89.4%), and patients' ages ranged from 2 weeks to 15 years, with a mean of 2.1 years; the majority were infants (Table 1). Females were slightly more (52.2%). Only 1.9% of patients and families were non-compliant. A total of 333 (15.8%) patients had previous OPT unit visits.

Most patients who were included were in clinical situations where possible sepsis or suspected bacteremia was the concern (Table 2). More than two-thirds had the symptoms for 1-2 days, with comorbidities in 26.4%. Suspected systemic infections were in 51.4% but only confirmed in 3.4%. The total length of OPT treatment for all patients during the study period was 3663 days (Table 2).

More than 90% had white blood cell (WBC) counts carried out before treatment initiation. Blood culture was carried out with a positivity rate of 2.1% and urine culture was carried out with a positivity rate of 30% (Table 3). Nitrites were checked for 1601 (75.3%) and were positive in 5.9%. One cerebrospinal fluid (CSF) culture was positive. Cephalosporins were mostly used in both the PEC observation areas and after discharge to the OPT unit, and few needed antibiotics changes while in the OPT unit (Table 4).

Third-generation cephalosporins were given to 75% of the patients; ceftriaxone was given to 1,556 (98.5%) patients. More than 95% stayed for less than 24 hours in the PEC observation areas, and most

Table 1 - Age and source of referral to the outpatient parenteral therapy unit.

Parameters	n (%)
Age	
0-29 days	260 (12.3)
1-12 months	1006 (47.3)
1-3 years	415 (19.5)
3-6 years	217 (10.2)
>6 years	228 (10.7)
Total	2126 (100)
Source of referral	
Main PEC	1901 (89.4)
PEC satellites	194 (9.1)
Other hospitals	31 (1.5)

Values are presented as numbers and percentages (%). PEC: pediatric emergency center

Table 2 - Clinical data for patients treated in the outpatient parenteral therapy unit.

Parameters	n (%)	
Diagnosis		
Rule out sepsis	789 (37.1)	
Urinary tract infection	531 (25)	
Lower respiratory tract infection	198 (9.3)	
Dermatological conditions	93 (4.4)	
Hematological and oncological	90 (4.2)	
Abscess including dental abscess	78 (3.7)	
Neurological conditions	70 (3.3)	
GIT including salmonella infection	51 (2.4)	
ENT (AOM, pharyngitis) infections	50 (2.4)	
Lymphadenitis and infected cysts	46 (2.2)	
Ophthalmological conditions	22 (1.0)	
musculoskeletal and joints	5 (0.2)	
Others	103 (4.8)	
Total	2126 (100)	
Duration of symptoms (days)		
1-2	1533 (73.0)	
3-4	366 (17.0)	
5-10	193 (9.0)	
≥11	19 (1.0)	
Total	2111 (100)	
Primary co-morbidities		
Neurological and metabolic	171 (30.0)	
Congenital anomalies	151 (27.0)	
Hematology, oncology, and allergy	144 (26.0)	
Renal and urologic disorders	46 (8.0)	
Prematurity-related disorders	22 (4.0)	
Others	28 (5.0)	
Total	562 (100)	
Length of stay in OPT unit (days)	n (%)	Total no. of days
1	1136 (54.5)	1136
2	366 (17.6)	732
3	533 (25.6)	1599
4	49 (2.3)	196
Grand total (days)		3663

Values are presented as numbers and percentages (%). GIT: gastro intestinal tract, ENT: ear, nose, and throat, AOM: acute otitis media, OPT: outpatient parenteral therapy

Table 3 - Laboratory workup prior treatment initiation in the outpatient parenteral therapy unit.

Parameters	n	Results
Cultures type, no growth		
Blood	2038	1913 (94.0)
Urine	1675	1041 (62.2)
CSF	717	716 (99.9)
Others	89	51 (57.3)
High blood WBC		
Neonates	280	19 (6.8)
Infants	1007	378 (37.5)
Older	1088	361 (33.2)
Low blood WBC		
Neonates	280	20 (7.1)
Infants	1007	5 (0.5)
Older	1088	47 (4.3)
Uncentrifuged urine WBC, high (>10/HPF)	1312	595 (45.3)

Values are presented as numbers and precentages (%). WBC: white blood cell count, CSF: cerebrospinal fluid, HPF: high power field

of the patients treated in the OPT unit completed the treatment within 2 days (Table 4). Infectious disease service consultations were carried out for 1.6% of those who needed antibiotic therapy.

The antibiotics were changed in 2.8%, primarily shifting from wider spectrum (third generation cephalosporin) to narrower spectrum (aminoglycosides) antibiotics or from more frequent to less frequent dosing intervals. The antibiotics were changed to every 24 hours for 47 patients and every 12 hours for another 10 patients. Gentamicin and amikacin were given for 67%, cephalosporin for 20%, and ertapenem for 12% of those changes.

The cure rate was 99.3%. The patients were considered to be cured by the resolution of the clinical manifestation during the follow-up until discharge from the OPT unit. There was no significant difference in the cure rate, but the complication rate was significantly different between ≤3 months of age and older age group (p<0.001; Table 5).

A total of 14 (0.7%) patients experienced disease worsening and were readmitted to the hospital, one of them needed pediatric intensive care unit (PICU) admission. However, all were discharged home. A total of 449 (21%) patients had complications. One patient had anaphylaxis, which responded well to the standard treatment, while the rest of the complications were related to vascular access. These complications were: cannula dislodgment or infiltration in 227 (11%) patients and blocked cannula in 222 (10%) patients. These were managed by one-time cannula re-insertion for 372 (83%) patients, 2-time re-insertion for 53 (12%) patients, 3-time reinsertion for 18 (4%) patients, and 4-time reinsertion for 6 (1%) patients. The treatment changed because of vascular access complications in only 10 (0.5%) patients.

A total of 8 patients were readmitted to the hospital for incision and drainage for pus collection which evolved during the antibiotic treatment in the OPT unit. The other 6 patients were readmitted because of persistent symptoms, possibility of immunodeficiency, or appearance of new symptoms suggested the probability of other diagnosis needed further workup. Of the readmitted patients only 27 days old neonate with fever, found to be mildly distressed in the OPT unit due to respiratory syncytial virus (RSV) bronchiolitis, readmitted to the observation unit in the PEC where the patient developed an apnea for which respiratory support was initiated including endotracheal intubation and admitted to the PICU then discharged home. Antihemophilic factors were continued in the OPT unit for 29 (1.4%) patients.

Table 4 - Treatment in the outpatient parenteral therapy unit.

Parameters	n (%)
Antibiotics in the observation areas	
Cephalosporins (ceftriaxone/cefotaxime/cefepime, cefuroxime)	1516 (75.0)
Amikacin/gentamycin	285 (14.0)
Clindamycin	170 (8.0)
Other antibiotics	83 (4.0)
IV antibiotics in OPT unit	
Cephalosporins (ceftriaxone/cefotaxime/cefepime, cefuroxime)	1556 (75.0)
Amikacin/gentamycin	300 (14.0)
Clindamycin	164 (8.0)
Other antibiotics	52 (3.0)
Duration of stay in observation areas (hours)	
≤24	2026 (96.5)
>24-48	33 (1.6)
>48	6 (0.3)
Duration of intravenous treatment in OPT unit (days)	
≤2	1403 (68.0)
3-4	489 (24.0)
5-6	130 (6.0)
≥7	27 (1.0)
Total duration of IV and oral treatment in OPT unit (days)	
≤2	1136 (55.0)
3-4	366 (18.0)
5-6	532 (26.0)
7-8	49 (2.0)

Values are presented as numbers and percentages (%). OPT: outpatient parental therapy, IV: intravenous

Discussion. Approximately 60% were infants and the majority were treated for sepsis or while ruling out sepsis, lower respiratory tract infection, and urinary tract infections. Starting parenteral antibiotics for such patients were considered to be safer awaited the

Table 5 - Primary outcomes in young infants and older age group.

Parameters	Age			*P*-values
	≤3 months	>3 months	Total	
Total number	739 (34.8)	1387 (65.2)	2126 (100)	
Cure rate	735 (99.5)	1377 (99.3)	2112 (99.3)	0.626
Vascular access complications rate	114 (15.4)	335 (24.2)	449 (21.1)	0.001

Values are presented as numbers and percentages (%). *P*-value significance of <0.05.

culture results or clinical improvement. However, it is a subjective decision. Only very few reports studied the direct referral for OPT from PED, among these is a study carried out in 49 children's hospitals EDs where 1.8% of their patients needed referral for OPT.[27] Our referral rate of only 0.34% is much lower. There could be differences in patient acuity.

We consider the total number of patients in our study relatively high compared to other series.[28-32] The OPT unit is in the same building of the main PEC but managed by medical and nursing team independent of the PEC coverage. Therefore, almost 90% of the patients who were referred to the OPT unit were from the main PEC, and the remaining were from PEC satellites or other institutional EDs with no patients from the hospital wards. This contrasts with other studies, where the main referral source to the OPT unit was from the wards.[23,31] The younger the child, the more precautions are taken by the clinicians because of their more subtle presentation and faster deterioration; for this reason, infants comprised approximately 60% of the patients, followed by toddlers and older children. Thus, the mean age in our study was approximately 2 years which is lower than in previous studies.[23,31]

The compliance rate was very high, probably due to the avoidance of admissions and the associated social and family work disturbances, assurance by the continuation of follow-up and reassessment by a senior pediatric emergency physician, and the need for cannula care by the unit staff. The satisfaction rate has been reported to be high with one variant of OPT.[33]

Ruling out sepsis and probable sepsis were the most common diagnostic groups, including only those who were not clinically ill. There was a large gap between the suspected and later confirmed diagnoses. However, this was understood as an aim to avoid missing a serious infection. The OPT has been used for a wide spectrum of illnesses, such as oncology patients with low-risk febrile neutropenia, moderate to severe skin infection, pre-septal cellulitis, urinary tract infection, and mastoiditis among several other studies.[18-26,31,32] The diagnosis in our study covered most of these conditions.

Blood and urine laboratory tests were carried out more for infants looking for more supportive parameters, and the majority were normal. More than 4,500 cultures, including blood, urine, and CSF, were carried out. Most of these did not show growth, yet they were clinically significant in a minority of patients.

Because of the need for initial wider broad-spectrum coverage, third-generation cephalosporins were given to 75% of the patients. Of these, ceftriaxone was given for 98.5%, which reasonably explained the more convenient dosing interval like several other studies.[27,29,31,32,34] Ceftriaxone has an overall cure rate of 94% for serious bacterial infections in children; it is generally safe, convenient, and covers a wide spectrum of organisms.[35] Though there were reports of severe adverse reactions in 30% of the ceftriaxone-related adverse reactions, such as anaphylaxis and even death.[36] We encountered only one episode of anaphylaxis out of 1,556 patients treated with ceftriaxone.

Most of our patients were seen only one day in the OPT unit because the first dose was received in the PEC observation unit before discharge. Based on the 48-hour culture results, the decision to stop antibiotics was carried out, and this length of stay was much shorter than other reports.[29,32] However, the nature of the disease is an important determinant for the duration of parenteral antibiotics. The changes carried out in the antibiotic coverage only for 2.8% of patients. Mainly a shift from a wider spectrum (third-generation cephalosporins) to a narrower spectrum (aminoglycoside). The shift to oral antibiotics and therapy discontinuation was based primarily on clinical assessment, this was why only 4% had a laboratory workup at the end of the therapy courses, which was consistent with the published systematic review and guidelines.[37] Hospital readmission during the treatment in the OPT unit was very low (0.7%). Those readmitted were mainly for surgical intervention, which was much lower than in a previous study.[34]

This study is the largest utilizing only peripheral vascular access compared to other studies where CVCs were used.[6,30,31] Our study supported previous ones that showed this service is possible and achievable with no serious adverse effects. We provided the first IV dose in the PED and then discharged the patient with a "capped" IV catheter and instructions to come back to a specific area in the ED for the subsequent doses of IV antibiotics and safety reassessment.[9] In our study, we had a lower complication rate than other reported studies.[29,30,32] Complications were mainly in the vascular access, but the majority were managed by only one-time cannula reinsertion, and only 0.5% needed a change in treatment because of vascular issues. The complication rate in young infants was significantly less than that in older infants and children. This may be related to reduced activity, mobility, and increased sleep time which potentially helped to maintain the cannula. Most of the infants received a short course of IV antibiotics because of negative cultures. Utilizing peripheral vascular cannulas in all patients in our unit helped in avoiding bloodstream infection and other central

venous catheter-related complications.[31,38] Vascular complications were also more frequent than antibiotic-associated complications.[37] Because of the increasing safety of OPT, pediatric oncology departments started to utilize this service for low-risk febrile neutropenic patients.[18,39]

Our study demonstrated an excellent cure rate most likely related to the early presentation in most patients; easily accessible health care services; assessment and re-assessment by a senior emergency physician; and skilled staff for peripheral vascular access care. The cure rate was much lower in previous reports, though there might be variations in the patient's acuity.[21-23,28] The comorbidities in our patients were also not of those predisposed to a severe infection or delayed recovery, such as oncology or immunodeficiency patients.[27]

Hospital daily cost in pediatric in-patient service was reported to be from 976.26-1,899.24 Euros, depending on the reason for admission.[40] If we apply the lowest cost to our OPT 3663 total days, the amount saved was around 3,576,040.38 Euros during the 15-month study period.

This study added confidence in using the OPT for patients evaluated and initially treated in the PED. It emphasized the need for an independent OPT unit away from the ED service. This avoided delay in providing the IV medications for these patients. This has been described previously.[28]

This study supports the practice of using a peripherally inserted cannula for an OPT and assuring the ED staff and families that possible complications can be managed effectively in most patients.

Study limitations. The study is limited by its retrospective design. Not all data were available from note review such as availability of the rate of return to the PEC during the first few days after completion of the treatment in the OPT unit. The study could have included the degree of the patient's acuity on their arrival to the PEC.

In conclusion, for carefully selected patients, OPT seems effective, safe with manageable complications, and may result in less family disturbance than hospital admission. Based on these quality and patient safety characteristics, we recommend the continuation and establishment of such safe and efficient service in the appropriate setup particularly in institutions with a limited in-patient bed capacity.

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