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The importance of the formulation in the effectiveness of Coenzyme Q10 supplementation in mitochondrial disease therapy

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ABSTRACT

This report describes the response of a patient treated with two different coenzyme Q10 extemporaneous pharmaceutical formulations that generated radical changes in her symptoms and life quality. It could explain why in some cases therapy with coenzyme Q10 does not work in patients with deficiency of this coenzyme. It is important that the scientific community dedicated to the area of health be aware and mindful of differences that can occur in extemporaneous preparations which are not as strict at the time of development and control as in pharmaceutical industry. The aim of this study was to demonstrate the need for extreme control in the coenzyme Q10 formulation administered to patients.

Keywords: Coenzyme Q10, formulation, mitochondrial disease

INTRODUCTION

Mitochondrial diseases are disorders caused by impairment in any of the numerous mitochondrial pathways including the mutation in Coenzyme Q10 (CoQ10) biosynthetic genes producing a primary CoQ10 deficiency [1]. It is known that primary CoQ10 deficiencies are the only treatable disorders since patients respond to oral CoQ10 supplementation with a remarkable improving of their life quality and a delay or interruption in the progress of the disease [2].

One major issue concerning to the use of CoQ10 in therapy is their potential efficacy, mainly determined by its absorption/bioavailability proprieties in the different formulations currently administered [3]. CoQ10 is a crystalline powder, insoluble in water, with high hydrophobicity (log P>10), and therefore, poorly absorbed by the organism. Since CoQ10 has a rather complex chemical structure, its formulation must be prepared with special care in order to obtain a product with acceptable bioavailability and efficacy [4]. Besides bioavailability of drug product can be altered by drug and excipients properties in the formulation and manufacturing process [5]. Unfortunately, in the case of extemporaneous pharmaceutical formulations, there is no consensus in their preparation and each pharmacist can prepare formulations “as art” in an unruled way. This report describes the response of a patient treated with two different CoQ10 extemporaneous pharmaceutical formulations that generated radical changes in her symptoms and life quality. The aim of this study was to demonstrate the need for extreme control in the CoQ10 formulation administered to patients.

MATERIALS AND METHODS

The patient (female, 65 kg body weight) disclosed clinical symptoms of mitochondrial disease at 16 years old with periods of amnesia, progressive muscular degeneration, difficulty to swallow, some episodes of epilepsy and mild mental retardation.

A treatment with 400 mg CoQ10/day (divided into 4 daily doses) was initiated showing an improvement of her neurologic and muscular condition.

The patient was treated for six months with a formulation containing: crystalline CoQ10 (50 mg) and lactose (300 mg) per capsule (treatment 1). At the seventh month, the patient began to be treated with a new lower-cost formulation prepared in another pharmacy containing: crystalline CoQ10 (50 mg), lactose (300 mg) and polyvinyl pirrolidone (PVP) (7 mg) per capsule (treatment 2). After a few days of treatment 2 the symptoms of mitochondrial disease returned. The label content of CoQ10 in both formulations and a blood sample after 1 month following both treatments were analyzed for comparative purposes of absorption/bioavailability by HPLC-UV method previously described [6].

Both capsules showed similar content in good agreement with the labeled values.

However, significative differences were observed in CoQ10 plasma concentration after1 month of both treatments (table1).

When PVP was added to CoQ10, the plasma CoQ10 concentration diminished respect to the formulation without PVP administered at the same dose and administration time and it was accompanied with the reappearance of the symptoms. From table 1 it can be observed that the variability between both results in plasma samples (70%) is higher than the intraindividual variability of CoQ10 (12%) [7]. These observations suggest that CoQ10 in the formulation containing PVP cannot reach acceptable concentration for therapeutic purpose causing inhibition instead of beneficial effects. In conclusion, the type of formulation must be controlled in order to obtain better effectiveness of CoQ10 therapy.

Table 1: CoQ10 content in capsules and CoQ10 concentration in plasma after 1-month treatments

Capsule Formulation	CoQ10 content (mg/capsule)	Plasma CoQ10 concentration* (µg/ml)
Treatment 1	47.6	2.3
Treatment 2	48.0	0.7

** Reference value: 0.4-1.4µg/mL (expected value after treatment 2.5- to 5-fold higher than the upper limit of reference value [8]*

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