Gaïes et al., J Clinic Case Reports 2012, 2:4
DOI: 10.4172/2165-7920.1000112

Journal of Clinical Case Reports

Case Report Open Access

Caffeine Medication Error in Newborn Inducing Therapeutic Inefficiency: A Case Report

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Keywords: Caffeine; Medication error; Therapeutic inefficiency; Therapeutic drug monitoring

Introduction

Caffeine citrate is commonly used for prophylaxis and treatment of apnea in preterm babies [1,2]. Its pharmaceutical form is presented as a solution used intravenously and orally. In clinical use, caffeine citrate needs generally a dilution protocol to be administrated in newborns. Such calculating may increase the risk of medication errors and so the risk of toxic side effects or therapeutic inefficiency. Medication errors inducing toxicity are frequently reported in pediatric inpatients [3,4] but therapeutic inefficiency seems to be not described.

We report a case of therapeutic inefficiency due to a medication error in caffeine dilution and illustrated by caffeine plasma monitoring.

Case Report

T. O. a premature baby was born at 25 weeks of gestation. Apgar was 7 in the first, fifth and tenth minute. For apnea and bronchopulmonary dysplasia, he was treated with a caffeine citrate loading dose 20 mg/kg/d and orally maintained dose of 5 mg/kg/d. He also received domperidone, omeprazole, alginates, valproic acid, vitamin E and ergocalciferol. Three months after the begining of caffeine, the newborn did not improve and continued to have apnea. Thus monitoring of caffeine has been required. Plasma levels measured by High Performance Liquid Chromatography (HPLC) showed a null concentration. After checking the team of neonatology, we found an error in the caffeine dilution protocol. In fact, the 2 ml flacon is dosed at 25 mg of caffeine base that corresponds to 50 mg of citrate caffeine. The 2 ml flacon must be diluted in 25 ml of saline to have a caffeine base concentration of 1 mg/ml, but the nurse added 50 ml of saline instead of 25 ml. So the newborn received the half dose (5 mg / day instead of 10 mg / day) during the three months.

Five days after the correction of the dilution error, another dosage of plasma caffeine level was done and the caffeine concentration is increased to 3,35 µg/ml.

Results and Discussion

Medication errors are defined as errors in medication ordering, transcribing, dispensing, administering or monitoring [5].

Newborns and children are at a greater risk than adults for medication errors because of their physiological immaturity and their difficulty to communicate. In an other hand the majority of medications are developed in concentrations appropriate for adults. We need so to calculate the appropriate dose to the weight or to the body surface area.

In addition, neonates have a rapidly changing body weight, a rapidly development of the drugs absorption system, metabolism and excretion [6].

In our case the newborn received caffeine which is a drug characterized by an important pharmacokinetics variability in the premature babies. It has been described previously that the elimination of caffeine from the blood of neonates is lower compared to adults with a blood half life averaging 100 hours [7,8]. Caffeine dilution protocol was also needed in our case to administrate the appropriate dose to the weight. For this reason the dose necessary to maintain caffeine plasma concentration at the therapeutic range (8-14 mg/l) varies remarkably and requires adjustment by the measurement of caffeine plasma levels if maintenance therapy is needed [9].

Medication errors leading to an overdose and toxicity side effects are frequently reported in literature. These errors are potentially dangerous as wrong calculation can result in a dose upto 10 times higher than necessary. This can cause serious toxicity, even death, especially when medication agents have a narrow therapeutic range [3].

The drug classes associated most frequently with errors were anti-infectives, electrolytes, fluids, analgesics and sedatives [4].

Our case is different with those described in litérature because the newborn did not present toxicity side effects but inefficency due to a medication error. Inefficiency is also threatening. In fact, it can prolonged the patient hospitalisation, increased health-care costs and, in sometimes can cause loss of confidence in the health-care system [10,11].

Despite the lack of improvement and the narrow therapeutic range of caffeine, plasma levels were done three months after the bigining of the treatment. In fact, some clinicians are not enough sensibilized for caffeine monitoring. They continue to give caffeine empirically and they have thought to monitoring only at the persistance of inefficiency.

Medication errors inducing inefficiency should be considered at the same order as errors inducing toxicity side effects. In fact, they seems under estimated because of the diagnosis difficulty. So it is necessary to check systemically these errors and to evaluate their frequency and therapeutic drug monitoring represent in some cases a solution to reduce medication errors and to verify adherence to treatment.

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Received December 19, 2011; **Accepted** February 22, 2012; **Published** February 27, 2012

Citation: Gaïes E, Sahnoun R, Jebabli N, Trabelsi S, Salouage I, et al. (2012) Caffeine Medication Error in Newborn Inducing Therapeutic Inefficiency: A Case Report. J Clinic Case Reports 2:112. doi:10.4172/2165-7920.1000112

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