

A Rare Case of Intravenous Metamizole Abuse



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SUMMARY

Given the very frequent prescription of non-opioid analgesics (NOA), their dependence potential has been a subject of research. Increased use of NOA in the last decade has led authors to publish case reports to describe the dependence potential of these agents. Metamizole (dipyrone) has become one of the most popular NOA agents, in being easily accessible and inexpensive. Its analgesic effect depends on the central inhibition of cyclo-oxygenase (COX-3) and activation of the opioidergic and cannabinoid systems. Recent research has also stressed its possible anxiolytic effects. Our Literature search indicated no previous reports regarding metamizole misuse.

Case of a 41 year old female patient is presented. She had self administered increasing doses of i.v. metamizole reaching up to 10 ampules per day. Considering the risk of mortality due to the metamizole's side effect of agranulocytosis, we thought that it could be a significant contribution to the literature to present a case of a possible metamizole abuse.

Keywords: Metamizole, abuse, dependence

INTRODUCTION

Given the very frequent prescription of non-opioid analgesics (NOA), their potential for causing user dependence has been the subject of research. With the increased use of NOA in the last decade, case reports are being presented in the literature in order to meet the need for detailed information on the potential of these agents for causing dependence (Bonnet et al. 2019).

Metamizole (dipyrone), the 4-methylaminomethanesulfonate sodium derivative of aminopurine, is the most popular agent among the NOA available. Being water soluble, it is suitable for injection after administration, the prodrug breaks down to biologically active and non-active antipyrenes (Brodgen 1986, Hintz et al. 2007). The persistent classification of metamizole as a non-steroidal anti-inflammatory drug (NSAID) has been opposed by many authors (Lorenzetti et al. 1985, Jaseicka et al. 2014).

The analgesic effect of metamizole is known to depend on central inhibition of the cyclo-oxygenase (COX-3) and activation of the opioidergic and cannabinoid systems. (Chandrasekharan et al. 2002, Munoz et al. 2010), The most serious adverse side effect of the drug is agranulocytosis due to its myelotoxic effects. For this reason, its use without

indication or abuse can present significant risks for human health (Jaseicka et al. 2014).

Considering the argument by Bonnet et al. (2019) in their report of the study on NOA dependence that metamizole abuse should be further studied to meet the need for data, we decided to present this case report. Literature scan indicated that metamizole abuse had not been reported previously.

CASE

The 41-year-old divorced mother of one, employed in shift work, consulted the outpatient clinic declaring that she used metamizole continually for pain relief and wished to be hospitalized for treatment. The patient admitted using up to 10 ampoules (10 x 2500 mg of metamizole per ampule) daily. After the required investigations she was admitted as an inpatient for treatment of metamizole misuse. The patient reported that 2 years previously she had been diagnosed with "chronic interstitial cystitis" and had started using metamizole on account of the pain and the fatigue caused by the working conditions of the time. After 2 months of starting on metamizole, the inadequate effect of a single ampule caused her to use 1 ampule before and 1 ampule after each 24-hour work shift, which relieved her pain and induced sleep. Within

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this period, she was diagnosed with major depressive disorder after consulting the psychiatry outpatient clinic and was started on venlafaxine treatment which she had been satisfied with. She expressed that the purpose of consulting the hospital was for the treatment of her drug dependence since in the 1-week period before hospitalization, she had maintained an open vein and self injected 10 ampules of metamizole per day.

In her psychiatric examination, the patient's appearance was compatible with her age and socioeconomic status. She did not have any visible physical defects. She was totally conscious with normal orientation, attention and psychomotor activity, speech, perception and memory. She was cooperative, comfortable in expressing herself and willing to tell her story with a tendency to weep in reference to her ex-husband. She had euthymic mood and broad affect. Pathology was not detected in her thought contents, associations and judgement. Her intelligence was clinically normal and she had insight. In the psychophysiological analysis, it was found that her sleep had decreased, her appetite had partially increased, and her libido was normal. She did not have a history of smoking, alcohol or other substance use.

After being discharged from the hospital, the patient was weekly followed up with venlafaxine (150 mg/day) treatment. When the patient stated that she did not use or abuse any pain relief agent after being discharged from the hospital, she was followed up with a routine of monthly controls.

DISCUSSION

The case was defined as “metamizole abuse” due to the increasing use of metamizole, daily repeated administration of the drug leading to problems at work and interpersonal relations, developing tolerance to the drug, and having withdrawal symptoms when not using it. Although metamizole use is prohibited Australia, Japan, United States of America, and 30 other countries on grounds of the risk of developing agranulocytosis. it is still widely used in the rest of the world to relieve pain and spasms and to reduce fever (Bonnet 2019). Since NSAIDs have hepatotoxic effects, metamizole is still widely used for pain control in elderly patients in Germany (Bonnet 2019). Since metamizole was easily accessible, our patient used this agent for many weeks, initially orally and later by i.v. administration at dosages above the therapeutic dose.

NOA dependence was determined in 124 out of 400 elderly individuals with the report of a “surprise finding” of “metamizole de novo addiction” in two patients without any previously known addictions. It was also stated that metamizole addiction had not been investigated previously (Bonnet et al. 2019). It is possible to say that there was a high incidence of NSAID abuse in these cases.

Research has shown that metamizole reduces glutamate-induced hyperalgesia. Metamizole, believed to have a low potential for addiction, cannot be expected to cause severe euphoria even if used at doses higher than therapeutic doses. The case of the patient discussed here is an example of psychological addiction. Although more research is required on the subject, metamizole addiction is not a common NOA addiction in everyday life (Bonnet and Scherbaum 2017).

Metamizole (dipyrone) is found similar to paracetamol in not having a strong effect on COX enzyme activity. Dipyrone efficacy in the central nervous system has been the subject of research for many years. Currently it is known that dipyrone affects central structures such as the periaqueductal grey matter, rostral ventromedial medulla, and the spinal cord, leading to the release of endogenous opioids and activation of the descending inhibitory pathways. In one of the recent studies on mice, dipyrone was found to produce anxiolytic-like effects (Topuz et al. 2019). It may be this anxiolytic activity that prepares the basis for abuse.

The most serious side effect of metamizole abuse is agranulocytosis that presents as an outcome of its myelotoxic effects. Therefore, its use without indication or abuse can be risky for human health (Jaseicka et al. 2014). In our patient haemogram data did not indicate haematological pathology.

In conclusion, given the particulars of the case presented here, it would be necessary to suspect the risk of abuse in patients known to be under regular NOA therapy.

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