USE OF TIGECYCLINE (TYGACIL) AGAINST DRUG RESISTANT ORGANISMS IN EASTERN REGION

[1]MUGHIS UDDIN AHMED, [2]JAVED MEMON, [3]SHABAN MOHAMMED, [4]NEARCHOS YIANNAKOU
[5]RIFAT REHMANI, [6]NADIA AL-HAWASHIM AND [7]MOTASIM AHMED

[1]Department of Pathology and Laboratory Medicine, King Abdulaziz Hospital (NGHA) Al-Ahsa KSA
[2]ICU King Abdulaziz Hospital (NGHA) Al-Ahsa KSA. [3-5]King Abdulaziz Hospital (NGHA) Al-Ahsa KSA
[6]Pathology Eastern Region. [7]Al-Moosa General Hospital, Al-Ahsa KSA

ABSTRACT

Objective:

This study was designed to look for sensitivity and resistant pattern of tigecycline in different gram positive and gram negative infections which were resistant to different antibiotics and also look for various methods to prevent drug resistance against tigecycline (tygacil) group of antibiotic.

Materials and Methods:

Three hundred seventy five (375) isolates which includes MRSA(Methicillin Resistant Staphylococcus Aureus), VRE (Vancomycin Resistant Enterocooci), ESBL (Extended Spectrum Beta Lactamase), Stenotrophomonas maltophilia and MDR (Multi Drugs Resistant) Acinetobacter species were identified with the help of colonial characteristics, gram staining, biochemical reactions including API strips system, and special techniques used for each organism. Sensitivity was done with help of disc diffusion (Kirby Bauer) method for tigecycline (tygacil) 15 ug disc provided by company.

Results:

This is a retrospective study which has showed that MRSA were 100% sensitive to tigecycline and VRE were also 100% sensitive to this antibiotic. The ESBL were 90% sensitive and Stenotrophomonas maltophilia 87% to tigecycline. The MDR Acinetbacter species were only 41% resistant which was high in 2008 as compared to overall sensitivity pattern. Male and female were almost equal in this study. Highest number of cases was reported from 70-80 years age group. The different isolates were from different locations from human body and different wards including ICU (Intensive Care Unit).

Conclusions:

Tigecycline exhibit high in vitro activity against most of the commonly encountered gram positive and gram negative resistant organisms which were pathgens in this region. We should take care not to get antibiotic resistance to be developed against tigecycline by appropriate uses and preventive measures (hand hygiene etc.)

Keywords:

Tigecycline (Tygacil), MRSA, VRE, ESBL, Antibiotic Resistance

INTRODUCTION

We come across different type of organisms including gram positives, gram negatives, atypicals, anaerobes, resistant gram positives and resistant gram negatives. Many organisms are sensitive to different antibiotics but some organisms like resistant

Gram positive (MRSA) and resistant gram negatives (ESBL) are problem to treat[1-8]. The new antibiotic by the name of tigecycline (tygacil) has very good in vitro activity against resistant gram positives and gram negatives besides other organisms mentioned earlier[9-13]. This antibiotic belongs to the family of glycycline which is semi-synthetic derivatives of the tetracycline. Tigecycline is the (tigecycline 9-t-butylglycylamide-minocycline) first compound in the new glycocycline class of antimicrobials to become available for clinical use[1,2,10,14,17] . A lot of work has been done on this

antibiotic in North America, Europe and other countries. One study was done on this antibiotic in the Beirut- Lebanon from Middle East. No published data on this antibiotic available from the Saudi Arabia[18-27].

As there is no data available locally. This study will provide a guide on product use of this antibiotic in this part of the world. It will also provide guideline to physicians and surgeons. It will also give information about the proper usage of this product in certain reserve situations like resistant infections. We should concentrate to stop misuse. disuse, overuse and abuse of this antibiotic among hospitalized patients as well as out-patients. This antibiotic should be kept as reserve medicine to be used in resistant cases where no other antibiotic is available[25-27].

MATERIALS AND METHODS

Three hundred seventy five (375) isolates which includes MRSA(Methicillin Resistant Staphylococcus Aureus), VRE (Vancomycin Resistant Enterocoocus), ESBL (Extended Spectrum Beta Lactamase), Stenotrophomonas maltophilia and MDR (Multi Drugs Resistant) Acinetobacter species were identified with the help of colonial characteristics, gram staining, biochemical reactions including API strips system, and special techniques used for each organism. Sensitivity was done with help of disc diffusion (Kirby Bauer) method for tigecycline (tygacil) 15 ug disc provided by company. API strips used were 20 E, NE, Staph.API, Vancomycin resistant identification disc & Etest. The other identifications disc like methicillin or cloxacillin, ESBL identifications disc, other biochemical reactions and specialized techniques for identification were also used.

RESULTS

This antibiotic has been used in 375 different organism isolated from January 2008-December 2010 from our hospital. In this is a retrospective study in which tigecycline was used on MRSA, ESBL, VRE, MDR Acinetobacter species and Stenotrophomonas maltophilia. This study showed that MRSA were 97 (100%) sensitive to tigecycline and VRE were also 07(100%) sensitive to this antibiotic. The ESBL were 173 (90%) sensitive and 20 (10%) were resistant to tigecycline. The Stenotrophomonas maltophilia 13 (87%) sensitive and 02 (13%) resistant to tigecycline. The MDR Acinetbacter species were only 26 (41%) sensitive, which was high in 2008 as compared to overall sensitivity pattern and 37 (59%) resistant to tigecycline (Table 1 & 2). ESBLs were Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca and Proteus mirabilis in different numbers and percentages. In this highest was Escherichia coli 144(74.6%) with sensitivity of 94.4%, followed by Klebsiella pneumoniae 40 (20.7%) with 82.5% sensitivity, Proteus mirabilis 08 (4.2%) with sensitivity around 62.5% and Klebsiella oxytoca which was 0.5% amongst organisms with sensitivity 100% (Table 3). Male and female were almost equal in this study. Highest number of cases were reported from 70-80 years age group (Table 4). The different isolated were from different locations from human body and different wards including (Intensive Care Unit) ICU (Table 5).

DISCUSSION

Our study has shown that tigecycline in vitro very good activity against different antibiotic resistance organisms like MRSA, VRE, ESBL and Stenotrophomonas maltophilia but it showed less activity against MDR Acinetobacter species, which was less in year 2008 and increased by the end of year 2010. We should look for factors responsible for this resistance. Different studies provided us tigecycline activity against different organisms. In USA sepsis caused by Elizabethkingia miricola successfully treated with tigecycline[29]. Bacterial isolates were consecutively collected between (2004-2007) from 24 countries of Eurpean Union, tigecycline was highly active in vitro against most of the pathogens monitored, including MDR pathogens. This activity was stable over the study period, which increasing resistance was noted for several comparator agents during the same period. Tigecycline is approvmamentarium used for the treatment of intra-abdominal and complicated Skin and soft tissue

TABLE NO.1
DIFFERENT ORGANISMS WITH SENSITIVITY AND RESISTANCE PATTERN FOR TIGECYCLINE

Name of organisms	Number of Sensitive organisms	Percentage of Sensitve organisms	Number of Resistant organisms	Percentage of Resistant organisms	Total Number of organisms	Percentage of Total Organisms
MRSA	97	100%	0	0%	97	100%
VRE	7	100%	0	0%	7	100%
ESBL	173	90.00%	20	10.00%	193	100%
Stenotrphomonas maltophila	13	87.00%	2	13.00%	15	100%
MDR Acinetobacter spp.	26	41.00%	37	59.00%	63	100%
Total	316	84.00%	59	16.00%	375	100%

TABLE NO.2
SEX DISTRIBUTION

Group	Male	Percentage	Female	Percentage	Total	Percentage
MRSA	54	56.00%	43	44.00%	97	100.00%
VRE	2	29.00%	5	71.00%	7	100.00%
ESBL	87	45.00%	106	55.00%	193	100.00%
Stenotrphomonas maltophila	12	80.00%	3	20.00%	15	100.00%
MDR Acinetobacter spp.	30	48.00%	33	52.00%	63	100.00%
Total=193(Male+Female)	185	49.00%	190	51.00%	375	100.00%

TABLE NO.3
ESBL ORGANISMS ISOLATED

Name of ESBL isolated	Number of isolated	Percentage of isolates	Number of Sensitive	Percentage of Sensitive	Number of Resistant	Percentage of Resistant
Escherichia coli	144	74.60%	136	94/4%	8	5.60%
Klebseilla pneumoniae	40	20.70%	33	82.50%	7	17.50%
Klebseilla oxytoca	1	0.50%	1	100%	0	0.00%
Proteus mirabilis	8	4.20%	5	62.50%	3	37.50%
Total	193	100%	175	91.00%	18	9.00%

TABLE NO.4
VARIOUS SITE FROM BODY ORGANISMS ISOLATED

Site of isolation	MRSA	VRE	ESBL	Stenotrophomonas maltophila	MDR Acinetobacter spp.
Nose	35	0	0	0	
Wound	18	1	29	2	25
Trachea	2	0	3	0	13
Endo	1	0	3	4	3
Abscess	17	0	5	1	1
Sputum	4	0	2	3	5
Tissue	2	0	6	0	2
Drain	2	0	3	0	1
Throat	1	0	0	0	0
Blood	3	5	14	3	2
Bed sore	1	0	0	0	0
Ear	1	0	0	0	0
Axilla	1	0	0	0	0
Hand	1	0	0	0	0
Abdomen	1	0	0	0	0
Synvial fluid	1	0	0	0	0
Urine	0	1	121	0	8
Tip	0	0	1	2	1
BF	0	0	1	0	0
Eye	0	0	5	0	1
NPA	0	0	0	0	1
Total	97	7	193	15	63

TABLE NO.5
DIFFERENT AGE GROUP FROM WHERE ORGANISMS ISOLATED

Age Group	MRSA	VRE	ESBL	Stenotrophomonas maltophila	MDR Acinetobacter spp.
0-10 years	15	0	7	3	0
10-20 years	2	0	11	1	5
20-30 years	9	0	14	0	4
30-40 years	6	0	18	0	6
40-50 years	7	2	22	0	10
50-60 years	9	0	23	2	6
60-70 years	20	0	27	1	16
70-80 years	22	4	31	5	11
80-90 years	7	1	35	1	3
90-100 years	4	0	3	2	1
100-110 years	0	0	2	0	1
Total	**97**	**7**	**193**	**15**	**63**

infections and retain potential to be a valuable part of the armamentarium used to combat MDR pathogen in Europe[12].

Tigecycline exhibits potent activity against Acinetobacter species in USA comparable to that shown against species of Enterobacteriaceae [2,8,9,13,22,23]. Resistance of this pathogen (Streptococcus pneumoniae) is prevalent and growing local resistance profiles should be consulted before selecting empiric therapy in USA[19]. Complicated Skin & Skin-structure infections, intra-abdominal infections, surgical site infections and surgical infections MDR infections can be controlled by proper and adequate treatment. Prevention of infections can be done by adopting hand hygiene, other preventive and antibiotic formulary resistance program (antibiotic stewardship) in USA[14]. Tigecycline appeared safe and efficacious in patients with selected serious infections due to resistant gram-negative organisms including Enterobacter species, Acinetobacter baumannii and Klebsiella pneumoniae in USA[15].

Tigecycline exhibits high in vitro activity against most of the commonly encountered ESBL producing and MDR bacterial pathogens in Beirut, Labanan Middle East[16]. There is significant data in favor of the clinical use of tigecycline in management of different infections in UK. Tigecycline satisfy the need for a new broad-spectrum antibiotic class from Latin America. The in vitro activity of Tigecycline against both gram-positive and gram negative isolates indicates that it may be a useful for the treatment of nosocomial infections caused by organisms resistant to other antibacterial agents[18].

Tigecycline demonstrated excellent activity against clinically resistant organisms in USA[19]. High tissue penetration into the epithelial lining fluid of infected and un-infected murine lungs by tigecycline in USA. Minimum Inhibitory Concentration (Mic.) of tigecycline is less than 2(.16) is sensitive and 4(13-15) is intermediate and more than >8(<12) is resistant for Acinetobacter species[10-11].

CONCLUSION

From this study we can draw following conclusion that gram positive and gram negative antibiotic resistance infections are quite prevalent in our region and tigecycline is new antibiotic which can be used in these resistant infections. We should also make proper guidelines for proper use of this antibiotic to avoid antibiotic resistance against this new class of semi-synthetic antibiotic. This antibiotic use is by proper healthcare professional permission who can understand gravity of antibiotic resistance. To prevent drug resistance antibiotic stewardship and preventive measures like hand hygiene are necessary. This magic bullet can be used for long period without problem of resistance.

RECOMMENDATIONS

It needs wider studies in different region of Saudi Arabia and a committee should be made to draw policies and guideline for antibiotics used in general and tigecycline in particular to overcome the problem of antibiotics resistance.

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