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Continuous beta-lactam intravenous antibiotic infusions over 24 hours for outpatient parenteral antimicrobial therapy, an audit

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ABSTRACT

BACKGROUND: According to actual PK/PD concepts, the use of continuous infusion (CI) of beta-lactams could increase their likelihood of therapeutic success. Although this strategy has been described in hospital setting, it is poorly documented for outpatient parenteral antimicrobial therapy (OPAT). We aimed to evaluate the efficacy, safety and global savings following the introduction of an OPAT pathway for CI of piperacillin/ tazobactam (TZP), temocillin (TMO) and ceftazidime (CAZ).

METHODS: This study is a monocentric retrospective data collection. Between June 2014 and December 2016, adult patients with the following criteria were included in the study; treated ≥48h with IV antibiotics in hospital, (ii) who still need IV antibiotics (TZP, TMO or CAZ) more than once a day and for at least 3 additional days and, (iii) who are suitable for OPAT. For CI, elastomeric devices were systematically used and placed through a peripherally inserted central catheter (PICC).

The clinical outcome was evaluated on infection markers, culture results, assessment of the patient clinical condition, relapse within 2 months. Savings were calculated as follow: saved bed days = duration of OPAT and cost savings = (duration of OPAT x cost of hospital bed) – (cost of OPAT team + antibiotic + PICC line + elastomeric device). Exclusions to bed and financial savings were: any patient(s) who had a clinical outcome of (failure, indeterminate or relapsed), developed an adverse reaction or died.

RESULTS: Fifty patients included. Patients were mainly treated for pulmonary infections and urosepsis. Clinical outcome and savings were as below:

- Infection resolution rate (%): 93 for TZP, 100 for TMO & 80 for CAZ
- Overall bed savings were a total of 641 days
- Estimated overall financial savings: £94347

CONCLUSIONS: OPAT is crucial to decrease bed and cost pressure in hospital while offering patients optimal treatment and improved quality of life. This goal is supported by use of CI in OPAT which (i) reduces the frequency of visiting by OPAT team, (ii) effective and well tolerated and (iii) economically profitable.

INTRODUCTION

Penicillins such as Piperacillin/tazobactam (TZP), Temocillin (TMO) & and β-lactam antibiotics such as ceftazidime (CAZ) exhibit time dependent bacterial kill. Maintaining free levels above the minimum inhibitory concentration (MIC) for a percentage of the dosing interval (50% for penicillins & 60% for cephalosporins), will ensure near maximal bactericidal effect [(1)].

There are relatively few intravenous (IV) antibiotics with gram negative action for once daily outpatient use to treat resistant Gram negative infections. It has been suggested that administering TZP by CI produces a drug concentration in excess of the MIC for a longer period which may achieve improved outcomes in critically ill patients [(2)]. Pharmacodynamics optimisation of TZP by manipulation of infusion times may be particularly useful in the treatment of infection caused by less susceptible pathogens [(3)].

Administering TMO as a CI produces a stable free serum concentration above the breakpoint [(4)] and stability by CI as well as elastomeric pumps were both published [(5,6)]. CAZ stability as CI is supported by literature [(7)].

Following the introduction of an OPAT pathway for CI, we aimed to evaluate the efficacy, safety and to calculate overall savings including bed days saved out of hospital and financial savings.

Methods:

Data from adult patients treated with TZP, TMO & CAZ for different gram negative Infections such as (Urosepsis, Infected exacerbation of Bronchiectasis) between June 2014 and December 2016 were reviewed retrospectively.

In our OPAT pathway, the administration of these antibiotics by continuous infusion over 24 hours is considered in patients: who need antibiotics to be given intravenously more than once a day AND who are suitable for hospital at home treatment under the care of our Healthcare at home (HAH) nursing team.

The patient must have had at least 48 hours of IV bolus/infusion to check for toxicity or adverse reaction and base line routine bloods: full blood count, LFT's, CRP and U&E's need to be taken. If the patient has tolerated the administration without adverse event then they can be changed to the use of a Surefuser (a designated Elastomeric 24 hourly Infusion device) through a peripherally inserted central catheter (PICC Line). We evaluated clinical outcome based on infection markers, culture results, re-admission to hospital within 2 months with the same diagnosis and assessment of the clinical condition of the patient by our HAH team through their daily visits.

Bed days saved was calculated by taking out number of treatment days spent in hospital from overall duration of treatment.

Cost savings were calculated by multiplying the number of bed days saved by the cost of hospital bed (£319.20) then taking out the cost of the daily visit of HAH (£78) + The cost of drug used via OPAT + the cost of the Surefuser devise used + the cost of the PICC line.

Exclusions included: any patient who had treatment through OPAT for less than 3 days. Exclusions to bed and financial savings included: any patient who had a clinical outcome of (failure, indeterminate or relapsed), developed an adverse reaction or died.

Results :

In total 65 patients were reviewed, Ten had OPAT not by CI and 5 didn't satisfy the inclusion criteria so Fifty included.

29 had TZP (most common indication was Infected exacerbation of bronchiectasis), 16 patients had temocillin (most common indication was urosepsis) and 5 had ceftazidime (4 bronchiectasis and 1 osteomyelitis).

Mean duration of treatment & OPAT, Infection resolution rate, adverse events and savings were as below:

	TZP (n=29)	TMO (n=16)	CAZ (n=5)	TOTAL (n=50)
Mean duration of antibiotic treatment (days)	17.1	16.4	29.6	18.2
Mean duration of OPAT (days)	11.7	11.1	24.8	12.8
Infection resolution rate (%)	93	100	80	94
Adverse event (n)	2*	0	0	2
Total bed days saved out of hospital	339	178	124	641
Estimated financial savings (£)	43504	25419	25424	94347
*** 1 diarrhoea and 1 rash**				

Some patients had successful prolonged therapy by CI such as:

- TZP for 52 days for left foot osteomyelitis which grew pseudomonas from a left foot swab that was sensitive to TZP and resistant to ciprofloxacin.
- TMO for 42 days for sepsis secondary to infected metal Hip replacement which grew Morganella morganii that was sensitive to TMO.
- CAZ FOR 86 days for left foot osteomyelitis which grew pseudomonas from a left foot swab that was sensitive to CAZ & TZP but patient had penicillin allergy with rash. This patient also grew MRSA from his left foot swab and was treated with Linezolid.

CONCLUSIONS

A continuous β-lactam intravenous Antibiotic infusion for (TZP, TMO & CAZ) over 24 hours for OPAT appears to be clinically effective, safe, practical and cost effective.

Only 2 patients in the PIP/TAZ group experienced adverse events (diarrhoea and rash) which were unlikely due to the infusion but the drug itself.

OPAT is crucial to decrease bed and cost pressure in hospital while offering patients optimal treatment and improved quality of life. This goal is supported by use of CI in OPAT which :

(i) reduces the frequency of visiting by OPAT team, (ii) effective and well tolerated and (iii) economically profitable.

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