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Dynamics of active pharmaceutical ingredients loads in a Swiss university hospital wastewaters and prediction of the related environmental risk for the aquatic ecosystems

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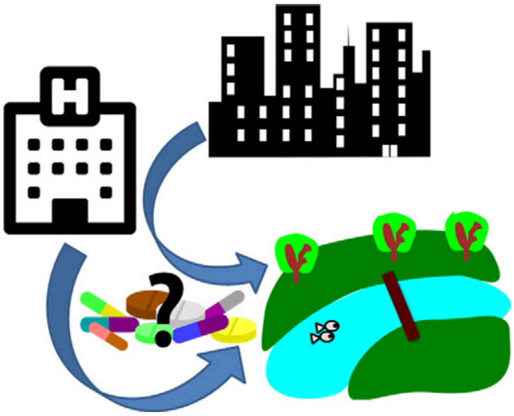
HIGHLIGHTS

- Pharmaceutical residues were studied in Geneva hospital wastewaters, Switzerland.
- Measured concentrations were compared to predictions based on consumption data.
- Risks for the aquatic ecosystems were assessed for hospital and urban contributions.
- The hospital fraction of ciprofloxacin and sulfamethoxazole threatened aquatic life.
- Urban consumption was likely more problematic with 7 risky compounds out of 14.

GRAPHICAL ABSTRACT



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ABSTRACT

The wastewater contamination of a Swiss university hospital by active pharmaceutical ingredient (API) residues was evaluated with a three months monitoring campaign at the outlet of the main building. Flow-proportional samples were collected with an automatic refrigerated sampler and analyzed for 15 API, including antibiotics, analgesics, antiepileptic and anti-inflammatory drugs, by using a validated LC–MS/MS method. The metals Gd and Pt were also analyzed using ICP-MS. Measured concentrations were compared to the predicted ones calculated after the drug average consumption data obtained from the hospital pharmacy. The hospital contribution to the total urban load was calculated according to the consumption data obtained from city pharmacies. Lastly, the environmental hazard and risk quotients (RQ) related to the hospital fraction and the total urban consumption were calculated. Median concentrations of the 15 selected compounds were ranging from 0.04 to 675 μg/L, with a mean detection frequency of 84%. The ratio between predicted and measured environmental concentrations (PEC/MEC) has shown a good accuracy for 5 out of 15 compounds, revealing over- and under-

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PEC
Risk assessment

estimations of the PEC model. Mean daily loads were ranging between 0.01 and 14.2 g/d, with the exception of paracetamol (109.7 g/d). The hospital contribution to the total urban loads varied from 2.1 to 100% according to the compound. While taking into account dilution and removal efficiencies in wastewater treatment plant, only the hospital fraction of the antibiotics ciprofloxacin and sulfamethoxazole showed, respectively, a high ($RQ > 1$) and moderate ($RQ > 0.1$) risk for the aquatic ecosystems. Nevertheless, when considering the total urban consumption, 7 compounds showed potential deleterious effects on aquatic organisms ($RQ > 1$): gabapentin, sulfamethoxazole, ciprofloxacin, piperacillin, ibuprofen, diclofenac and mefenamic acid. In order to reduce inputs of API residues originating from hospitals various solutions can be envisioned. With results of the present study, hospital managers can start handling this important issue.

1. Introduction

Active pharmaceutical ingredients (API) are continuously released into the aquatic environment through urban wastewater treatment plants (WWTP) (Götz et al., 2010; Kümmerer, 2010; Michael et al., 2013). A non-negligible proportion of this point source pollution comes from hospitals and health care facilities, which differentiate itself from domestic ones by the nature of administrated molecules (Kümmerer, 2001; Mullot, 2009), as well as a higher proportion of antibiotic-resistant bacteria (Czekalski et al., 2012; Lyko et al., 2012). In general, the main pharmaceutical classes consumed in hospitals are X-ray contrast media, laxatives, analgesics and anti-inflammatory drugs, as well as antibiotics (McArdell et al., 2011; Le Corre et al., 2012). Other classes of pharmaceuticals mainly administrated at the hospital are of environmental concerns, such as cytostatic agents (Weissbrodt et al., 2009; Ferrando-Climent et al., 2014). On average, hospital contribution represents 10 to 25% of the urban API load found at the watershed outlet (Kümmerer, 2010; Le Corre et al., 2012). But, this fraction can vary from 3 to 74% according to the compound and the hospital beds/inhabitants ratio of the watershed (Santos et al., 2013).

Once in the environment, API residues can cause some adverse effects in wildlife (Fent et al., 2006; Santos et al., 2010). For example, the non-steroidal anti-inflammatory drug (NSAID) diclofenac has been shown to alter the kidney functions in fishes and birds (Oaks et al., 2004; Hoeger et al., 2005). Therefore, environmental risk assessment (ERA) of API is recommended at the pre-commercial stage already (EMEA, 2006). In ERA approach, risk quotients (RQ) are calculated according to the ratio between organisms exposure, by means of predicted or measured environmental concentrations (PEC or MEC), and water quality criteria or potential hazards, usually their predicted no effect concentrations (PNEC) (European Commision, 2003; Cooper et al., 2008). These latter are derived from dose–response curves obtained with ecotoxicological tests, usually performed on the three trophic levels of aquatic ecosystems (algae, daphnia, fish). PNEC values found in the literature are scarce, often modeled, and can vary as much as three orders of magnitude between studies according to test conditions and endpoints (Santos et al., 2010; Helwig et al., 2013).

In Switzerland, several studies have been recently conducted to evaluate the environmental risk (Escher et al., 2011), and the possible treatment options regarding hospital wastewaters (Kovalova et al., 2012, 2013). Concerning API environmental risk assessment, 30–40 API contributed to the mixture risk quotient (Escher et al., 2011). However, this was done based on predicted concentrations, and many uncertainties remained about ecotoxicological data for several compounds. Concerning treatment options, there is still an active debate whether or not a dedicated treatment of the hospital effluents is necessary, and if so which kind of treatment (Verlicchi et al., 2015). In the end, possible options are site-specific and should be evaluated case-by-case (Kümmerer, 2010).

In this context, the present study aimed at evaluating the wastewater contamination of a university hospital in western Switzerland by API residues, as well as the risk for the aquatic ecosystems. A monitoring campaign of 3 months of the main building's sewer was implemented, and the comparison of measured concentrations with predictions based on the pharmaceutical consumption data was performed. Daily loads were calculated based on flow measurements, and the hospital contribution to the total urban load was estimated according to pharmacy sales data. Lastly, the environmental risk of API residues in hospital effluents was assessed based on measurements and PNEC values found in the literature. This work intended to help the hospital managers to find a solution to reduce the inputs of pharmaceutical residues into the urban network and, subsequently, their potential deleterious effects for the aquatic biota.

2. Material and methods

2.1. Study site

The Geneva University Hospitals (HUG) are among the most important hospitals of Switzerland. They comprise eight hospitals and about 40 other health care facilities, providing both primary and tertiary care. In 2014, 9068 full-time equivalent collaborators and a total of 656,598 days of hospitalization were registered, for 1781 beds, and over 960,000 outpatient consultations. Mean daily water consumption was almost 800 m^3/d in 2014, which gives 450 L/bed × day. The effluents of the HUG main site (1200 beds) as well as those of other health care facilities (approx. 300 beds) are ending in the Geneva main WWTP (Fig. 1). This latter can treat wastewaters from 600,000 population equivalent, and discharge up to 2.5 m^3/s wastewaters in the Rhône River. Treatments consist of classic stages of screening, grit and grease removal and primary settling, biological treatment and clarification. Thus, the bed density of the studied catchment is about 3.75 beds/1000 inhabitants.

2.2. Sampling

In most of the studies dealing with APIs in wastewaters, 24 h time-proportional composite samples are reported, where a flow-proportional sampling is desirable, especially in the case of hospital effluents (Weissbrodt et al., 2009; Ort et al., 2010). Thus, the sewer pipe of the HUG main building (741 beds) was equipped with a sharp-crested rectangular weir for the flow rate determination. An ultrasonic flow meter device (ISCO 4210) was installed upstream of this latter, and the wastewater height measurements was done every 2 min and checked for accuracy at least every 2 weeks. The flow rate was then calculated according to the Kindsvater–Carter equation (Kindsvater and Carter, 1959):

$$Q = C_e \, \frac{2}{3} \sqrt{2g} \, b_e \, (h_e)^{3/2} \qquad (1)$$

where Q = discharge [m^3/s], C_e = discharge coefficient [$m^{1/2}/s$], g = acceleration of gravity [m/s^2], b_e = effective width [m], h_e = effective height [m].

The uncertainty with this kind of measurements was estimated at 5% by the metrology section of the Water Ecology Service of the Geneva State (SECOE-GE). It is worth to stress that rain water contributes to the waste water flow as roof gutters are not connected to separate