Therapeutic Drug Monitoring of caffeine in preterm neonates

Sint Franciscus Gasthuis

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INTRODUCTION

The methylxanthine caffeine decreases the frequency of apnea in prematurity and the need for mechanical ventilation. The pharmacokinetics of caffeine in neonates shows interindividual and intraindividual variability. Therefore therapeutic drug monitoring (TDM) of caffeine is used to optimise individual dosing to prevent toxicity and treatment failure. Because blood sampling is an invasive procedure, the question arises whether routine drug monitoring is necessary.

In a literature review there is no indication found for routine TDM for caffeine. The main reason to perform TDM is a relation between serum level and clinical effect. For caffeine this relationship is limited, due to intra- and interday variability. When using standard dosages the risk of toxic caffeine is low.

PURPOSE

Since routine TDM is still advised in our setting. We wanted to evaluate the caffeine levels found in preterm neonates.

METHODS

A retrospective study was conducted at Sint Franciscus Gasthuis, Rotterdam, The Netherlands. Preterm neonates treated with caffeine were identified in the period January 2008 until June 2010. Patients with at least one plasma caffeine level were included. The medical charts of preterm neonates with a caffeine level > 30 mg/ml were screened for adverse events.

RESULTS

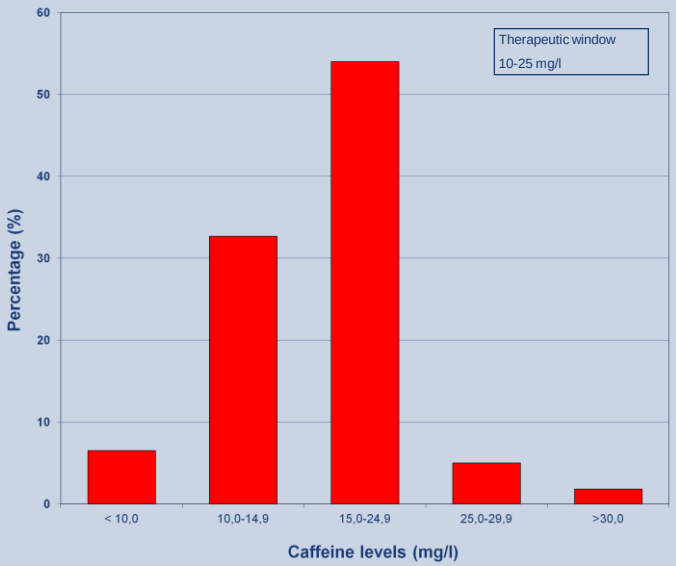

Figure 1: Caffeine levels measured during routine TDM

CONCLUSION

The majority of preterm neonates attain plasma levels between 5 and 25 mg/l using a standard caffeine dosage. In the subgroup of patients with serumlevels > 30 mg/l only one adverse event was recorded. Based on these results routine TDM is not longer advocated in our setting.

RESULTS

A total of 601 caffeine plasma levels were measured in 149 patients. The average dosage was an induction dose of 20 mg/kg caffeine citrate and a maintenance dose of 10 mg/kg/day.

In the subgroup of 11 patients with a plasma level > 30 mg/l, in two patients an adverse event was recorded. In one patient tachycardia and feeding intolerance was observed and in a second patients a limited growth was seen.

Table 1. Patients with caffeine levels > 30 mg/l

Age* (weeks)	Dose /kg	Level (mg/l)	Action	Adverse events
32+1	5.5	35,7	Skip 2 dosages and decrease dosage	tachycardia, feeding intolerance
31+0	4.7	33,7	Continue dosage	-
31+6	4.8	37,2	Continue dosage	-
31+1	6.0	32,4	Skip 1 dosage and decrease dosage	-
31+1	4.3	30,2	Continue dosage	-
30+4	5.3	32,0	Continue dosage	-
31+3	4.9	37,4	Decrease dosage	Growth failure
32+2	3.7	32,4	Continue dosage	-
30+1	5.2	32,4	Skip 1 dosage	-
31+3	5.2	34,5	Skip 1 dosage and decrease dosage	-
30+5	5.7	33,3	Skip 1 dosage	-

** gestational age (weeks)*

DISCUSSION

In our retrospective study the majority of serum levels are within the therapeutic window and only one adverse event was registered. When a high serum level was found, no action was undertaken for half of the patients in scope for the study.

Although this is a retrospectively conducted research, a large number of serum levels are evaluated and the results found are consistent with the literature. Based on these results routine TDM of caffeine is no longer advocated in our clinic.

References:

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