Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20184853

Original Research Article

Cost effective analysis of tab. nitrofurantoin vs. inj. ceftriaxone as an empirical therapy in patients of urinary tract infection at a tertiary health care centre

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Received: 28 September 2018
Accepted: 25 October 2018

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ABSTRACT

Background: Urinary tract infections (UTI) are commonly seen in adults, Urinary tract infection and asymptomatic bacteriuria in adults are a significant health care burden. In a developing country it is necessary to minimize the cost of therapy while giving maximum health benefits to the patient. Appropriate antimicrobial selection is clearly important, as treatment failures will increase the cost of care and result in additional morbidity for patients. Empirical treatment of urinary tract infection is common at tertiary health care center, authors conducted a pharmacoeconomic study to evaluate cost effectiveness of the empirical treatment.

Methods: Patients with similar symptoms suffering from UTI were divided into 5 groups with 10 patients in each group. Each group was subdivided into two subgroups with subgroup A having five patients receiving tab nitrofurantoin and subgroup B having 5 patients receiving inj ceftriaxone. Out of the total cost of therapy, percentage of cost attributed to tab nitrofurantoin was compared with inj ceftriaxone. Most cost-effective antibiotic was analysed. Average number of admission days for groups of UTI patients receiving tab nitrofurantoin and inj ceftriaxone were calculated and compared. Group of UTI patients receiving antibiotic with least number of admission days was calculated.

Results: Percentage of cost attributed to Nitrofurantoin therapy out of total cost in urinary tract infection patient was less than percentage of cost attributed to inj Ceftriaxone in all five groups of patients and was found to be statistically significant ($p < 0.05$). However, there was no statistically significant difference in average number of admission (IPD) days between groups of patients receiving tab nitrofurantoin and inj ceftriaxone ($p > 0.05$).

Conclusions: In current study authors found tab nitrofurantoin to be more cost effective than inj ceftriaxone as an empirical therapy in UTI patients.

Keywords: Cost effectiveness, Nitrofurantoin, Urinary tract infection

INTRODUCTION

Urinary tract infection involves upper urinary tract (kidneys and ureter) and/or lower urinary tract (urethra and urinary bladder), urinary tract infections are caused by wide range of pathogens including *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Staphylococcus aureus*, clinically urinary tract infections are divided into complicated and uncomplicated urinary tract infections.[1] Uncomplicated urinary tract infections takes place in healthy individuals with no structural defects and neurological deficits, complicated UTI are defined as those compromising host defence, urinary tract (obstruction) and neurological integrity which leads to urinary tract infections.[2] Urinary tract infections are common in developing countries affecting women more than men, it is necessary to minimize the cost of therapy while providing optimum health benefits to the patients. Patients of UTI are prone to recurrence and high costs of treatment leads to increase burden of costs of treatment on patients.

Urinary tract infections are a frequent cause of hospitalisation and have a great economic impact on healthcare systems. The annual cost of UTI acquired through community is significant and goes beyond 1.6 million dollars.[3] In developing countries because of increased antimicrobial resistance and increased cost of treatment, patients are left with few therapeutic options.[4,5]

Intravenous antibiotic given in urinary tract infection requires admission of patient, despite admission the other costs incurred by the patient is increased i.e. price of intravenous antibiotics and cost of syringes and needles. Injection ceftriaxone shows wide spectrum of antibiotic activity especially in urinary tract infection, it is highly efficacious against many gram negative UTI causing Enterobacteriaceae i.e. *E coli*, *Klebsiella*, however increased cost of antibiotic and other cost (syringes and needles) required for ceftriaxone should restrict its use in developing country like India.[6]

Nitrofurantoin has been found to be effective in causing remissions of symptoms in patients of urinary tract infections.[7] Nitrofurantoin is a bactericidal antibiotic with a broad-spectrum activity and can be used to treat urinary tract infection caused by *Enterobacter spp, Klebsiella spp, Staphylococcus aureus* spp and *Enterococcus spp*. Nitrofurantoin is the first choice recommended for treatment of uncomplicated cystitis and pyelonephritis in women. Nitrofurantoin has become the choice of antibiotic in UTI due multi drug resistant pathogens, especially in developing countries like India and is highly effective against gram negative and gram positive bacteria causing UTI and is also cost effective with fewer adverse effects.[8]

Pharmacoeconomics is the application of economics to assess the pharmaceutical and health care products that helps evaluate economic, clinical and humanistic outcomes of health care products and interventions. In a developing country like India where there are so many prevalent infections and limited resources, study of pharmaeconomics of antibiotics is of utmost importance.[9] In authors' tertiary health care center antibiotics are sometimes prescribed empirically with most of the patients of UTI being admitted, therefore we planned a study to compare cost effectiveness of two most commonly prescribed antibiotics for urinary tract infection i.e. nitrofurantoin and ceftriaxone.

The aim of the present study was to Compare cost effectiveness of tab. nitrofurantoin with inj. ceftriaxone in adult IPD patients suffering from Urinary tract infection.

Objectives

- To calculate percentage of cost of total therapy attributed to tab. nitrofurantoin
- To calculate percentage of cost of total therapy of attributed to inj. ceftriaxone
- To compare percentage of cost of total therapy attributed to tab. nitrofurantoin with inj. ceftriaxone and find out most cost-effective antibiotic for urinary tract infection
- To find out average number of admission days until patients (receiving tab nitrofurantoin) became symptom free
- To find out average number of admission days until patients (receiving inj. ceftriaxone) became symptom free
- To compare average number of admission days of patients receiving tab nitrofurantoin with average number of admission days of patients receiving inj ceftriaxone and find out the antibiotic with least number of admission days.

METHODS

The study was undertaken after receiving letter of approval from Institutional Ethical Committee, DMIMS, dated 31/03/2017 with Ref. No. DMIMS(DU)/IEC/2017-18/6348.

Table 1: patients were grouped into five groups based on symptoms each group divided into two subgroups.

Groups	Subgroup	Symptoms
Group I	Subgroup I A (receiving nitrofurantoin)	Burning micturition, lower abdominal pain, increased frequency of urination, fever
	Subgroup I B (receiving ceftriaxone)	
Group II	Subgroup II A (receiving nitrofurantoin)	Burning micturition, fever, increased frequency of urination
	Subgroup II B (receiving ceftriaxone)	
Group III	Subgroup III A (receiving nitrofurantoin)	Burning micturition, lower abdominal pain, increased frequency of urination
	Subgroup III B (receiving ceftriaxone)	
Group IV	Subgroup IV A (receiving nitrofurantoin)	Lower abdominal pain, increased frequency of urination, fever
	Subgroup IV B (receiving ceftriaxone)	
Group V	Subgroup V A (receiving nitrofurantoin)	Burning micturition, increased frequency of urination
	Subgroup V B (receiving ceftriaxone)	

The study was performed on 50 cases of urinary tract infection in adult population admitted at Acharya Vinoba Bhave rural hospital (Sawangi). The study was carried out from 1st April 2017 till 1st June 2017 (two months). Inclusion criteria for this study was male and female patient admitted in medicine/surgery/Obgy ward with patient age >18 years. Exclusion criteria for the study was

patient age less than 18 years, patients suffering from complicated urinary tract infection, patients not willing to participate in the study and OPD patients. This study was an observational study with sample size of 50 patients. Patients with similar symptoms suffering from UTI were divided into 5 groups (Figure1) with 10 patients in each group. Each group was subdivided into two subgroups with subgroup A having five patients receiving tab nitrofurantoin and subgroup B having 5 patients receiving inj ceftriaxone as shown in Table 1. Five patients from each group were receiving Tab Nitrofurantoin and Five patients were getting Inj Ceftriaxone as an empirical therapy for UTI. Average total cost of therapy (which includes cost of all medicines for UTI patient), average total cost of antibiotic therapy in each group (ceftriaxone or nitrofurantoin) and average total no of IPD (admission) days until patients became symptom free were calculated. Out of the total cost of therapy, percentage of cost attributed to tab nitrofurantoin was compared with inj ceftriaxone. Most cost-effective antibiotic was analysed. Average number of admission days for groups of UTI patients receiving tab nitrofurantoin and inj ceftriaxone were calculated and compared. Group of UTI patients receiving antibiotic (nitrofurantoin or ceftriaxone) with least number of admission (IPD) days was calculated.

Statistical analysis

Statistical analysis was done by using descriptive and inferential statistics using student's unpaired t test and software used in the analysis was SPSS 22.0 version and $p<0.05$ is considered as level of significance.

RESULTS

The average number of admission days of urinary tract infection patients in group IA (receiving nitrofurantoin) was 4.4 days, total average cost of therapy for urinary tract infection in group IA was 277 rupees out of which 70.4 rupees was attributed to nitrofurantoin therapy. Percentage of cost attributed to nitrofurantoin out of total cost of therapy was 26% as shown in Table 2.

The average number of admission days of group IB (receiving inj ceftriaxone) was 5.2 days, total average cost of therapy for urinary tract infection in group IB was 911 rupees out of which 676 rupees was attributed to ceftriaxone therapy. Percentage of cost attributed to ceftriaxone out of total cost of therapy was 75% as shown in Table 3.

By using unpaired student t test statistically significant difference was found between average cost (in percentage) attributed to injection ceftriaxone (group IB) and tablet nitrofurantoin (group IA) (p-value <0.05) Table 12. By using unpaired student t test no statistical significant difference between average number of admission days was found within each group receiving Inj ceftriaxone (group IB) and tablet nitrofurantoin (group IA) (p-value>0.05) Table 13.

Table 2: No of admission (IPD) days of UTI patients in group IA and percentage of cost of therapy attributed to nitrofurantoin out of total cost.

Age (yrs)	No. of IPD days	Cost of nitrofurantoin (rupees)	Total cost of therapy for UTI (rupees)	Percentage of cost attributed to nitrofurantoin out of total cost (%)
45	3	48	213	23
42	4	64	258	25
47	4	64	260	25
48	5	80	304	27
44	6	96	349	28
Avg.	4.4 days	70.4 rupees	277 rupees	26%

Table 3: No of admission (IPD) days of UTI patients in group IB and percentage of cost of therapy attributed to ceftrixone out of total cost.

Age (yrs)	No. of IPD days	Cost of ceftrixone (rupees)	Total cost of therapy for UTI (rupees)	Percentage of cost attributed to ceftriaxone out of total cost (%)
60	6	780	1040	76
55	5	650	880	74
48	4	520	720	73
56	5	650	876	75
58	6	780	1040	75
Avg.	5.2 days	676 rupees	911 rupees	75%

Table 4: No of admission (IPD) days of UTI patients in group IIA and percentage of cost of therapy attributed to nitrofurantoin out of total cost.

Age (yrs)	No. of IPD days	Cost of nitrofurantoin (rupees)	Total cost of therapy for UTI (rupees)	Percentage of cost attributed to nitrofurantoin out of total cost (%)
26	4	64	264	25
45	4	64	274	25
50	5	80	304	27
47	4	64	269	24
44	4	64	260	25
Avg.	4.2 days	67.2 rupees	274.2 rupees	25%

Table 5: No of admission (IPD) days of UTI patients in group IIB and percentage of cost of therapy attributed to ceftrixone out of total cost.

Age (yrs)	No. of IPD days	Cost of ceftrixone (rupees)	Total cost of therapy for UTI (rupees)	Percentage of cost attributed to ceftriaxone out of total cost (%)
40	4	390	555	71
44	4	520	720	73
21	5	650	885	74
55	5	650	876	75
48	4	520	725	72
Avg.	4.4 days	546 rupees	752.2 rupees	73%

The average number of admission days of urinary tract infection patients in group IIA (receiving nitrofurantoin) was 4.2 days, total average cost of therapy for urinary tract infection in group IIA was 274.2 rupees out of which 67.2 rupees was attributed to nitrofurantoin therapy. Percentage of cost attributed to nitrofurantoin out of total cost of therapy was 25% as shown in Table 4.

The average number of admission days of group IIB (receiving inj ceftriaxone) was 4.4 days, total average cost of therapy for urinary tract infection in group IIB was 752.2 rupees out of which 546 rupees was attributed to ceftriaxone therapy. Percentage of cost attributed to ceftriaxone out of total cost of therapy was 73% as shown in Table 5.

By using unpaired student t test statistically significant difference was found between average cost (in percentage) attributed to injection ceftriaxone (group IIB) and tablet nitrofurantoin (group IIA) (p-value <0.05) as shown in Table 12. By using unpaired student t test no statistical significant difference between average number of admission days was found within each group receiving inj ceftriaxone (group IIB) and tablet nitrofurantoin (group IIA) (p-value >0.05) as shown in Table 13.

The average number of admission days of urinary tract infection patients in group IIIA (receiving nitrofurantoin) was 5.4 days, total average cost of therapy for urinary tract infection in group IIIA was 312.40 rupees out of which 86.4 rupees was attributed to nitrofurantoin therapy. Percentage of cost attributed to nitrofurantoin out of total cost of therapy was 28% as shown in Table 6.

The average number of admission days of group IIIB (receiving inj ceftriaxone) was 5.6 days, total average cost of therapy for urinary tract infection in group IIIB was 984 rupees out of which 728 rupees was attributed to ceftriaxone therapy. Percentage of cost attributed to ceftriaxone out of total cost of therapy was 74% as shown in Table 7.

By using unpaired student t test statistically significant difference was found between average cost (in percentage) attributed to injection ceftriaxone (group IIIB) and tablet nitrofurantoin (group IIIA) (p-value <0.05) as shown in Table 12. By using unpaired student t test no statistical significant difference between average number of admission days was found within each group receiving inj ceftriaxone (group IIIB) and tablet nitrofurantoin (group IIIA) (p-value >0.05) as shown in Table 13.

The average number of admission days of urinary tract infection patients in group IVA (receiving nitrofurantoin) was 5.2 days, total average cost of therapy for urinary tract infection in group IVA was 339.5 rupees out of which 83.2 rupees was attributed to nitrofurantoin therapy. Percentage of cost attributed to nitrofurantoin out of total cost of therapy was 25% as shown in Table 8.

The average number of admission days of group IVB (receiving inj ceftriaxone) was 5.4 days, total average cost of therapy for urinary tract infection in Group IVB was

980.6 rupees out of which 702 rupees was attributed to ceftriaxone therapy. Percentage of cost attributed to ceftriaxone out of total cost of therapy was 72%, as shown in Table 9. By using unpaired student t test statistically significant difference was found between average cost (in percentage) attributed to injection ceftriaxone (group IVB) and tablet nitrofurantoin (group IVA) (p-value <0.05) as shown in Table 12. By using unpaired student t test no statistical significant difference between average number of admission days was found within each group receiving inj ceftriaxone (group IVB) and Tablet nitrofurantoin (group IVA) (p-value >0.05) as shown in Table 13.

Table 6: No of admission (IPD) days of UTI patients in group IIIA and percentage of cost of therapy attributed to nitrofurantoin out of total cost.

Age (yrs)	No. of IPD days	Cost of nitrofurantoin (rupees)	Total cost of therapy for UTI (rupees)	Percentage of cost attributed to nitrofurantoin out of total cost (%)
35	5	80	294	28
45	5	80	294	28
37	6	96	340	29
45	5	80	294	28
44	6	96	340	29
Avg.	5.4 days	86.4 rupees	312.40 rupees	28%

Table 7: No of admission (IPD) days of UTI patients in group IIIB and percentage of cost of therapy attributed to ceftrixone out of total cost.

Age (yrs)	No. of IPD days	Cost of ceftrixone (rupees)	Total cost of therapy for UTI (rupees)	Percentage of cost attributed to ceftriaxone out of total cost (%)
50	5	650	864	76
36	6	780	1024	76
54	6	780	1124	70
56	5	650	864	76
48	6	780	1024	75
Avg.	5.6 days	728 rupees	984 rupees	74%

Table 8: No of admission (IPD) days of UTI patients in group IVA and percentage of cost of therapy attributed to nitrofurantoin out of total cost.

Age (yrs)	No. of IPD days	Cost of nitrofurantoin (rupees)	Total cost of therapy for UTI (rupees)	Percentage of cost attributed to nitrofurantoin out of total cost (%)
56	5	80	332	24
57	6	96	376	26
53	5	80	301	27
38	5	80	388	21
46	5	80	301	27
Avg.	5.2days	83.2 rupees	339.5 rupees	25%

Table 9: No of admission (IPD days) of UTI patients in group IVB and percentage of cost of therapy attributed to ceftrixone out of total cost.

Age (yrs)	No. of IPD days	Cost of ceftrixone (rupees)	Total cost of therapy for UTI (rupees)	Percentage of cost attributed to ceftriaxone out of total cost (%)
60	5	650	902	72
56	6	780	1112	70
55	6	780	1060	74
47	5	650	871	75
52	5	650	958	68
Avg.	5.4days	702 rupees	980.6 rupees	72%

The average number of admission (IPD) days of urinary tract infection patients in group VA (receiving nitrofurantoin) was 4.4 days, total average cost of therapy for urinary tract infection in Group VA was 227.60 rupees out of which 67.2 rupees was attributed to nitrofurantoin therapy. Percentage of cost attributed to nitrofurantoin out of total cost of therapy was 30%, as shown in Table 10.

The average number of admission (IPD) days of group VB (receiving inj ceftriaxone) was 5 days, total average cost of therapy for urinary tract infection in Group VB was 848 rupees out of which 650 rupees was attributed to ceftriaxone therapy. Percentage of cost attributed to ceftriaxone out of total cost of therapy was 77% as shown in Table 12.

Table 10: No of admission (IPD days) of UTI patients in group VA and percentage of cost of therapy attributed to nitrofurantoin out of total cost.

Age (yrs)	No. of IPD days	Cost of ceftrixone (rupees)	Total cost of therapy for UTI (rupees)	Percentage of cost attributed to nitrofurantoin out of total cost (%)
20	5	80	208	38
36	4	64	221	29
45	4	64	244	26
48	4	48	244	20
55	5	80	221	36
Avg.	4.4 days	67.2 rupees	227.60 rupees	30%

Table 11: No of admission (IPD) days of UTI patients in group VB and percentage of cost of therapy attributed to ceftrixone out of total cost.

Age (yrs)	No. of IPD days	Cost of ceftrixone (rupees)	Total cost of therapy for UTI (rupees)	Percentage of cost attributed to ceftriaxone out of total cost (%)
45	5	650	850	77
53	6	780	990	79
37	5	650	820	79
43	5	650	860	76
60	4	520	720	72
Avg.	5 days	650 rupees	848 rupees	77%

Table 12: Comparison of cost effectiveness (% of cost attributed to each antibiotic) within each group (between ceftriaxone and nitrofurantoin).

	Nitrofurantoin	Ceftriaxone	t-value	p-value
Group I	25.60±1.94	74.60±1.14	48.51	0.0001, S
Group II	25.20±1.09	73±1.58	55.56	0.0001, S
Group III	28.40±0.54	74.60±2.60	38.77	0.0001, S
Group IV	25±2.55	71.80±2.86	27.29	0.0001, S
Group V	27.80±5.76	76.60±2.88	16.93	0.0001, S

Table 13: Comparison of average number of admission days (IPD) within each group (between ceftriaxone and nitrofurantoin).

	Nitrofurantoin	Ceftriaxone	t-value	p-value
Group I	4.40±1.14	5.20±0.83	1.26	0.24, NS
Group II	4.20±0.44	4.40±0.54	0.63	0.54, NS
Group III	5.40±0.54	5.60±0.54	0.57	0.58, NS
Group IV	5.20±0.44	5.40±0.54	0.63	0.54, NS
Group V	4.40±0.54	5±0.70	1.50	0.17, NS

By using unpaired student t test statistically significant difference was found between average cost (in percentage) attributed to injection ceftriaxone (group IVB) and tablet nitrofurantoin (group IVA) (p-value <0.05) as shown in

Table 12. By using unpaired student t test no statistical significant difference between average number of admission (IPD) days was found within each group receiving inj ceftriaxone (group IVB) and Tablet nitrofurantoin (group IVA) (p-value >0.05) as shown in Table 13.

Average cost (in percentage) out of total cost attributed to nitrofurantoin and ceftriaxone in group I was 25.60±1.94 and 74.60±1.14 respectively, in group II it was 25.20±1.09 and 73±1.58 respectively, in group III it was 28.40±0.54 and 74.60±2.60 respectively, in group IV it was 25±2.55 and 71.80±2.86 respectively, in group V it was 27.80±5.76 and 76.60±2.88 respectively. By using unpaired student t test statistically significant difference was found between average cost (in percentage) attributed to injection ceftriaxone and tablet nitrofurantoin (p-value <0.05) in each group. Avera average number of admission (IPD) days in patients receiving nitrofurantoin and ceftriaxone in group I was 4.40±1.14 and 5.20±0.83 respectively ,in group II it was 4.20±0.44 and 4.40±0.54 respectively, in group III it was 5.40±0.54 and 5.60±0.54 respectively, in group IV it was 5.20±0.44 and 5.40±0.54 respectively, in group V it was 4.40±0.54 and 5±0.70 respectively. By using unpaired student t test no statistically significant difference between average number of admission (IPD) days was found within each group receiving Inj ceftriaxone and tablet nitrofurantoin (p-value >0.05) in each group.

DISCUSSION

In present study authors have calculated and compared cost effectiveness of tablet nitrofurantoin with injection ceftriaxone, authors have compared average number of admission (IPD) days of patients receiving tablet nitrofurantoin and injection ceftriaxone as an empirical therapy for urinary tract infections. Percentage of cost of therapy attributed to nitrofurantoin was found to be less than ceftriaxone (p <0.05) in all the five groups, nitrofurantoin was found to be more cost effective as compared to ceftriaxone in adult UTI patients. In a study Mckinell et al, nitrofurantoin was found to be the most low cost antibiotic used as an empirical therapy in uncomplicated UTI when compared to other antibiotics such as cotrimoxazole and other fluoroquinolones, this study was a cost minimization study and high sensitivity and low resistance of nitrofurantoin was the reason of selecting it as a favourable antibiotic.[10] However in one study by Lin et al, comparing effectiveness and cost of three antibiotics (ceftriaxone, ertapenem and levofloxacin) ceftriaxone was found to be more cheaper than ertapenem and levofloxacin.[11] In one study by Bosmans et al, comparing cost effectiveness between cranberry capsules and tablet cotrimoxazole as a prophylactic therapy for recurrent UTI in women, cotrimoxazole was found to be more cost effective.[12] In a study by Friedland et al, comparing oral cefixime and inj ceftriaxone in adolescents patients suffering from gonococcal cervicitis no cost advantages was seen in between cefixime and ceftriaxone.[6] In a study by Huang et al, for economic assessment of three antibiotics i.e. ciprofloxacin, cotrimoxazole and nitrofurantoin, cotrimoxazole was found to be more cost effective as compared to other antibiotics.[13]

In a study by Hutner et al, 5 days of nitrofurantoin resulted in significant clinical resolution of uncomplicated UTI in women compared to single dose fosfomycin at 14th and 24th day respectively, however in present study no significant difference was found in between average number of admission (IPD) days in between nitrofurantoin and ceftriaxone.[7] In a systematic review and meta-analysis by Price et al, comparing prophylactic capacity of nitrofurantoin with other antibiotics, nitrofurantoin had shown similar efficacy to antibiotics such as norfloxacin, cotrimoxazole, cefaclor etc but more adverse effects.[14]

CONCLUSION

In current study authors found tab nitrofurantoin to be more cost effective than inj ceftriaxone as an empirical therapy in UTI patients however there was no significant difference between the average number of admission (IPD) days in patients receiving Tablet nitrofurantoin and injection ceftriaxone for urinary tract infection as an empirical therapy.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee of DMIMS (On 31/03/2017 Ref. No. DMIMS(DU)/IEC/2017-18/6348)

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Cite this article as: Yadav NS, Pathak SS. Cost effective analysis of tab. nitrofurantoin vs. inj. ceftriaxone as an empirical therapy in patients of urinary tract infection at a tertiary health care centre. Int J Basic Clin Pharmacol 2018;7:2393-400.