COMPOSITION AND PRODUCTION RATE OF CYTOSTATIC PHARMACEUTICAL WASTE FROM THEAGENIO CANCER HOSPITAL IN THESSALONIKI, GREECE

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EXTENDED ABSTRACT
The objective of this work was to determine the composition and production rate of cytostatic pharmaceutical waste produced by Theagenio Cancer Hospital in Thessaloniki, Greece. This information is extremely important for the design and costing of management systems for cytostatic pharmaceutical waste. Furthermore, the quantification of pharmaceutical waste production is significant for assessing their environmental impact, when they are released in the environment. Specific objectives were: (1) To determine the daily production (g/d) and unit production rates (g/patient/d and g/bed/d) of cytostatic pharmaceutical waste by individual wards and Theagenio hospital as a whole. (2) To determine the daily production of residual amounts of cytostatic pharmaceutical waste by individual wards and the hospital as a whole. (3) To determine possible correlations between daily waste production and daily number of patients. A total of 412 kg cytostatic pharmaceutical waste was collected, manually separated and weighed over a period of six working weeks.

Total cytostatic pharmaceutical waste was classified in two categories, vial waste comprising 89.5% and syringe waste with 10.5% of the total. The overall pharmaceutical waste production by the hospital was 9811(5425) g/d, with numbers in parenthesis representing standard deviations. The main cytostatic pharmaceutical waste producers were interdisciplinary day clinic with 42.1%, pathology with 38.9% and hematology with 10.4% w/w of the total. The total residual amount of waste cytostatic pharmaceuticals over the 42 days of the study was 4.5 kg. The overall residual waste production (visually assessed) was 109(84) g/d. This is the average daily amount (g/d) of drugs contained in the vials and syringes, which pass to the waste stream. The overall average unit production rates of cytostatic pharmaceutical waste were 46(12) g/patient/d and 86(48) g/bed/d. The larger producer was pathology with production rates of 59(21) g/patient/d and 55(29) g/bed/d, followed by hematology with 49(14) g/patient/d and 38(14) g/bed/d. The smallest producer was gastroenterology department with 34(29) g/patient/d and 38(25) g/bed/d. The respective unit production rates were: (1) for vial waste 6.4(1.6) g/patient/d and 13 (2.6) g/bed/d and (2) for syringe waste 5(1.5) g/patient/d and 9(5) g/bed/d.

Keywords: cytostatic, antineoplasmatic waste, vial waste, syringe waste, unit production rate

1. INTRODUCTION
The cytostatic drugs are used for cancer therapy. They affect the metabolism of cancer cells, thus, hindering their division (Eitel et al., 1999). Undesired effects of cytostatic drugs include nausea, hair loss and depression of the immune system and they affect not only cancer patients, but also handling health care personnel. There are more than 50
different cytostatic drugs, used with both intravenous and oral administration (BMA, 2006).

Previous investigations have shown that mismanagement of cytostatic waste may cause adverse effects in the environment and human health. Concentrations for specific cytostatic pharmaceuticals up to 100 ng/L were reported in hospital wastewater effluents (Kümmerer et al., 1997; Steger-Hartmann et al., 1996). Aherne et al. (1990) reported concentrations up to 17 ng/L in river water in South East England, for the cytostatic drug “Bleomycin”. Buarge et al. (2006) reported concentration of cyclophosphamide in wastewater treatment plant effluents in Switzerland from 0.15 to 0.17 ng/L.

Occupational exposure to some kinds of cytostatic pharmaceutical waste (e.g., antineoplastic drugs and other hazardous drugs) may result in adverse health effects, such as skin rashes, infertility, miscarriage, birth defects, and possibly leukemia or other cancers (DHHS, 2004).

In the European Union, pharmaceutical waste is classified in chapter 18 of the European Waste Catalogue. Specifically, cytostatic pharmaceutical waste is classified with code numbers 18 01 08* and 18 02 07*, as potentially hazardous waste.

Although there are a large number of papers on production of infectious waste by hospitals, no such information is available for production of pharmaceutical and specifically cytostatic pharmaceutical waste (Voudrias et al., 2012). This information, however, is extremely important for the design and costing of management systems for cytostatic pharmaceutical waste. The choice of treatment technology is also important. Quantification of cytostatic pharmaceutical waste production is crucial for health and safety considerations and for assessing their environmental impact, when they are released in the environment.

This work was designed with an overall objective to determine the composition and production rates of cytostatic pharmaceutical waste produced by Theagenio Cancer Hospital, in Thessaloniki, Greece. Specific objectives were: (1) To determine the daily production (g/d) and unit production rates (g/patient/d and g/bed/d) of cytostatic pharmaceutical waste by individual wards and the hospital as a whole. (2) To determine the daily production of residual amounts of pharmaceutical waste by individual wards and the hospital as a whole.

2. MATERIALS AND METHODS

2.1. Activity at Theagenio Cancer Hospital

The following wards/departments of Theagenio Cancer Hospital (with the number of beds in parenthesis) participated in this study and are the main cytostatic pharmaceutical waste producers: Interdisciplinary day clinic (43 beds), Pathology (69 beds), Hematology (23 beds) and Gastroenterology (22 beds). The study lasted 42 days and was conducted in 2011. At that time, the hospital had 357 beds for patient care. The average daily number of patients during the study period was 195±87 and the total number of patients over the same period was 8194.

2.2. Cytostatic pharmaceutical waste at Theagenio Cancer Hospital

For the purpose of this study, the cytostatic pharmaceutical waste was distinguished in two types: (1) vial and (2) syringe waste. Vial waste comprised the initial containers (usually plastic or glass) with residual amounts of cytostatic pharmaceuticals in liquid or
solid form. Vials were labeled by drug manufacturers with the name and initial quantity of cytostatic pharmaceutical. Syringe waste comprised used syringes without needles, containing residual amounts of cytostatic pharmaceuticals in liquid form. Used syringes were not labeled and, therefore, it was not possible to sort the waste based on the pharmaceutical content, but they were all lumped together for every ward/department.

2.3. Collection of cytostatic pharmaceutical waste

The regular waste collection took place from May to September 2011 for 6 working weeks, one week per month randomly selected during the sampling month. The following types of containers were used for waste collection.

- Red plastic bags which were placed next to the biosafety chamber.
- An electronic balance.

Source separation of cytostatic pharmaceutical waste was conducted by nurses at each ward/department. The cytostatic waste was collected in the red bags, which were placed next to biosafety chamber. Specifically, vials containing residual amounts of pharmaceuticals and used syringes with no needles, following medical praxis, and expired medicine were placed by collection in the red plastic bags. Plastic bags were collected at the end of the working shift on each collection day and were transported by waste collection crew with wheel-containers in a storage room, where they were weighed.

2.4. Separation, weighing and recording

An electronic balance with precision of 1 g was used in all measurements. First, the whole content of each red bag was weighed, followed by bag opening and separation of the vials, based on the name of their cytostatic pharmaceutical content in the label (e.g., Epibra, a known cytostatic antibiotic). All syringes were grouped together, regardless of their content. Small quantities of undesired waste components included in the bags were not taken into account and discarded. Then, vials of each cytostatic pharmaceutical type were weighed together and recorded in Microsoft Excel spreadsheets. In addition, the residual amounts contained in each vial were visually estimated (without weighing) based on the original content, summed and recorded.

Separation of syringe waste according to their content was not possible, because used syringes were not labeled. However, assessment of their residual amounts was more accurate than in the vials, because of syringe graduation. In all cases, the sorted waste after weighing was returned to the main collection area of the hospital, for proper management.

Along with the amount of waste collected, the number of beds in each ward and the hospital as a whole, the number of patients entering the hospital on the particular sampling days was also recorded in excel spreadsheets. Therefore, the term “patient” refers to everybody entering the hospital for medical examination, regardless if he was then hospitalized or not. The number of patients was used in order to compute the waste unit production rates, as g/patient/d. The number of beds was used to compute the unit production rates, as g/bed/d. In wards/departments with beds, the unit production rate g/patient/d is equivalent to g/occupied bed/d. More details are presented in Voudrias et al. (2012).

The person involved in waste separation, weighing and recording took all necessary health and safety measures for accident prevention. These included a white laboratory coat, glasses, a paper mask, double pair of plastic gloves and surgeon’s foot covers.
3. RESULTS AND DISCUSSION

3.1. Total production of cytostatic pharmaceutical waste by Theagenio Cancer Hospital in Thessaloniki and comparison of waste categories

The average daily production and unit production rates of vial and syringe cytostatic waste by wards/departments of Theagenio Cancer Hospital are presented in Tables 1-2. Numbers in parentheses represent standard deviations. The total amount of cytostatic pharmaceutical waste produced by all wards/departments at Theagenio Cancer Hospital equals the sum of vial waste and the syringe waste. The total amount of cytostatic pharmaceutical waste, which was collected and analyzed over the 42 days of the study, was approximately 412 kg and the total number of patients producing the waste was 8194. The columns in Table 3 resulted from addition of total production columns from previous Tables 1, 2 and show the total amount of cytostatic pharmaceutical waste produced by Theagenio Cancer Hospital. The overall cytostatic pharmaceutical waste production by the hospital was 9811 (5425) g/d.

Comparing the cytostatic pharmaceutical waste categories, vial waste was found in the largest quantity with 8782 (1719) g/d (89.5 %), followed by syringe waste with 1029 (573) g/d (10.4 %) (Tables 1,2,3). The main cytostatic pharmaceutical waste producers were Interdisciplinary day clinic with 42.1 % and Pathology with 38.9% w/w of the total.

The overall residual cytostatic waste production (visually assessed) was 109 (84) g/d. This is the average daily amount (g/d) of cytostatic drugs contained in the vials and syringes, which pass to the waste stream. The total residual amount of cytostatic pharmaceutical waste over the 42 days of the study was 4.5 kg. Residual waste contained in vials was found in the largest quantity with 105 (79) g/d (96.8 %), followed by syringe with 3 (6) g/d (3.2 %) (Tables 1,2).

The overall average unit production rates of cytostatic pharmaceutical waste by Theagenio Cancer Hospital were 46 (12) g/patient/d and 86 (48) g/bed/d (Table 3). The larger producer was Pathology with production rates of 59 (21) g/patient/d and 55 (29) g/bed/d. The smallest producer was Gastroenterology with 34 (29) g/patient/d and 38 (25) g/bed/d.

Comparing the cytostatic pharmaceutical waste categories, vials were found in the largest production rate, with 41 (11) g/patient/d and 77 (46) g/bed/d, followed by syringe waste with 5 (1.5) g/patient/d and 9 (5) g/bed/d (Tables 1,2).

Figure 1 presents the correlation between daily production of total cytostatic pharmaceutical waste and the respective number of patients. An approximately linear trend is presented and the correlation is strong, as indicated by the high value of the correlation coefficient (R²=0.9117). A visual inspection of Figure 1 shows a gap between
Table 1. Average daily production of vial cytostatic pharmaceutical waste, of residual amount of cytostatic pharmaceuticals and unit production rates by wards/departments of Theagenio Cancer Hospital of Thessaloniki. Numbers in parentheses are standard deviations.

<table>
<thead>
<tr>
<th>Ward/department</th>
<th>Vial cytostatic pharmaceutical waste, g/d</th>
<th>% of total</th>
<th>Residual amount, g/d</th>
<th>% of total</th>
<th>Vial cytostatic pharmaceutical waste, g/patient/d</th>
<th>Vial cytostatic pharmaceutical waste, g/bed/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interdisciplinary day clinic</td>
<td>5168(1719)</td>
<td>42.0</td>
<td>67(57)</td>
<td>45.3</td>
<td>38(10)</td>
<td>-</td>
</tr>
<tr>
<td>Pathology</td>
<td>3465(1819)</td>
<td>39.5</td>
<td>39(26)</td>
<td>37.4</td>
<td>54(19)</td>
<td>50(26)</td>
</tr>
<tr>
<td>Hematology</td>
<td>877(317)</td>
<td>10.0</td>
<td>9.2(6)</td>
<td>8.7</td>
<td>42(14)</td>
<td>38(14)</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>749(500)</td>
<td>8.5</td>
<td>9(9.2)</td>
<td>8.6</td>
<td>35(22)</td>
<td>34(23)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>8782(4883)</strong></td>
<td><strong>100</strong></td>
<td><strong>105(79)</strong></td>
<td><strong>100.0</strong></td>
<td><strong>41(11)</strong></td>
<td><strong>77(46)</strong></td>
</tr>
</tbody>
</table>

Table 2. Average daily production of syringe cytostatic waste, of residual amount of cytostatic pharmaceuticals and unit production rates by wards/departments of Theagenio Cancer Hospital of Thessaloniki. Numbers in parentheses are standard deviations.

<table>
<thead>
<tr>
<th>Ward/department</th>
<th>Syringe cytostatic waste, g/d</th>
<th>% of total</th>
<th>Residual amount, g/d</th>
<th>% of total</th>
<th>Syringe cytostatic waste, g/patient/d</th>
<th>Syringe cytostatic waste, g/bed/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interdisciplinary day clinic</td>
<td>624(220)</td>
<td>43.3</td>
<td>0.7(2)</td>
<td>15.1</td>
<td>5(2)</td>
<td>-</td>
</tr>
<tr>
<td>Pathology</td>
<td>348(223)</td>
<td>33.8</td>
<td>2(4)</td>
<td>58.1</td>
<td>5.4(2.8)</td>
<td>5(3.2)</td>
</tr>
<tr>
<td>Hematology</td>
<td>140(55)</td>
<td>13.6</td>
<td>0.3(2)</td>
<td>7.6</td>
<td>7(3)</td>
<td>6(2)</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>96(73)</td>
<td>9.3</td>
<td>1(2)</td>
<td>19.2</td>
<td>4.6(3)</td>
<td>4(3)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1029(573)</strong></td>
<td><strong>100</strong></td>
<td><strong>3(6)</strong></td>
<td><strong>100</strong></td>
<td><strong>5(1.5)</strong></td>
<td><strong>9(5)</strong></td>
</tr>
</tbody>
</table>
Table 3. Average daily production of total cytostatic pharmaceutical waste, of residual amount of cytostatic pharmaceuticals and unit production rates by wards/departments of Theagenio Cancer Hospital of Thessaloniki. Numbers in parentheses are standard deviations.

<table>
<thead>
<tr>
<th>Ward/department</th>
<th>Total cytostatic pharmaceutical waste, g/d</th>
<th>% of total</th>
<th>Residual amount, g/d</th>
<th>% of total</th>
<th>Total cytostatic pharmaceutical waste, g/patient/d</th>
<th>Total cytostatic pharmaceutical waste, g/bed/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interdisciplinary day clinic</td>
<td>5792(1882)</td>
<td>42.1</td>
<td>67(58)</td>
<td>44.4</td>
<td>43(11)</td>
<td>No beds</td>
</tr>
<tr>
<td>Pathology</td>
<td>3813(1999)</td>
<td>38.9</td>
<td>41(28)</td>
<td>38.0</td>
<td>59(21)</td>
<td>55(29)</td>
</tr>
<tr>
<td>Hematology</td>
<td>1017(336)</td>
<td>10.4</td>
<td>9(7)</td>
<td>8.7</td>
<td>49(14)</td>
<td>38(29)</td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>845(556)</td>
<td>8.6</td>
<td>9.7(10.2)</td>
<td>8.9</td>
<td>34(29)</td>
<td>38(29)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>9811(5425)</strong></td>
<td><strong>100</strong></td>
<td><strong>109(84)</strong></td>
<td><strong>100</strong></td>
<td><strong>46(12)</strong></td>
<td><strong>86(48)</strong></td>
</tr>
</tbody>
</table>
measurements. This was due to the significant difference in the number of patients and the
quantities of the waste between weekends and weekdays. The linear form of the equation is
\[ y = 59.853x - 1865.8 \]. Both linear parameters are statistically significant at \( \alpha = 0.05 \), since the
respective 95% confidence intervals do not contain zero. In addition, residuals of the linear
model followed an approximately normal distribution with a zero mean, which is a necessary
condition for the model (Berthouex and Brown, 2002). The standard errors of the linear
parameters are 33.6 and 4.9% of the intercept and the slope, respectively.

The regression equation of Figure 1 can be used to calculate the approximate amount of
total cytostatic pharmaceutical waste produced by a hospital for a period of time, when the
number of patients is known. For example, a hospital with 500 patients per day will produce
\[ 1865.8 - (59.85 \times 500 \text{ patients/d}) \times (365 \text{ d/y}) = 10241608 \text{ g/y} \] or approximately 10.2 ton/y of total
cytostatic pharmaceutical waste. From the management point of view, this has to be treated
only by incineration.

In Theagenio Cancer Hospital, cytostatic pharmaceutical waste is source-separated and
ends up in hazardous medical waste with only toxic character waste fraction, which is
subject to incineration.

4. CONCLUSIONS

The following conclusions were drawn about the composition and production rate of
cytostatic pharmaceutical waste from Theagenio Cancer Hospital:

- The main pharmaceutical waste producer at the hospital was Interdisciplinary day
clinic with 42.1% of the total. The smallest producer was Gastroenterology with 8.6
% of the total.
- The unit production rates for total cytostatic pharmaceutical waste for the hospital
were 46 (12) g/patient/d and 86 (48) g/bed/d. The respective unit production rates
were: (1) for vial waste 41 (11) g/patient/d and 77 (46) g/bed/d and (2) for syringe
waste 5 (1.5) g/patient/d and 9 (5) g/bed/d.
- Based on g/patient/d, the larger producer of total cytostatic pharmaceutical waste
was Pathology with unit production rates of 59 (21) g/patient/d and 55 (29) g/bed/d.
while the smallest producer was Gastroenterology with 34 (29) g/patient/d and 38 (25) g/bed/d.

- Statistically significant and strong linear correlation was established between the daily production and the respective number of patients for total cytostatic pharmaceutical waste ($R^2=0.9117$).
- The residual amount of cytostatic pharmaceutical (visually estimated) contained in the vial waste was 96.8 % w/w of the total and in the syringe waste was 3.2% of total residual waste.

REFERENCES