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infectio

ARTÍCULO ORIGINAL

Cost-effectiveness of ceftolozane/tazobactam for the treatment of complicated intraabdominal and urinary tract infections in Colombia

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Abstract

Objective: To evaluate the cost-effectiveness of ceftolozane/tazobactam + metronidazole (C/T+M) and ceftolozane/tazobactam (C/T) compared with 8 alternatives used in the treatment of complicated intraabdominal infection (cIAI) and complicated urinary tract infection (cUTI) respectively.

Methods: A Monte Carlo simulation decision model was used for the estimation and comparison of treatment-related costs, and quality adjusted life years for patients with cIAI treated with C/T+M in comparison with cefepime + metronidazole, ciprofloxacin + metronidazole, doripenem, levofloxacin + metronidazole, meropenem, piperacillin/tazobactam, ceftazidime + metronidazole or imipenem/cilastatin and patients with cUTI treated with C/T in comparison with cefepime, ciprofloxacin, doripenem, levofloxacin, meropenem, piperacillin/tazobactam, ceftazidime or imipenem/cilastatin. Local costs were estimated using base cases identified by experts and consulting local databases. Sensitivity values of the PACTS (Program to Assess Ceftolozane/Tazobactam Susceptibility) study in Latin America were used in the model.

Results: C/T+M and C/T obtained incremental cost-effectiveness ratios (ICER) that were below the Colombian cost-effectiveness threshold (3 GDP per capita) in most comparisons, and were dominated by meropenem, considering only gram-negative microorganisms. Sensitivity assessments were also carried out, in which only the population with *P. aeruginosa* infections was considered, showing positive results for C/T+M and C/T (cost-effective or dominant with regards to all comparators).

Conclusions: C/T+M and C/T could be cost-effective alternatives in the treatment of CIAI and CUTI in Colombia, when there is an adequate and rational use of antibiotics. The results of the sensitivity analyses showed dominance and cost-effectiveness with regards to every comparator in patients infected with *P. aeruginosa*

Keywords: Ceftolozane; Tazobactam; cost-effectiveness; urinary tract infections; intraabdominal infections

Costo-efectividad de ceftolozano/tazobactam para el tratamiento de las infecciones intraabdominales e infecciones del tracto urinario complicadas en Colombia

Resumen

Objetivo: Evaluar la costo-efectividad de ceftolozano/tazobactam + metronidazol (C/T + M) y ceftolozano/tazobactam (C/T) en comparación con 8 alternativas utilizadas en el tratamiento de las infecciones intraabdominales complicadas (IAAc) e infecciones del tracto urinario complicadas (ITUc) respectivamente.

Métodos: Se usó un modelo de decisión de simulación de Monte Carlo para la estimación y comparación de los costos relacionados con el tratamiento y los años de vida ajustados por calidad para pacientes con IAAc tratados con C/T + M, en comparación con cefepima + metronidazol, ciprofloxacina + metronidazol, doripenem , levofloxacina + metronidazol, meropenem, piperacilina / tazobactam, ceftazidima + metronidazol o imipenem/cilastatina, y pacientes con ITUc tratados con C/T en comparación con cefepime, ciprofloxacina, doripenem, levofloxacina, meropenem, piperacilina / tazobactam, ceftazidima o imipenem/cilastatina . Los costos locales se estimaron por medio de casos base identificados por expertos y consultando bases de datos locales. Se utilizaron los valores de sensibilidad bacteriana del estudio PACTS (Programa para evaluar la susceptibilidad al ceftolozano/tazobactam) en América Latina para poblar el modelo.

Resultados: C/T + M y C/T obtuvieron razones de costo-efectividad incrementales (RCEI) que estaban por debajo del umbral de costo-efectividad colombiano (3 PIB per cápita) en la mayoría de las comparaciones, y fueron dominados por meropenem, considerando solo microorganismos gran-negativos También se llevaron a cabo análisis de sensibilidad, en los que solo se consideró la población con infecciones por *P. aeruginosa*, mostrando resultados positivos para C/T + M y C/T (costo efectivo o dominante con respecto a todos los comparadores).

Conclusiones: C/T + M y C/T podrían ser alternativas costo efectivas en el tratamiento de IAAc e ITUc en Colombia, cuando existe un uso adecuado y racional de antibióticos. Los resultados de los análisis de sensibilidad mostraron dominio y costo-efectividad en relación con todos los comparadores en pacientes infectados con *P. aeruginosa*.

Palabras clave: Ceftolozano; Tazobactam; rentabilidad; infecciones del tracto urinario; infecciones intraabdominales

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Recibido: 11/05/2018; Aceptado: 24/02/2019

Cómo citar este artículo: F. Hernández, *et al*. Cost-effectiveness of ceftolozane/tazobactam for the treatment of complicated intraabdominal and urinary tract infections in Colombia. Infectio 2020; 24(1):9-23

Introduction

Intra-abdominal infections (IAI) encompass a wide spectrum of pathological alternations that can be defined as the peritoneal response to the infectious process. They are an important cause of morbidity and mortality and represent the second most common cause of severe sepsis in intensive care units[1]. Complicated intra-abdominal infections (cIAI) extend beyond the affected organ towards the peritoneal space so they are generally associated to diffuse or localized peritonitis. Treatment of these patients requires an adequate control of the infected focus and antibiotic treatment, with the purpose of avoiding spread of the infection[2].

On the other hand, urinary tract infections (UTI) are among the most common types of infections in clinical practice[3], with greater prevalence and incidence in women due to the short distance between the urethra and the vaginal opening[4]. Complicated UTI (cUTI) are associated to factors that compromise the host's immunologic response or the physiology of the urinary tract, such as renal failure, immune suppression, kidney stones, kidney transplant, and others[5].

The most commonly used antibiotics in the empiric therapy of cIAI are beta-lactam antibiotics due to their wide spectrum and low rate of resistance[6]. According to different studies carried out in Colombia, the most used antibiotics for the treatment of UTI are: ciprofloxacin, ampicillin/sulbactam, nitrofurantoin and trimetoprim/sulfamethoxazole, out of which nitrofurantoin is the antibiotic to which isolated cultures present a higher susceptibility[7].

However, extended use of wide spectrum antibiotics has increased bacterial resistance during the last decade, decreasing therapeutic options; the need of new therapeutic alternatives has become even more important[8,9]. Ceftolozane/tazobactam (C/T) is a new cephalosporin associated to a beta-lactam inhibitor that has shown activity in strains that produce extended spectrum beta-lactamases (ESBL) and has proven to be stable to the most common resistance mechanisms to *Pseudomonas aeruginosa* such as: overexpression of efflux pumps and closing of porins[8]. In Colombia, C/T is approved in combination with metronidazole (M) for the treatment of cIAI caused by the following Gram positive and Gram negative microorganisms: *P. aeruginosa*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Bacteroides fragilis*, *Streptococcus anginosus*, *Streptococcus constellatus*, and *Streptococcus salivarius*. It is also approved for the treatment of complicated urinary tract infections including pyelonephritis caused by the following organisms: *P. aeruginosa, E. coli*, *K. pneumoniae* and *P. mirabilis*[10].

The objective of this study is to estimate the cost-effectiveness of C/T + M in the treatment of cIAI and C/T in cUTI from the perspective of the Colombian health system.

Methods

Target population and perspective: The population considered in this evaluation are adult patients with a diagnosis of cIAI and cUTI. This evaluation was carried out from a third party payer perspective (Colombian health system).

Comparators: In the case of cIAI, intervention was C/T combined with metronidazole (C/T+M), as approved in the Colombian regulatory agency. Comparators were cefepime + metronidazole, ceftazidime + metronidazole, meropenem, doripenem, imipenem/cilastatin, piperacillin/tazobactam, ciprofloxacin + metronidazole and levofloxacin + metronidazole.

For cUTI, intervention was C/T and comparators were cefepime, ceftazidime, meropenem, doripenem, ertapenem, imipenem/cilastatin, piperacillin/tazobactam, ciprofloxacin and levofloxacin.

Time horizon and discount rate: The time horizon for this economic evaluation was defined as the patient's life expectancy, considering that the long-term consequences of an acute event would be modeled (including mortality). A 5% discount rate was considered for costs and utilities, according to the recommendations of IETS, the Colombian health technology assessment agency[11]. The use of a life expectancy time horizon is reasonable in this model, since one of the outcomes included was death due to infection and this event has repercussions in QALY lost due to premature death.

Efficacy measurements and outcomes: The individual patient antibiograms results reported in the PACTS (Program to Assess Ceftolozane / Tazobactam susceptibility) study in Latin America[12] were used as the efficacy measurement. This study measured antimicrobial sensitivity of 2,415 isolated gran-negative bacillus gathered in 12 centers in 4 countries in Latin America (Brazil, Chile, Argentina, and Mexico), between January 1, 2013 and December 31, 2015. Only data from 2015 were used. Infections considered were: blood infections, pneumonia associated to health care, skin infections, intra-abdominal infections, urinary tract infections, and other infections.

Outcomes are expressed in quality-adjusted life years (QALY) that allow to combine the impact of each technology on target population's quality of life and life expectancy. The utility measurement for survivors in each infection was extracted from Senekjian et al.[13] and Thomas et al.[14],for cIAI and cUTI respectively.

Analytic Model: A Monte Carlo simulation decision model was used for a hypothetical cohort of 1,000 patients in each indication. For cUTI, the patient enters the model after diagnosis, and begins to receive empiric treatment while urine samples are taken for culture. The culture is then assessed to see whether the microorganism is sensitive to the empiric therapy or not. If it is sensitive, the patient may continue with the initial empiric therapy or be de-escalated to the less costly alternative to which the microorganism is sensitive.

Otherwise, the patient will be escalated to the sensitive therapy with the lower cost. In any case, the patient ends up either healed or deceased. As for the cIAI case, the patient follows the same path as for the cUTI. If the patient is a non-responder, imaging analyses and surgical procedures may be considered, ending up in healing or death; if the patient responds to the therapy they may also heal or die. Figure 1 shows the analytical models used. Model parameters values are summarized in Table 1.

Model assumptions: The patient will always be de-escalated from the adequate empiric therapy, when there is a less expensive appropriate alternative. Microbial sensitivity to each antibiotic found in the countries included in the PACTS study is similar to the one of Colombian infections isolates (Table S1). There are no differences in the response to antimicrobial therapy, mortality, and length of inpatient stay between men and women.

Resource use estimation and costs: The resources used to treat each condition were identified through an expert consultation. Resource cost estimation was carried out using local tariff manuals and databases, according to the recommendations of the Colombian technology assessment agency[11]. Table 2 summarizes the estimated costs for this evaluation.

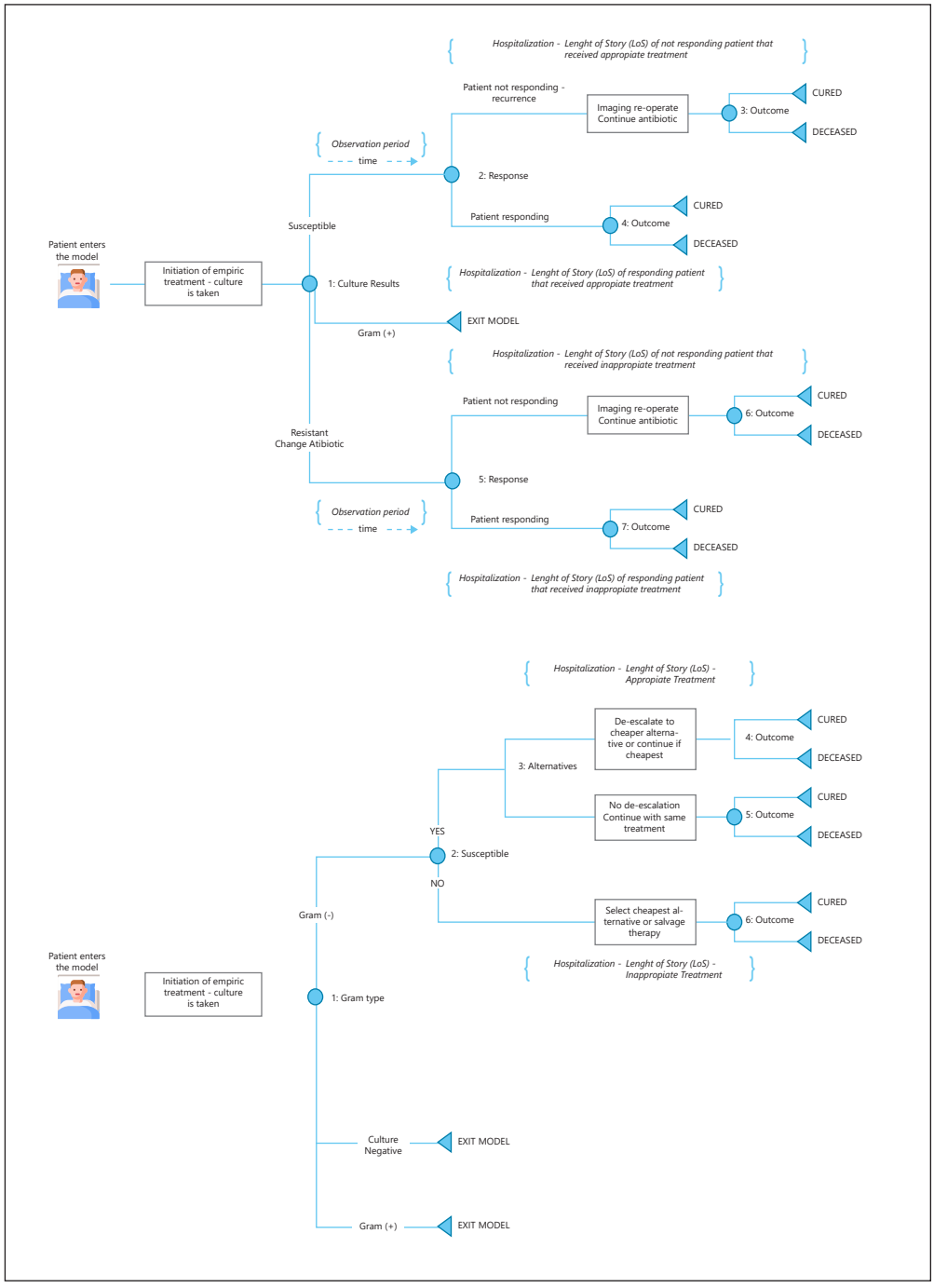

Figure 1. Decision models used in the evaluation. A). Model used in cIAI. B). Model used in cUTI.

Table 1. Model parameters for cUTI and cIAI evaluation

Model parameters for cUTI evaluation					
Parameter	Base case	Sensitivity analysis		Distribution	Source
		Upper	Lower		
Duration of empiric therapy (days)	3	2	3	Gamma	Experts
Length of stay with initial appropriate therapy (days)	12	10	14	Gamma	Experts
Additional length of stay with initial inappropriate therapy (days)	3	2	3	Gamma	Experts
Mortality rate with appropriate empiric treatment	0.10	0.09	0.13	Beta	Experts
Mortality rate with inappropriate empiric antibiotic	0.33	0.30	0.40	Beta	Experts
Health utility for survivors	0.93	0.92	0.94	Beta	(14)
Discount rate	0.05	0.03	0.07	Gamma	(11)
Model parameters for cIAI evaluation					
Parameter	Base case	Sensitivity analysis		Distribution	Source
		Lower	Upper		
Duration of empiric therapy (days)	4	3	5	Gamma	Experts
Length of stay with initial appropriate therapy (days)	12	10	14	Gamma	Experts
Additional length of stay with initial inappropriate therapy (days)	15.5	10	21	Gamma	Experts
Additional days of hospitalization for re-operation	4.5	2	7	Gamma	Experts
Percentage of appropriately treated patients who require re-operation	0.75	0.30	1	Beta	Experts
Percentage of inappropriately treated patients who require re-operation	0.76	0.30	1	Beta	Experts
Mortality rate with appropriate empiric treatment	0.175	0.15	0.20	Beta	Experts
Mortality rate with inappropriate empiric antibiotic	0.40	0.35	0.50	Beta	Experts
Health utility for survivors	0.85	0.84	0.86	Beta	(13)
Discount rate	5%	3%	7%	Gamma	(11)

Sensitivity analyses: The impact of some parameters on the final results was assessed through one-way and probabilistic sensitivity analyses (supplementary material). Additionally, another sensitivity analysis was carried out, considering only *P. aeruginosa* isolates.

Results

C/T+M was a cost-effective option for the empiric treatment of cIAI in the base case compared to cefepime + metronidazole, ceftazidime + metronidazole, ciprofloxacin + metronidazole, levofloxacin + metronidazole, piperacillin/tazobactam, doripenem and imipenem cilastatin, under the of 3GDP per capita for 2017 (18,609 USD; 1 USD = 2,984.5 COP) and is dominated by meropenem in the base case. Likewise, C/T in the empiric treatment of cUTI resulted to be a cost-effective option compared with cefepime, ceftazidime, ciprofloxacin, levofloxacin, piperacillin/tazobactam, doripenem and imipenem/cilastatin under the same criteria. The incremental cost-effective ratios (ICER) obtained for each comparison are summarized in Table 3. According to the one-way sensitivity analyses results, variation of antibiotic sensitivity rates has a marked effect on the QALYs gained, contrasting with the minimal impact observed on the final costs of the whole cohort (Supplementary material). Probabilistic sensitivity analyses showed that C/T+M was cost-effective in all simulations when compared with ceftazidime + metronidazole, cefepime + metronidazole, ciprofloxacin + metronidazole, levofloxacin + metronidazole and piperacillin/tazobactam for cIAI treatment. Similarly, C/T was cost-effective in all simulations against cefepime, ciprofloxacin, ceftazidime, levofloxacin and piperacillin/tazobactam (Supplementary material). Also, when only information from the *P. aeruginosa* isolates was used, the technology was found to be cost-effective or dominant against all comparators in both indications. These results are shown in Table 4.

Discussion

C/T+M and C/T resulted to be cost-effective alternatives with regards to most comparators for the empiric treatment of cIAI and cUTI, respectively. Even though meropenem was dominant compared with C/T+M and C/T, the difference in utilities and costs between the two alternatives was small. Univariate sensitivity analyses showed that the variation in antibiotic resistance increases, in the range upper limit, the difference in efficacy between the compared alternatives. The sensitivity analysis considering only patients with *P aeruginosa* showed that C/T + M ends up being cost-effective in comparison to meropenem and cost-saving in comparison with doripenem and imipenem/cilastatin. In any case, these results seem to indicate that C/T+M and C/T are valid options for the empiric treatment of patients with cIAI and cUTI, respectively.

Table 2. Hospitalization, surgical and imaging procedures costs for each infection. Costs in USD

Infection	Parameter	Base case	Sensitivity analysis		Distribution	Source
			Upper	Lower		
cUTI	Hospitalization cost per day	$271	$217	$320	Gamma	Experts and tariff manual
	Imaging procedures cost per patient	$39	$31	$47	Gamma	Experts and tariff manual
cIAI	Hospitalization cost per day	$272	$217	$327	Gamma	Experts and tariff manual
	Surgical procedures cost per patient	$199	$160	$239	Gamma	Experts and tariff manual
	Imaging procedures cost per patient	$95	$76	$114	Gamma	Experts and tariff manual

In general, the comparators selected for this assessment are not common comparators used in other investigations[15–17], taking into account that many of the alternatives evaluated in this study are not considered first choice options in the treatment of cUTI. However, according to the spectrum and the place that C/T will occupy in the therapeutic arsenal for the treatment of cUTI, the evaluated alternatives can be considered reasonable comparators. Likewise, some studies use clinical healing rates directly derived from clinical trials as efficacy measure, which can result in different conclusions for one same comparison[18–20].

On the other hand, Kauf et al., (2017)[21] and Prabhu et al., (2017)[22] used a similar approach to evaluate the cost-effectiveness of C/T versus piperacillin/tazobactam as initial empiric therapy for the treatment of cUTI and cIAI, respectively, in the United States, obtaining similar results to those of this study.

The main strength of this study is the use of real-world data in the Monte Carlo simulation to model resistance profiles and treatment strategies for cIAI and cUTI. However, the de-escalation assumption to the less costly alternative in all the patients is perhaps one of the model's limitations, since it is slightly distant from the real clinical practice. Even though this can be reasonable practice, it is not necessarily done automatically and in all patients. The use of resistance percentages as a success measure of the antimicrobial therapy is also part of the consideration of the therapeutic response, but it can depend on other factors also. Another potential limitation is the use of Latin American antibiograms, but not Colombian, for this assessment. Considering the importance of the resistance of microorganisms in the sensitivity analysis, a point for future research could be the implementation of Colombian isolate data to improve the reliability of the results.

The calculation of ICER for uncertainty scenarios suggested in the univariate sensitivity analysis shows consistency in the results obtained in the base cases, since in all variations applied, intervention with C/T+M and C/T continue to be a cost-effective alternative with regards to non-carbapenem comparators. In the case of the comparison with carbapenems, ICER showed to be highly sensitive to the variation in the antibiotic resistance, making C/T+M and C/T be dominated in some cases. According to the information included in the model, the variation of the antibiotic resistance has a marked impact on the total QALYs of the entire cohort, in contrast with the minimal change in the cohort's total cost. In the case of the probabilistic sensitivity analysis, for comparisons regarding non-carbapenem alternatives, the simulations are under the cost-effectiveness threshold for the Colombian context.

As for the sensitivity analysis, considering only the population infected by *P. aeruginosa*, the rationale of this scenario is the available evidence indicating that microorganisms of this genus are prevalent in Colombian cIAI isolated elements[23] and cUTI[24]. Taking this into account, it is reasonable to assume that there is a population niche where CZT+M and C/T are cost-effective with regards to all comparators. Likewise, according to the model design and the assumptions used, C/T+M and C/T are cost-effective alternatives when antibiotics use is carried out in a rational way.

Table 3. Base case results of the cost-effectiveness analyses for C/T vs. comparators in cIAI and cUTI. *Combined with metronidazole in cIAI. 1000 patients simulated cohort results are shown. Costs in USD

Antibiotic	cUTI			cIAI		
	Incremental cost (USD)	Incremental effectiveness (QALY)	Incremental cost effectiveness ratio (USD/QALY)	Incremental cost (USD)	Incremental effectiveness (QALY)	Incremental cost effectiveness ratio (USD/QALY)
Ceftolozane/Tazobactam*	-	-	-	-	-	-
Cefepime*	$393,438	404.0	$974	$96,081	327.2	$294
Ceftazidime*	$479,007	317.6	$1,508	$313,031	256.7	$1,219
Ciprofloxacin*	$395,185	536.6	$737	$36,805	442.9	$83
Doripenem	$318,927	61.7	$5,171	$347,210	50.8	$6,838
Imipenem/cilastatin	$356,021	67.8	$5,248	$405,156	39.5	$10,259
Levofloxacin*	$449,319	363.9	$1,235	$285,428	290.5	$982
Meropenem	$532,806	-55.5	Dominated	$749,559	-50.8	Dominated
Piperacillin/tazobactam	$431,056	293.0	$1,471	$271,113	248.2	$1,092

Table 4. Sensitivity analyses considering only population infected with *P. aeruginosa* in cIAI and cUTI. * Combined with metronidazole in cIAI. 1000 patients simulated cohort results are shown. Costs in USD

Antibiotic	cUTI			cIAI		
	Incremental cost (USD)	Incremental effectiveness (QALY)	Incremental cost effectiveness ratio (USD/QALY)	Incremental cost (USD)	Incremental effectiveness (QALY)	Incremental cost effectiveness ratio (USD/QALY)
Ceftolozane/tazobactam*	-	-	-	-	-	-
Cefepime*	$375,204	415.6	$903	$64,421	335.2	$192
Ceftazidime*	$451,179	357.6	$1,262	$274,559	288.6	$951
Ciprofloxacin*	$352,534	470.3	$750	$108,036	396.5	$273
Doripenem	$158,517	592.7	$267	-$32,174	492.7	Dominant
Imipenem/cilastatin	$205,453	567.0	$362	-$188,763	469.3	Dominant
Levofloxacin*	$386,675	541.2	$714	$42,134	454.8	$93
Meropenem	$367,708	492.9	$746	$17,285	408.1	$42
Piperacillin/tazobactam	$398,568	351.1	$1,135	$208,803	291.5	$716

Conclusions

C/T+M and C/T are cost-effective alternatives for the empiric treatment of complicated intra-abdominal infections and complicated urinary tract infections, respectively, when there is an adequate escalation and de-escalation of antibiotics. In the sensitivity analyses, the model estimates that C/T+M and C/T are cost-effective with regards to all comparators, when only *P. aeruginosa* isolates are considered.

Ethical disclosure

Protection of human and animal subjects. This research do not use animal nor human material or data.

Confidentiality of data. Not applicable

Conflict of interest statement. The authors received grants from MSD Colombia to perform this study.This work was funded by MSD Colombia, however the authors had complete independency on data acquisition and analysis.

References

1. Lopez N, Kobayashi L, Coimbra R. A Comprehensive review of abdominal infections. World J Emerg Surg. 2011;6(1):7.
2. Sartelli M, Catena F, Ansaloni L, Moore E, Malangoni M, Velmahos G, et al. Complicated intra-abdominal infections in a worldwide context: an observational prospective study (CIAOW Study). World J Emerg Surg. 2013;8(1):1.
3. Stamm WE, Norrby SR. Urinary Tract Infections: Disease Panorama and Challenges. J Infect Dis. 2001 Mar;183(s1):S1–4.
4. Foxman B. Urinary Tract Infection Syndromes. Infect Dis Clin North Am. 2014 Mar;28(1):1–13.
5. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol. 2015 May 8;13(5):269–84.
6. File TM. New Guidelines for the Management of Complicated Intra-Abdominal Infections. Infect Dis Clin Pract. 2010 May;18(3):195–7.
7. Cortes JA, Perdomo D, Morales RA, Alvarez CA, Cuervo SI, Leal AL, et al. Guía de práctica clínica sobre diagnóstico y tratamiento de infección de vías urinarias no complicada en mujeres adquirida en la comunidad. Rev la Fac Med. 2015 Dec 10;63(4):565–81.
8. Mawal Y, Critchley IA, Riccobene TA, Talley AK. Ceftazidime–avibactam for the treatment of complicated urinary tract infections and complicated intra-abdominal infections. Expert Rev Clin Pharmacol. 2015 Nov 2;8(6):691–707.
9. Mikamo H, Yuasa A, Wada K, Crawford B, Sugimoto N. Optimal Treatment for Complicated Intra-abdominal Infections in the Era of Antibiotic Resistance: A Systematic Review and Meta-Analysis of the Efficacy and Safety of Combined Therapy With Metronidazole. Open Forum Infect Dis. 2016 Jul;3(3):ofw143.
10. Instituto Nacional de Vigilancia de Medicamentos y Alimentos. Acta No. 15 de 2016. 2016.
11. Instituto de Evaluación Tecnológica en Salud. Manual para la elaboración de evaluaciones económicas en salud. Bogotá D.C.; 2014.
12. Pfaller MA, Shortridge D, Sader HS, Flamm RK, Castanheira M. Ceftolozane–tazobactam activity against drug-resistant Enterobacteriaceae and Pseudomonas aeruginosa causing healthcare-associated infections in Australia and New Zealand: Report from an Antimicrobial Surveillance Program (2013–2015). J Glob Antimicrob Resist. 2017 Sep;10(6):186–94.
13. Senekjian L, Nirula R, Bellows B, Nelson R. Interval Appendectomy: Finding the Breaking Point for Cost-Effectiveness. J Am Coll Surg. 2016 Oct;223(4):632–43.
14. Thomas JA, Tubaro A, Barber N, Thorpe A, Armstrong N, Bachmann A, et al. The Continuing Story of the Cost-Effectiveness of Photoselective Vaporization of the Prostate versus Transuretheral Resection of the Prostate for the Treatment of Symptomatic Benign Prostatic Obstruction. Value Heal. 2015 Jun;18(4):376–86.
15. Perrault L, Dahan S, Iliza AC, LeLorier J, Zhanel GG. Cost-Effectiveness Analysis of Fosfomycin for Treatment of Uncomplicated Urinary Tract Infections in Ontario. Can J Infect Dis Med Microbiol. 2017;2017:1–11.
16. Rubin N, Foxman B. The cost-effectiveness of placing urinary tract infection treatment over the counter. J Clin Epidemiol. 1996 Nov;49(11):1315–21.
17. Carlson KJ. Cost-Effectiveness Analysis of Single-Dose Therapy of Urinary Tract Infection Compared to Conventional Treatment. Eur Urol. 1987;13(1):45–7.
18. Attanasio E, Russo P, Carunchio G, Basoli A, Caprino L. Cost-Effectiveness Study of Imipenem/Cilastatin versus Meropenem in Intra-Abdominal Infections. Dig Surg. 2000;17(2):164–72.
19. Jansen JP, Kumar R, Carmeli Y. Cost-Effectiveness Evaluation of Ertapenem versus Piperacillin/Tazobactam in the Treatment of Complicated Intraabdominal Infections Accounting for Antibiotic Resistance. Value Heal. 2009 Mar;12(2):234–44.
20. Barie PS, Rotstein OD, Dellinger EP, Grasela TH, Walawander CA. The Cost-Effectiveness of Cefepime plus Metronidazole versus Imipenem/Cilastatin in the Treatment of Complicated Intra-Abdominal Infection. Surg Infect (Larchmt). 2004 Sep;5(3):269–80.
21. Kauf TL, Prabhu VS, Medic G, Borse RH, Miller B, Gaultney J, et al. Cost-effectiveness of ceftolozane/tazobactam compared with piperacillin/tazobactam as empiric therapy based on the in-vitro surveillance of bacterial isolates in the United States for the treatment of complicated urinary tract infections. BMC Infect Dis [Internet]. 2017;17(1):314. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28454524
22. Prabhu VS, Solomkin JS, Medic G, Foo J, Borse RH, Kauf T, et al. Cost-effectiveness of ceftolozane/tazobactam plus metronidazole versus piperacillin/tazobactam as initial empiric therapy for the treatment of complicated intra-abdominal infections based on pathogen distributions drawn from national surveillance data in. Antimicrob Resist Infect Control [Internet]. 2017;6:107. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29090091
23. Vallejo M, Cuesta DP, Flórez LE, Correa A, Llanos CE, Isaza B, et al. Características clínicas y microbiológicas de la infección intra-abdominal complicada en Colombia: un estudio multicéntrico. Rev Chil infectología. 2016 Jun;33(3):261–7.
24. Rodriguez-Triana DA. Caracterizacion de uropatógenos en un hospital de cundinamarca periodo abril 2009 - abril 2010. [Tesis] Bogotá: Universidad Nacional de Colombia. Facultad de Ciencias. Departamento de Farmacia; 2011. Disponible en: http://www.bdigital.unal.edu.co/3847/1/01192269.2011.pdf