

Toxidromes and multimorbidity: Do we need more case reports?

Salvatore Greco, Alfredo De Giorgi, Fabio Fabbian

One of the most frequent causes of accidental death is poisoning, and it is frequently ascribed to pharmaceutical agents. Already Paracelsus, in the 16th century, stated that the difference between remedy and medicine was the dose (“All things are poison, and nothing is without poison; the dosage alone makes it so a thing is not a poison”). However, some drugs could become dangerous even at therapeutic dose, depending on patient’s clinical conditions and on the interactions with different molecules.

“Drug abuse” is a common medical condition involving a high percentage of the world population. It was estimated that a quarter of a billion people, or around 5% of the global adult population, used drugs at least once in 2015 [1]. The most abused substances are alcohol, opioids, cannabinoids, sedative-hypnotics, cocaine, and many other stimulants such as caffeine, hallucinogens, tobacco, and volatile solvents. Not all these substances are equally harmful and many of them have different “harm ratings” to users themselves and/or to third persons [2].

The term “drug abuse” is still of common use, even if it is no longer considered a medical diagnosis in both the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (DSM), and the World Health Organization’s International Statistical Classification of Diseases (ICD), the most used diagnostic tools in the world. The DSM-5, released in 2013, revisited the terminology, and both the terms “substance abuse” and “substance dependence” were merged into the bigger

category of “substance use disorders,” with three different degrees of severity: mild, moderate, and severe.

It is to remember as well that the term “drug abuse” does not have to be confused with “drug misuse,” defined as the use of a substance not consistent with legal or medical guidelines and may lead to drug dependence [3] or to harmful behaviors [4].

The effects on the central nervous system and autonomic nervous system by such substances could be depression or stimulation [5]. In 2015, The American College of Medical Toxicology published data from their registry and showed that an intentional pharmaceutical exposure was the most frequent reason for medical consultation (more than 52%) and the 69% of such events represented an attempt at self-harm; in particular, 85.6% of these self-harmful attempts were suicide attempts. Non-opioid analgesics, sedative-hypnotics, and antidepressant agents were the agents most frequently reported, and about one-third of cases involved a diagnosed toxidrome (a portmanteau of “toxic” and “syndrome”), with sedative-hypnotic toxidromes being the most frequently described. Fatalities involved 1.2% of cases, while adverse drug reactions 4.3%. More than 65% of cases received a toxicological treatment and one in three patients was treated with specific antidotal therapy [6].

Several drugs such as acetaminophen, anesthetics and some cardiotoxins, β -adrenergic blockers, calcium channel blockers, digitalis glycosides, iron, isoniazid, methotrexate, neuroleptics, sulfonyleureas, insulin, tricyclic antidepressants (and related compounds with sodium channel blocking properties), valproic acid, anticoagulants could be the cause of toxidromes [7, 8].

In many cases, to better evaluate toxicity it is necessary to contemplate the renal function. Pharmacotherapy and toxicology should be, in fact, classified on the base of kidney physiology and nephrologists should be consulted also considering the utility of dialysis and extracorporeal therapies in the treatment of poisoned patients [9, 10].

Modern medicine is complicated by multimorbidity and this is among the major determinants of outcome in admitted patients [11]. Physicians must be trained in the recognition of those symptoms related to poisoning, especially in aged subjects with

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multimorbidity. Furthermore, the presence of a high load of multimorbidity is associated with polypharmacy: this could favor, through the interaction of many molecules, the development of drug toxicity [12]. Confounding factors, such as multimorbidity itself and interfering drugs, should be taken into consideration; heart and respiratory rate, blood pressure, body temperature, and mental status could be altered both by clinical conditions and drugs.

In complicated patients, performances could depend on the time spent in the analysis of their clinical case: in such cases, sharing the experience with qualified colleagues could be helpful. Drug over dosage in general, intentional, or unintentional, is a clinical challenge made more difficult by the possible multi-organ complications in comorbid patients.

Financial, psychological, and social factors should be always taken into account when evaluating a patient with drug abuse and this often leads to the need for a multi-disciplinary approach; besides this, age and multimorbidity represent unchangeable risk factors for a worse outcome.

The current literature does not dedicate much attention to the relationships existing between toxidromes and multimorbidity. An interesting retrospective study by Mühlberg et al. on 5883 patients reported higher mortality rates in the elderly patients (2.17% vs. 0.24%), with age and ingestion of multiple drugs, found to be strongly associated with mortality and prolonged stay in the Intensive Care Units after acute poisoning [13]. A more recent work on 156 subjects by a group of Indian researchers, focused on aged patients with a recent history of acute poisoning, showed high mortality rates (16.9% overall mortality), more often consequent to systemic shock, aspiration pneumonia, and acute liver injury [14].

In conclusion, we think that sharing different practical experiences between healthcare professionals plays a role of primary importance in the everyday clinical practice, and it allows both the growth of the entire scientific community and a better approach to patients. This is even more important in case of complex comorbid and pharmacologically multi-treated patients, regardless of the drugs involved.

Keywords: Drug misuse, Multimorbidity, Substance use disorders, Toxidromes

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Salvatore Greco – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Alfredo De Giorgi – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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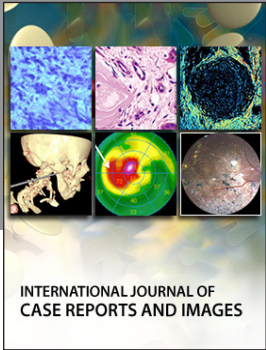
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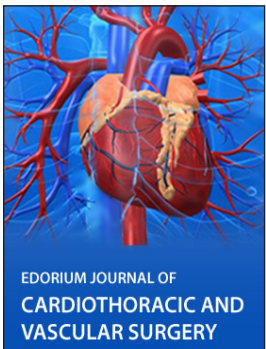
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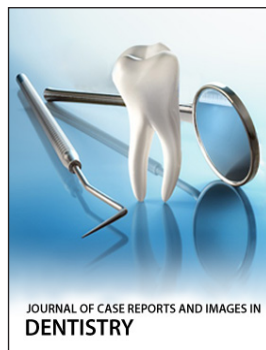
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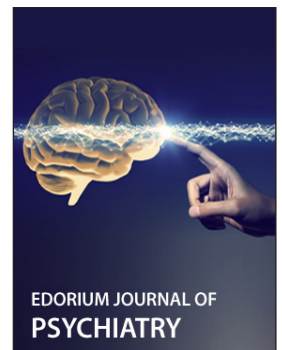
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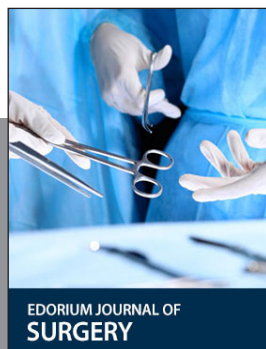
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