Wastewater-based epidemiology biomarkers: Past, present and future

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A B S T R A C T

Wastewater is a complex matrix containing a wide range of chemical and biological markers of human activity. Relating concentrations of these “waste” materials in wastewater influent streams to population-scale use, consumption, or rates of exposure, can provide important qualitative or quantitative information on the activity of inhabitants within a given wastewater catchment. Many publications in this field of study have focussed on the usage of pharmaceuticals, illicit drugs, tobacco and alcohol. However, many other potential applications are emerging which can contribute useful knowledge on human health, exposure to industrial chemicals, infectious diseases or pathogens and antibiotic resistance. This review summarises the established wastewater based epidemiology (WBE) biomarkers, and presents a critical review of the current capabilities of WBE. We further discuss possible future strategies and challenges anticipated in analysing wastewater to measure chemical markers of population health as well as biological markers of microbial exposure and disease.

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1. Introduction

The analysis of wastewater for concentrations of human-use substances, pharmaceuticals, chemicals, exogenous contaminants, and nutrient concentrations has been employed for decades. The main focus of analyses has generally been to determine substance concentrations entering the wastewater treatment process, to monitor removal efficiencies of wastewater treatment processes, and to evaluate wastewater effluent as a point source for environmental contamination. More recently, Wastewater-Based Epidemiology (WBE), defined here as the normalisation of analyte concentration to per capita mass loads using the daily flow and wastewater treatment plant (WWTP) population, provides population-scale information on human activity within catchment boundaries. This allows for community-level assessments on per-capita consumption, use, exposure, or release of chemical or biological agents. Therefore, the amount of a target chemical or biological agent in the wastewater stream can provide qualitative or quantitative information on the total and mean population exposure to the agent in a given sewer catchment. Assessments of spatial or temporal trends, or response(s) to events within catchments can also be conducted. The method is non-invasive and is done on a population-scale level, so individuals are not targeted and privacy is respected [1]. In addition, the population normalisation of data allows for direct comparisons to be made between catchments of different population sizes.

After entering the sewer network, these excreted agents arrive at a wastewater treatment plant (WWTP) where wastewater samples can be collected over a defined sampling period, Fig. 1. To obtain a quantitative estimate of a given agent with WBE, representative samples are collected over a given period (typically 24 h) using autosamplers that collect time or flow proportional samples of wastewater entering the WWTP [3]. One important consideration in WBE studies is the solubility and partitioning of analytes of interest into the aqueous phase, which allows for adequate and representative sampling within wastewater samples. For small molecules such as drugs, per capita daily consumption of a parent compound in a given catchment is calculated using an equation such as Equation (1) [4].
Daily chemical consumption of drug residue $i$ can be estimated by the formula:

$$\frac{\text{mass}}{\text{day per 1000 people}} = \frac{C_i \cdot F \cdot R_i}{P} \quad (1)$$

where, $C_i$ is the concentration of a given drug residue $i$ (parent drug or metabolite) measured in raw wastewater samples, $F$ is the total wastewater volume during the sampling period (typically 24 h), $P$ is the number of people in the catchment, $R_i$ is the ratio of molar mass of parent drug to its metabolite and $E_i$ is the average excretion rate of a drug residue $i$.

Compared to wastewater analysis, WBE is a relatively young and growing field with new advancements being made continuously, as evidenced by the growing number of new publications in this field (Fig. 2). A number of recently published reviews also summarise important advancements in aspects of the field, in terms of specific biomarkers [5–7] or analytical techniques and challenges [8,9]. The present review focuses on WBE studies, critically presenting progress made to date, and offers insights into new areas where WBE could be applied in future and shows explorative promise, such as pathogen and health indicator monitoring.

2. Illicit and licit drugs

Drugs can be broken down into several groupings and classes, including licit and illicit substances. Here, we briefly summarise the previous and ongoing WBE efforts. Each class will be discussed in turn, beginning with the illicit drugs: established stimulants, heroin, cannabis, ketamine, and finally, the New Psychoactive Substances (NPS). A more comprehensive list of biomarkers can be found in SI1.

2.1. Illicit drugs

2.1.1. “Established” drugs — MDMA, methamphetamine, amphetamine, cocaine

Methamphetamine, MDMA (3,4-methylenedioxymethamphetamine), and cocaine have been widely analysed in WBE since the key studies in the field were published in 2005 and 2008 [4,10]. Subsequently, hundreds of publications have focussed on illicit drug use due to their ubiquitous prevalence across the globe. MDMA and methamphetamine have been predominantly monitored through their parent drugs, and not their metabolites. This is mainly driven by the high elimination of the parent drugs in urine, and the non-selective nature of many of the dominant metabolites. For example, methamphetamine also metabolises to amphetamine, and so confounds amphetamine load estimates. Therefore in regions where methamphetamine consumption is much higher than amphetamine (e.g. Australia, United States of America, and some Eastern European countries), estimating consumption of amphetamine can be problematic due to the contribution from methamphetamine metabolism, whereas for areas where methamphetamine consumption is low to non-existent (e.g. much of Western Europe), then the effect is not as pronounced [2]. Similarly, MDMA metabolises to MDA (3,4-methylenedioxyamphetamine), an illicit drug in its own right,
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