The Efficacy of Using Different Antibiotics to Prevent Maternal Surgical Site Infections in COVID-19-Infected Cases

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Abstract:

Medical costs go up as a result of surgical site infections (SSIs). Women with COVID-19 infection are more susceptible to infection. Maxipime and Unictam have been evaluated to determine how well they prevented post-cesarean SSIs in pregnant COVID-19 carriers. On the day of surgery, 100 cases received either Maxipime or Unictam treatment. Two groups of patients were created: Group 1 included 50 patients taking Maxipime, and Group 2 included 50 patients taking Unictam. For two weeks, the patients underwent daily SSI following up. Infections at the surgical site occurred at a rate of 21.4% in group 1 and 28.6% in group 2. In 33% of the positive cultures in group 1 and 25% in group 2, Pseudomonas was isolated. Staph-aureus was isolated in 67% of the positive cultures in group 1 and 75% in group 2. By comparing the rates of post-cesarean surgical site infections after using Maxipime or Unictam in COVID-19 cases, we found an increase in the SSI rate in group2 more than in group1. Compared to women without COVID-19 infection, women with COVID-19 infection had a higher rate of post-cesarean SSI. In COVID-19 cases, we advise using Maxipime to prevent SSI following a caesarean delivery. This is due to the fact that Maxipime has a dual action as an antiviral effect besides an antibacterial effect against various types of bacteria.

Keywords: surgical site infection; cesarean; SARS-CoV-2; COVID-19; Maxipime; Unictam

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1. Introduction

Coronavirus is highly contagious and spreads rapidly through contact between humans. [1-3] Little is known about what happens when SARS-CoV-2, the virus that causes COVID-19, infects a pregnant woman.[4, 5] The US Centres for Disease Control and Prevention reported that, after accounting for age, the presence of underlying conditions, race, and ethnicity, the risks of intensive care unit admissions and mechanical ventilation were significantly higher among pregnant women than among non-pregnant women in a study of 8207 pregnant women with COVID-19 between January 22 and June 7, 2020. According to research from Sweden, pregnant women who had COVID-19 were five times more likely to be admitted to an intensive care unit and four times more likely to require mechanical ventilation than women who were not pregnant. [6-8] Then, the risk of surgical site infections after caesarian section may be higher in COVID-19 infected women than in non-infected women.

Managing comorbidities in COVID-19 infected pregnant women at an earlier stage leads to a reduction in SSI. The SSI rate is not influenced by COVID-19 status, but hospital facilities and overcrowding have an effect. [9-11]

SSI may be prevented by receiving an antibiotic which has an antiviral effect, such as Maxipime. [12]

Maxipime is an antibiotic that has antiviral activity and is effective against many viruses, including coronavirus. [12]

So, in this study, we aimed to determine the effectiveness of Maxipime and Unictam as a prophylactic therapy to prevent SSI post-cesarean in COVID-19 infected pregnant women.

2. Materials and Methods

2.1. Study design

This prospective cohort study included 100 pregnant women who were infected with COVID-19. It was conducted at Beni-Suef University Hospital. Patient nasopharyngeal swab samples were collected, and a Real-time reverse

transcription-polymerase chain reaction (RT-PCR) was used to confirm their infection with Covid-19. All patients were admitted for the first time for COVID-19 treatment and scheduled for Caesarian section. The data was collected from those patients between January and December of 2021. All the patients met the inclusion criteria. The study protocol was reviewed and approved by the Research Ethical Committee of the Faculty of Pharmacy, Beni-Suef University. Patients who participated wrote informed consent.

2.2. Inclusion Criteria

- Pregnant women within the age group of more than18 years
- Cases of Covid-19 infection detected as positive by RT-PCR at anytime during pregnancy.

2.3. Exclusion criteria

- Severe hepatic disease in women.
- Cases with age less than 18 years.
- Women with medical disorders such as pre-gestational diabetes, hypertension, or preeclampsia.

The patients were divided into two groups: Patients in Group 1 received maxipime® (cefepime) (50 patients); patients in Group 2 received Unictam® (ampicillin-sulbactam) (50 patients).. The dose of maxipime was 1000 mg three times on the operation day, and the dose of Unictam was 1000 mg three times on the operation day.

2.4. Data collection

In this study, the cases were collected from January to December 2021 in Egypt. We gathered clinical data to determine the rate of SSI incidence after using Cefebime or Unictam as a prophylactic therapy on the day of Caesarean section for pregnant women infected with coronavirus at any time during pregnancy.

2.5. Outcomes

Surgical site infection is the outcome measure in this study and was detected in the form of superficial SSI, deep SSI, endometritis, abscess formation, pus-like incisional drainage, irritation & vaginal dryness, postoperative fever, and positive blood culture.

The patients were followed up daily for SSI for two weeks or until complete recovery to detect the rate of SSI incidence.

2.6. Statistical analysis

Data was analyzed using IBM SPSS advanced statistics version 22 (SPSS Inc., Chicago, IL). The mean and standard deviation of numerical data were used as appropriate. The qualitative data is expressed as frequency and percentage. The comparison between subgroups was performed using an independent T-test regarding scale variables, while the comparison regarding categorical variables was done using Chi-squared, Mann-Whitney, or Fisher exact tests. P-value <0.05 was considered statistically significant.

3. Results

3.1. The baseline characteristics and laboratory data of the studied groups

The mean age ± SD for the Maxipime group was (28.2±5.9) and for the Unictam group was (24.9±5.5). The mean weight for the Maxipime group was (72.9±12.1) and for the Unictam group was (68.9±14.8). The mean gestational age for the Maxipime group was (36.4±2.7) and for the Unictam group was (37.1±2.6). The mean Pre-operative hemoglobin for the Maxipime group was (10.1±1.5) and for the Unictam group was (10.5±1.1). The mean caesarean section duration for all the study cases was (35.9±7.4). The mean C-reactive protein (CRP) for the Maxipime group was (104.4±92.9) and for the Unictam group was (53.5±70.4). The mean D. dimer for the Maxipime group was (1680.5±1615.7) and for the Unictam group was (916.8±811.8). The mean ferritin for the Maxipime group was (430.6±338.6) and for the Unictam group it was (336.1±277.8).

For the Maxipime group, 89.3% of the cases were suffering from lymphopenia, 21.4% from increased SGPT.

For the Unictam group, 92.9% of the cases were suffering from lymphopenia.

Tables 1 and 2 show the baseline features and laboratory findings of the groups under study.

Table 1. Baseline characteristics of the studied groups.

Items	Maxipime group (no=50)	Unictam group (no=50)	P-value
Age	28.2±5.9	24.9±5.5	0.024* (MW)
weight	72.9±12.1	68.9±14.8	0.271
Gestational age	36.4±2.7	37.1±2.6	0.324
cesarian section duration	35.9±7.4	35.9±7.4	>0.999
medical disorders /pregestational diabetes / hyprttension/preeclampsia	0(0%)	0(0%)	

MW=mann whitney test
FET=Fisher exact test

Table 2. Laboratory data of the studied groups.

Items	Maxipime group (no=50)	Unictam group (no=50)	P-value
Pre-opearive hemoglobin	10.1±1.5	10.5±1.1	0.282
CRP	104.4±92.9	53.5±70.4	0.001*(MW)
median (IQR)	96(48-132.25)	24(6-96)	
D. dimer	1680.5±1615.7	916.8±811.8	0.012*(MW)
median(IQR)	1400(776.25-1950)	675(402.5-1175)	
ferritin	430.6±338.6	336.1±277.8	0.258(MW)
median(IQR)	371(96-648)	305.5(66.25-518)	
Lymphocyte			
normal	6(10.7%)	4(7.1%)	0.639
low	44(89.3%)	46(92.9%)	
SGPT			
normal	39(78.6%)	50(100%)	0.012* (FET)
increased	11(21.4%)	0(0.0%)	

MW=mann whitney test
FET=Fisher exact test

3.2. Comparison between the studied groups regarding the occurrence of surgical site infections:
For the Maxipime group, 21.4% of the patients suffered from SSI, including Superficial SSI, Deep SSI, abcess formation, pus-like incisional, postoperative fever, irritation, and vaginal dryness. 21.4% resulted in a positive culture; 33% of them were Pseudomonas and 67% were Staph aureus.

For the Unictam group: 28.6% of the patients suffered from SSI including Superficial SSI, Deep SSI, Abcess formation, pus-like incisional, Postoperative fever, irritation & vaginal dryness. 28.6% resulted in a positive culture, 25% of them were Pseudomonas and 75% were Staph aureus.
Table 3 shows how often surgical site infections happened in each of the groups that were looked at.

Table 3. Comparison between the studied groups regarding the occurrence of infections.

Items	Maxipime group (no=28)	Unictam group (no=28)	P-value
Superficial SSI			
No	39(78.6%)	36(71.4%)	0.537
Yes	11(21.4%)	14(28.6%)	
Deep SSI			
No	39(78.6%)	36(71.4%)	0.537
Yes	11(21.4%)	14(28.6%)	
Endometritis			
No	46(92.9%)	46(92.9%)	>0.999
Yes	4(7.1%)	4(7.1%)	
Abcess formation			
No	39(78.6%)	36(71.4%)	0.537
Yes	11(21.4%)	14(28.6%)	
pus-like incisional drainage			
No	39(78.6%)	36(71.4%)	0.537
Yes	11(21.4%)	14(28.6%)	
Postoperative fever			
No	39(78.6%)	36(71.4%)	0.537
Yes	11(21.4%)	14(28.6%)	
irritation & vaginal dryness			
No	39(78.6%)	36(71.4%)	0.537
Yes	11(21.4%)	14(28.6%)	
Culture (SSI)			
negative	39(78.6%)	36(71.4%)	0.537
positive	11(21.4%)	14(28.6%)	
Isolated Organism			
Pseudomonas	4/11 (33.3%)	4/14 (25%)	0.733
Staph aureus	7/11 (67.7%)	10/14 (75%)	

4. Discussion

Surgical site infection is a problem and leads to increased healthcare costs.[13-15] The risk of surgical site infections increases after caesarean section for women,[16] especially if they were infected with COVID-19 due to the immunity fall in COVID-19 pregnant women compared to non-infected pregnant women. Pregnant women with COVID-19 have a lower white blood cells (WBC) count than other pregnant women. [17, 18] Therefore, using prophylactic antibiotics may limit the incidence of surgical site infection.[19-21]

SSI may be superficial or it may be more dangerous, affecting the deep tissue or organ, as in Endometritis.[22]

SSI is the outcome measured in our study and was detected in the form of superficial SSI, deep SSI, endometritis, abscess formation, pus-like incisional drainage, irritation & vaginal dryness, postoperative fever, and positive blood culture.

The rate of SSI in the maxipime group it was 21.4% and in the unictam group was 28.6%. A previous study reported that the overall rate of SSI in non-COVID-19 cases was 4.3%. [23] and in another study, it was 5.5%. [24] That means that COVID-19 patients have a higher rate of SSI than people who haven't been infected with COVID-19 because their immunity is going down.[25-27]

In this study, we reported that the main gestational age for the maxipime group± standard deviation was 36.4±2.7 weeks and for the unictam group it was 37.1±2.6 weeks. The normal gestational age ranges from 38 to 42 weeks.[28] That indicates the adverse outcome of COVID-19 infection on pregnant women, which causes early-term birth. In contrast, a previous study showed an insignificant relationship between COVID-19 infection and early-term birth. [29]

This study reported that the main pre-operative hemoglobin for the maxipime group± standard deviation was 10.1±1.5 g/dL and for the unictam group it was 10.5±1.1 g/dL. The normal pre-operative hemoglobin is 11.5 to 12.5 g/dL.[30] It was reported previously that anemia is associated with COVID-19. [31]

Maxipime is a fourth-generation cephalosporin with a lower bacterial resistance association that has a broad spectrum of activityagainst Gram-negative and Gram-positive bacteria. [32] Unictam is a combination of ampicillin and sulbactam, which are both -lactam antibiotics and -lactamase inhibitors. [33, 34]

β-lactam antibiotics are the first-line therapy for the protection against surgical site infections, and the resistance to these antibiotics may cause the infection to worsen..[35]

The most common microorganisms causing SSI reported in this study were Staphylococcus aureus and pseudomonas aeruginosa. That was also reported in previous studies.[36, 37]. Staphylococcus aureus is a gram-positive bacteria [38-40]

Pseudomonas aeruginosa belongs to the family Pseudomonadacae and is a gram negative bacillus. [41]

The results of this study demonstrated that Cefebime showed a better effect as a protective agent against surgical site infections than Unictam. That may be due to the presence of the bacterial enzymes which inactivate penicillins in Unictam (that is also known as penicillinase-resistant penicillins). [19, 42-44] This resistance may have developed due to the empirical use of unictam in hospitals.

A study from the past said that maxipime works better than other broad-spectrum β-lactams and non-β-lactams.[32]

The lower efficacy of unictam than maxipime may be due to the lower efficacy of unictam against gram-negative bacteria than gram-positive bacteria. Some antibiotics, such as β-lactam antibiotics that target peptidoglycan in the bacterial cell wall, are ineffective against gram-negative bacteria because their chemical properties prevent them from using these pathways to effectively penetrate the outer membrane.[45-47]

On the other hand, maxipime has efficacy for improvement of symptoms in moderate and severe coronavirus cases as its antiviral activity against many viruses, such as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), as recorded in the study of Eid, R.A., et al. [12] From the chemistry point of view, cefepime has a high potential for inhibiting SARS CoV-2 by targeting the MPro enzyme. [12]

We conclude that Maxipime has dual activity against various types of bacteria which cause SSI and COVID-19 infection. Therefore, Maxipime is recommended for use as a prophylactic against SSI after caesarean delivery in COVID-19 cases due to its extra benefit of having an antiviral effect besides its antibacterial effect.

When we compared the rates of post-cesarean surgical site infections after using Maxipime or Unictam in COVID-19 cases, we found an increase in the rate of surgical site infections in the Unictam group more than in the Maxipime group. In a recent Egyptian study, it was found that the rate of post-cesarean surgical site infections in COVID-19 infected women was higher than that in non-infected women, which was reported to be 5.34%. [48] We recommend using Maxipime to protect against surgical site infections after a caesarean delivery in COVID-19 cases because of its dual action as an antiviral effect besides an antibacterial effect against various types of bacteria.

The main strength of this study is that, it is the first study to demonstrate the efficacy of Maxipime for protection against surgical site infections after caesarean delivery in COVID-19 cases.

The main limitations of this study, on the other hand, were (i) the relatively small sample size used in the study and (ii) its location (i.e., It was a study from a single-center).

5. Conclusions

Regarding the rates of post-cesarean surgical site infections after using Maxipime or Unictam in COVID-19 cases, there was an increase in the rate of surgical site infections in the Unictam group more than in the Maxipime group. The rate of post-cesarean surgical site infections in COVID-19 infected women was higher than in non-COVID-19 infected women. We recommend using Maxipime for protection against surgical site infections after caesarean delivery in COVID-19 cases because of its dual action as an antiviral effect besides an antibacterial effect against various types of bacteria.

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