Introduction

There has been much concern globally and nationally regarding the misuse of antibiotics leading to suboptimal treatments and a high incidence of resistance.\(^1\)\(^2\) Antibiotic resistance is now regarded as a major public health issue because infections by multi-drug resistant bacteria lead to increased mortality, morbidity and increased hospital stays and the armamentarium against these bacteria is dwindling rapidly. Many prescriptions are inappropriate and there is some evidence of compulsive antibiotic prescribing.\(^3\) It is generally recommended that antibiotic prophylaxis is given in most types of surgery, but the choice of therapy is controversial.\(^4\)

The antibiotic guidelines in Oman were last published in 1998 and covered therapeutic and prophylactic use.\(^5\) The guidelines for Lower Segment Caesarian Sections (LSCS) surgical prophylaxis give two possible regimens. These are; a single doses of 2 g cefradine, or a single dose of 1.2 g of co-amoxiclav administered intravenously, immediately after clamping the cord. All prescribers are supposed to follow the Ministry of Health guidelines as much as possible, but there is still the freedom to prescribe according to clinical need on a case-by-case basis.

The definition of prudent antibiotic prescribing has recently been defined as:

“The use of antimicrobials in the most appropriate way for the treatment or prevention of human infectious diseases, having regard to the diagnosis (or presumed diagnosis), evidence of clinical effectiveness, likely benefits, safety cost (in comparison with alternative choices), and propensity for the emergence of resistance. The most appropriate way implies that the choice of route, dose, frequency and duration of administration have been rigorously determined.”

As part of its remit, the directorate of rational use of medicines (DRUM) in the Ministry of Health is charged with ensuring the rational use of antibiotics throughout government health facilities in Oman. Therefore, investigative studies were planned to evaluate the use of antibiotics in major hospitals. This study focussed on the perioperative use of antibiotics in lower segment caesarean sections (LSCS). This area was chosen because international reviews, meta-analyses and guidelines are widely available for comparison.

Methods

A retrospective examination of patient records was conducted for the year 2004 (the nearest full year to the start of the study in 2005). The data was collected from four major hospitals located in different regions of the Sultanate. The sample size chosen at each hospital was approximately 20% of the annual number of LSCS surgeries (Table 1). Both elective and emergency LSCS...
surgeries were included to discover if there were major differences in approaches to treatment as emergency LSCS are considered to carry the highest risk.

Data was retrieved from the hospital registries by a systematic random sampling method and the total patient records evaluated was 510 from a possible 2,242 cases. The drug regimen and all antibiotics administered perioperatively were recorded for each patient. Checking of each patient’s notes was done to determine if the antibiotics were being used therapeutically and/or prophylactically although in many cases it was quite difficult to determine.

Each hospital was asked to provide:
• a copy of any written guidelines or protocols they were using
• the number of infections recorded, per month, in LSCS surgeries for the study period, including details of the attendant surgeons
• laboratory information about culture and sensitivity data and nosocomial infections if appropriate

The data obtained were analyzed in Excel using pivot tables and SPSS Version 14.

Results

Table 1 shows the collective statistical data in obstetrics and gynaecology for the four hospitals in the study.

Table 1: Obstetrics & Gynaecology Statistics for Study Hospitals in Oman (2004)

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Total Deliveries</th>
<th>Total LSCS</th>
<th>LSCS (of Total Deliveries)</th>
<th>Emergency</th>
<th>% Emergency</th>
<th>Elective</th>
<th>% Elective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Khoula</td>
<td>3,232</td>
<td>550</td>
<td>17</td>
<td>445</td>
<td>80.9</td>
<td>105</td>
<td>19.1</td>
</tr>
<tr>
<td>Sohar</td>
<td>5,394</td>
<td>599</td>
<td>11.1</td>
<td>517</td>
<td>86.2</td>
<td>83</td>
<td>13.8</td>
</tr>
<tr>
<td>Nizwa</td>
<td>3,318</td>
<td>465</td>
<td>14</td>
<td>337</td>
<td>72.6</td>
<td>127</td>
<td>27.4</td>
</tr>
<tr>
<td>Sultan Qaboos Hospital</td>
<td>3,822</td>
<td>638</td>
<td>16.7</td>
<td>513</td>
<td>80.5</td>
<td>124</td>
<td>19.5</td>
</tr>
</tbody>
</table>

Table 2 shows the surprising variety of regimens that have developed in Oman since 1998. Each of the four study hospitals had a different schedule and none were found to be following the MoH recommendations.

Table 2: Results Table for each of the 4 Study Hospitals in Oman

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Khoula</th>
<th>Sohar</th>
<th>Sultan Qaboos Salalah</th>
<th>Nizwa</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of LSCS patients</td>
<td>120</td>
<td>134</td>
<td>125</td>
<td>131</td>
</tr>
<tr>
<td>Written policy?</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Main Prophylactic Regimen (% cases)</td>
<td>(C2 (84%; 76-90 (M (97%; 91.7-99 + C1 (16%; 10.6-23 or (C2 (64%; 55.4-71.6 (C3 (55%; 46-64 (M (98%; 94.3-99.8 (G (22% (C2 (43%; 34.4-54.3) or + Amp (92%; 86.4-95.7) + Amox oral (90%; (83.6-94.03 (M (21%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additional therapeutic ABs</td>
<td>Varies</td>
<td>(M (26%</td>
<td>(M (26%</td>
<td></td>
</tr>
<tr>
<td>Avg Length of prophylactic treatment (days)</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>% on a single AB</td>
<td>(1.9-10.6) 5%</td>
<td>(3.1-11.4) 6%</td>
<td>(0.02-4.3) 0.8%</td>
<td>(0.19-4.1) 1%</td>
</tr>
<tr>
<td>% on single dose of AB</td>
<td>(27.3-45.1) 35.8%</td>
<td>0.7%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Median Stay in days</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Max Doses of any i/v AB to any one patient</td>
<td>28</td>
<td>23</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>No on Oral ABs</td>
<td>(17.6-33.7;25.2% 30</td>
<td>(24.9-44.5;32.8%) 44</td>
<td>(13.4-28.1;20%) 25</td>
<td>(87.4-96.9%;93%) 122</td>
</tr>
<tr>
<td>Infection Rate (all LSCS patients)</td>
<td>(0.15-1.4) 0.5%</td>
<td>(6.3-9.7) 8%</td>
<td>N/A</td>
<td>(1.8-5.3) 3.2%</td>
</tr>
</tbody>
</table>

Percentage ± 95% CI (%) where appropriate, C1 = 1st generation cephalosporin (1g stat then 500mg/1000mg 1 to 15 doses), C2 = 2nd generation cephalosporin (1.5g stat then 750mg - 1 to 15 doses), C3 = 3rd generation cephalosporin (2g – 1 to 6 doses), M = metronidazole (500mg - 3 to 19 doses), Amp = ampicillin (1 or 2g stat then 1g or 500mg (2 to 25 doses), Amox = amoxicillin (250mg – 15 doses), G = gentamicin, El = Elective, Em = Emergency, AB = antibiotic
Khoula and Sohar hospitals were found to be using a combination of cephalosporin and metronidazole routinely but in Sultan Qaboos Hospital, Salalah a third generation cephalosporin was used in roughly half of the studied cases and a second generation cephalosporin (cefuroxime) in just over 40% of cases. Khoul hospital in Muscat governorate used cefuroxime in more than 80% of cases and 97% of cases received metronidazole in addition. In Sohar hospital, North Batinah region, a small number of cases (16%) were given a first generation cephalosporin (cephalexin) with 64% receiving cefuroxime.

Metronidazole was apparently only given therapeutically in this hospital and in only 26% of the cases. In Nizwa hospital (Adh Dakhliyah region) the regimen was radically different to the others and cephalosporins were not used at all prophylactically. 92% of cases were given iv ampicillin combined with an oral dose of amoxicillin (90% of cases).

In Sultan Qaboos Hospital in Salalah (Dhofar region), 43% of cases were given a second generation cephalosporin and 55% received a third generation cephalosporin (ceftriaxone). Almost all of the cases (98%) received additional metronidazole prophylactically. In all 4 hospitals, there was no significant difference in the prophylaxis regimens for elective or emergency LSCS patients. A very small percentage of patients received only a single antibiotic during their stay but a significant number (36%) received a single dose of antibiotic at Khoul hospital. Other antibiotics, especially aminoglycosides, were introduced usually following post-partum complications e.g. fever spikes, UTI or wound sepsis. In a few of the cases bilateral tubal ligations or hysterectomies were performed after delivery and often further antibiotics were used therapeutically. The average length of prophylaxis ranged from 1 day in Sohar to 5 days in Salalah with the overall average being 2 days.

When oral antibiotics were analyzed, a range of 12 different antibiotics were used, from 5 different groups with the majority being penicillins (52%), cephalosporins (22%) and imidazoles (22%). The number of patients receiving oral antibiotics during their stay ranged from 20% - 32% in three hospitals and was 93% in Nizwa where oral amoxicillin was part of the main regime.

To try and discover any significant difference between the regimens used, the hospitals were asked to provide data governing their infection rates for the same period of the study. The infection rate data was requested by date, theatre and surgeon as well as the causative organisms. The procedures for gathering and recording the data was the same at each of the three hospitals which provided information. The results are displayed in Table 2. The infection rates at Khoul and Nizwa hospitals were low to moderate (0.5 - 3.2%), but in Sohar the infection rates were much greater (8%). Only 3 hospitals were able to provide infection control data and only one of the hospitals was able to provide a copy of a written protocol. Other indicators studied included the average length of prophylaxis, median bed stay, maximum doses of iv antibiotics to any one patient and number of oral antibiotics. However, none of these revealed any further tangible evidence of a significant difference between the facilities.

Discussion

The Ministry of Health Antibiotic Chemotherapy Policy & Guidelines were published in 1998 and cover the use of antibacterials in prophylaxis and treatment. In all, but the rarest cases of infection, a recommendation is given based on sound, evidence-based microbiological principles. As a method of controlling resistance, antibiotics are divided into three groups. Group 1 is a range of common antibiotics prescribable at all levels. Groups 2 and 3 can only be prescribed by senior physicians or consultants respectively, in defined circumstances and following culture and sensitivity testing. The lists and groups are somewhat dynamic and changes do occur over time depending on the prevailing evidence.

Prophylactic use of antibiotics in various surgical procedures is controversial and full of misconceptions such as, always using broad spectrum antibiotics and for longer durations. Also, it is often thought that prophylaxis should continue until "all tubes are out."8

Ideally, a single dose of a single antibiotic with a spectrum appropriate to cover the most common infecting organisms is considered the most judicious practice. There have been many reviews and published guidelines to cover most instances where prophylaxis is recommended and where it is not considered appropriate. However, there remains the complex problem of appropriate antibacterial selection, and then frequency, duration and timing of each dose. There are many examples of irrationality in this field. One in particular was the choice of four antibiotics including two cephalosporins e.g. cephadrine, ceftriaxone, gentamicin and metronidazole which was used in one community hospital in Saudi Arabia.9

A caesarean section is classified as a clean-contaminated operation. The most common negative outcomes are endometritis, wound infection, urinary tract infections or occasionally more
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serious septicaemias. The most common infecting organisms are *Staphylococcus aureus*, *E. coli* and *beta haemolytic Streptococci*. Much research has been conducted on the use of antibiotics during LSCS in countries throughout the world, ranging from developed to developing. Many regimens have been tried and tested and there seems to be very little significant benefit of one over another. It is now well established that antibiotic prophylaxis in LSCS surgery reduces the risk of infection and endometritis in all types of patients and has proven to be of benefit even to those at the lowest risk.10

The conclusion from all of these studies is not whether to use an agent but rather which agent to use. In addition to the choice of different antibacterials and combinations, there have been reported differences in the route of administration and the timing of administration. 5,10-15 Although administration after clamping of the cord is most common and prevents exposure of the infant, a recent meta analysis concluded that preoperative administration considerably reduced the risk of post-partum endometritis and other infections.15 Results from several randomised trials indicate that ampicillin or a first generation cephalosporin are suitable choices and a single dose is considered sufficient. One recent study showed no statistical significant difference in infection rates between the use of ceftriaxone versus ampicillin/cloxacillin prior to caesarean sections in Sudan.16 A recent literature review concluded that a narrow spectrum agent prior to incision or an extended spectrum regimen (with metronidazole) after cord clamp offers the best outcome for patients but stresses that the two regimes have not yet been compared. 17

Although the Omani MoH Antibiotic policy and therapeutic guidelines were about 6 years old at the time of this study they are still mainly relevant to much of today’s practice. However, many health workers considered the guidelines to be out-dated and in consequence, it appears that most major hospitals in Oman have established their own “in house” guidelines for almost all antibiotic use. In the case of prophylactic use of antibiotics in LSCS, the recommendation of a single dose of a first generation cephalosporin or broad spectrum penicillin is still a very commonly used regimen worldwide. However, the results found in this study were surprising and indicate that there is much diversity in this field.

This is possibly dictated by the background, training and experience of the senior clinicians in obstetrics and gynaecology and their junior staff at the hospitals under study. There may be a feeling amongst healthworkers that the MoH guidelines need to be changed because of the elapsed time since publication. The nature of the patients in the different health regions may also play a role in the choice and the duration of prophylaxis. The different health regions in Oman do differ somewhat, socially and culturally but whether this can explain the findings is controversial. Also, the infrastructure and the environment may have a bearing on the current findings, however, there was no direct association found between the age of the facility and the procedures used or outcomes achieved. Whatever the situation may be in the particular health region, five days of prophylaxis and the use of 3rd generation cephalosporins cannot be justified and can only lead to much greater bacterial resistance as well as having a negative economic impact.

It is not possible to state that reiteration of a blanket policy on antibiotic prophylaxis in surgery by MoH would necessarily be better than some of the evolved protocols described, however, such a policy might help to reduce some of the excesses witnessed in this study.

Conclusion

Many diverse regimes for prophylaxis and treatment during LSCS surgery have evolved at major hospitals in different regions of Oman. Those hospitals that had a consistent policy and especially a written policy, made known to all staff, had better outcomes as far as post operative infections were concerned.

The results found in this study will be disseminated to all health workers at workshops and seminars. The work will continue to investigate and, where necessary, educate prescribers, other health workers and the general public about rational use of medicines and rational use of antibiotics in particular.

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References


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