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Case Series

Planning, Scheduling and Period of Drug Vulnerability Impact Pharmacodynamics Result throughout Morphogenesis

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Abstract

When nutrients and drugs share the same absorption and disposition mechanisms, significant interactions between the two substances can occur. Because these processes undergo ontogenesis throughout the postnatal period, the outcomes of drug-nutrient interactions may change with postnatal age during development. Cefepime-carnitine, a significant drug-nutrient interaction, was found to be dependent on drug exposure timing and duration in relation to postnatal age in our study. Cefepime (5 mg/kg) was given to rat pups twice daily by subcutaneous injection on various dosing schedules. In the postnatal day 1-4, 1-8, and 8-11 groups, cefepime caused severe degenerative changes in the ventricular myocardium and significantly reduced serum and heart L-carnitine levels. Additionally, the ontogeny of a number of important L-carnitine homeostasis pathways was altered by cefepime. The time and duration of exposure to cefepime affected the qualitative and quantitative changes in hepatic -butyrobetaine hydroxylase mRNA and activity, hepatic trimethyllysine hydroxlase mRNA, intestinal organic cation/carnitine transporter (Octn) mRNA, and renal Octn2 mRNA. With cefepime exposure, all treatment groups maintained the same levels of ATP, carnitine palmitoyltransferase mRNA and activity, heart Octn2 mRNA, and lower levels of heart L-carnitine. However, rats with normal serum L-carnitine levels showed changes in other high energy phosphate substrates and decreased phosphocreatine/ATP ratios. In conclusion, our findings point to a significant drug-nutrient transport interaction in developing neonates, whose nature is affected by exposure timing and duration in relation to postnatal age.

Keywords: Drug-nutrient interaction, Ontogeny, L-carnitine, Cefepime

INTRODUCTION

Early postnatal life is a particularly vulnerable time for salutary changes that may have a long- term impact on a person's health and may affect growing biochemical and physiological processes (Chang RL et al., 1975). Depending on factors like the stage of physiological development, the duration of the nutritive revision, and whether the revision occurs during a critical window of vulnerability, developing individualities can acclimatize to nutritive changes to favour survival. These acclimations can be subtle or egregious, and they can be temporary or endless. Pharmacological interventions are constantly needed to lessen the burden of complaint- associated morbidity and mortality in babe who come ill. Limited exploration has examined the goods of pharmacological interventions on the developing bambino, particularly when medicines impact the vacuity of nutrients in the body, despite the wide recognition that medicine use may affect normal physiological system development. Postnatal ontogenesis may be significant for nutrient homeostasis pathways and medicine pharmacokinetics processes in new born (Takakura Y et al., 1990). A significant medicine- nutrient commerce during postnatal development is possible, and this commerce could affect the ontogeny of these pathways when a medicine and nutrient par take the same immersion and/ or disposition

medium. These goods may be temporary, when the normal inheritable programming is restored after the medicine exposure is removed, or they may be endless, when the medicine exposure occurs during a critical vulnerability window. Since the maturity of studies on medicine-nutrient relations concentrate on the effect of nutrients on medicine pharmacokinetics and/ or pharmacodynamics in adult populations, it's largely academic whether similar changes are possible. The impact of medicines on nutrient homeostasis (Yamamoto et al., 2003) (Kaneda Y et al., 2004)

DISCUSSION

A process (either for distribution or elimination from the body) that's constantly participated by both a medicine and a nutrient is the transport of substrates across epithelial walls into and out of cell and cellular organelles via a transport prot. In order to make nutrients available to the physiological system and maintain nutrient homeostasis, transport systems are particularly important (Tsunoda S wet al., 2000) medicine remedy in the bambino may affect in implicit reversible relations between a medicine and a nutrient that may alter the developing existent's nutrient immersion and disposition (and vice versa) when a transporter mediates both medicine and nutrient transport across membranes. There's presently a lack of information regarding the implicit troubles of medicine-nutrient relations at transport systems that may alter the nutritive status of the invigorated. In addition, the significance of an implicit medicine- nutrient transporter commerce in a invigorated case may change grounded on the magnitude, duration, and timing of a medicine exposure during postnatal development. When the affected nutrient is essential for neonatal development, these factors may affect in distinct adaptive strategies to optimize nutrient homeostasis in an invigorated and, as a result, significant changes in neonatal development. The question of whether pharmacological interventions in the bambino can alter the growing biochemical and physiological processes involved in medicine immersion/ disposition processes and nutrient homeostasis is thus an important bone (Cicek H et al., 2005)

We used the conditionally essential nutrient L- carnitine and the- lactam antibiotic cefepime in a evidence- of-conception study because both are known to be substrates for L- carnitine transporters that are expressed at epithelial walls and cellular membranes. Normal mitochondrial and epithelial/ endothelial functions, which are essential for normal neonatal growth and development, bear L- carnitine situations to be maintained. The major pathways that are involved in L- carnitine homeostasis suffer significant ontogenesis after birth 3 L- carnitine homeostasis is particularly dependent on the organic cation/ carnitine transporter 2(Octn2). A wide range of therapeutically used cationic medicines, similar as- lactam antibiotics, are included in Octns' substrate particularity. Significant competitive relations between these specifics and L-carnitine have been set up in both in vivo and in vitro studies We used the known L- carnitine and cefepime competitive transporter commerce as the underpinning premise to a significant medicine- nutrient commerce in the bambino to identify possible differences in the ontogeny of L- carnitine homeostasis pathways in recognition of the lack of information regarding medicine- nutrient relations in the early postnatal period (Mi FL et al., 2002). Also, we delved whether the timing and duration of medicine exposure in relation to postnatal development are related to the implicit goods of this medicine- nutrient transporter commerce. Our study's overall thing was to demonstrate for the first time experimentally that significant medicine- nutrient transporter commerce during postnatal development alters the ontogeny of nutrient homeostasis pathways. As a result of our study's design, we were unfit to determine whether these changes were simply temporary or on- going. This would be the focus of posterior exploration. For numerous physiological and biochemical processes considerable development of these processes continues throughout neonatal development. In the rat, numerous factors involved in the L- carnitine homeostasis pathway suffer significant ontogeny in the period from birth to weaning (handwriting in medication). In this study, treatment of rat pups with cefepime, a given asset of L- carnitine transport, altered colourful L- carnitine homeostasis mechanisms during postnatal development. The qualitative and quantitative changes in these pathways depended upon when during postnatal development the bambino was exposed to the medicine, as well as to the duration of the exposure. still, despite compensatory changes in renal and intestinal L-carnitine transport systems, rat pups treated at postnatal day 1- 4, 1- 8 and 8- 11 couldn't maintain serum and heart L- carnitine attention at situations associated with their undressed counterparts. As well, these pups showed more severe histopathological changes in the heart relative to their undressed counterparts and to aged treated pups. These data suggest that although youthful babes have the capability to mount an adaptive response to exogenous factors that impact nutrient status, this adaptive response may not be sufficient depending upon the magnitude of the environmental personality (Zhang Y et al., 2002). Our data also generally showed that babes exposed to cefepime latterly in postnatal development or throughout the postnatal period sounded to mount an adaptive response that was sufficient to maintain serum and towel L- carnitine situations and help pathological changes in the heart (Abraham GA et al., 2003) (Calandrelli L et al., 2002)

CONCLUSION

It appeared that exposure duration and timing relative to postnatal maturation influenced the qualitative and quantitative changes in these L-carnitine homeostasis pathways; however, it is unknown whether these changes are permanent. Following a cefepime-L-carnitine interaction, it is anticipated that subsequent studies will

examine the potential for metabolic programming of L-carnitine homeostasis mechanisms as well as the long-term effects of this interaction on the risk of disease in later life. Nevertheless, our findings highlight the potential requirement for nutritional interventions during drug therapy in this population and could have significant repercussions for the treatment of paediatric patients, particularly new born.

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CONFLICT OF INTEREST

None

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