BioFactors 9 (1999) 359–363
IOS Press

Clinical implications of the correlation between coenzyme Q_{10} and vitamin B_6 status

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Abstract. The endogenous biosynthesis of the quinone nucleus of coenzyme Q_{10} (CoQ_{10}) from tyrosine is dependent on adequate vitamin B_6 nutriture. Lowered blood and tissue levels of CoQ_{10} have been observed in a number of clinical conditions. Many of these clinical conditions are most prevalent among the elderly. Kalen et al. have shown that blood levels of CoQ_{10} decline with age. Similarly, Kant et al. have shown that indicators of vitamin B_6 status also decline with age. Blood samples were collected from 29 patients who were not currently being supplemented with either CoQ_{10} or vitamin B_6. Mean CoQ_{10} concentrations was 1.1 ± 0.3 μg/ml of blood. Mean specific activities of EGOT was 0.30 ± 0.13 μmol pyruvate/hr/10^8 erythrocytes and the mean percent saturation of EGOT with PLP was 78.2 ± 13.9%. Means for all parameters were within normal ranges. Strong positive correlation was found between CoQ_{10} and the specific activity of EGOT ($r = 0.5787$, $p < 0.001$) and between CoQ_{10} and the percent saturation of EGOT with PLP ($r = 0.4174$, $p < 0.024$). Studies are currently in progress to determine the effect of supplementation with vitamin B_6 of blood CoQ_{10} levels. It appears prudent to recommend that patients receiving supplemental CoQ_{10} be concurrently supplemented with vitamin B_6 to provide for better endogenous synthesis of CoQ_{10} along with the exogenous CoQ_{10}.

1. Introduction

In 1983, Olson and Rudney [1] reviewed the work which led to the elucidation of the biosynthetic pathway for coenzyme Q (Fig. 1). Most higher organisms have lost the ability to produce non-steroidal aromatic compounds from simple precursors. They, instead, rely on dietary precursors for aromatic compounds. Coenzyme Q (CoQ) biosynthesis begins with the conversion of tyrosine to 4-hydroxybenzoic acid. 4-Hydroxybenzoic acid is the key precursor to the benzoquinone nucleus of CoQ. The isoprenoid side chain is added at the next step and its length is variable according to species. Humans and most mammals synthesize CoQ_{10}.

Vitamin B_6, as pyridoxal 5′-phosphate (PLP), is required for the initial transamination step which produces 4-hydroxyphenylpyruvic acid from tyrosine. Thus, an adequacy of vitamin B_6 nutriture is essential for the synthesis of CoQ.

Lowered blood and tissue levels of CoQ_{10} have been observed in a number of clinical conditions. Many of these clinical conditions are most prevalent among the elderly. Kalen et al. [2] have shown that blood levels of CoQ_{10} decline with age. As can be seen in Fig. 2, the CoQ content of rat tissues peaks in early adulthood and, with the exception of heart tissue, declines dramatically with age. The tissues levels of CoQ in 300 day old rats declined 72.3% in lung, 47.0% in spleen, 72.9% in liver and 56.5% in kidney from the levels found in 30 day old rats. (Heart increased 7.5%.)

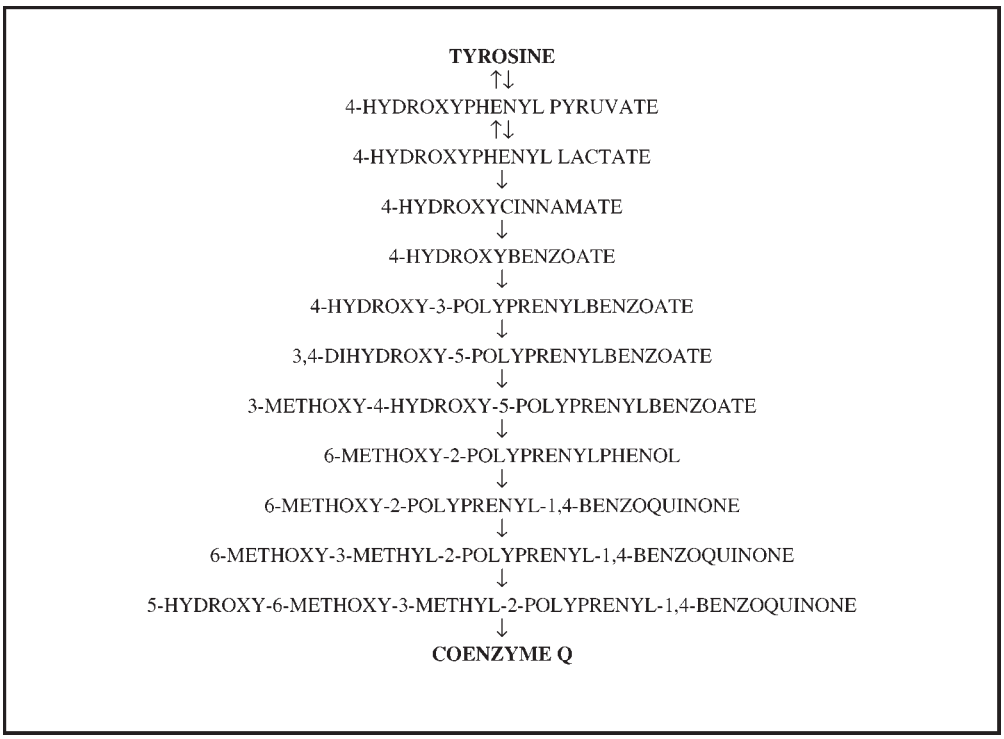

Fig. 1. Biosynthetic pathway for coenzyme Q in higher organisms. From [1].

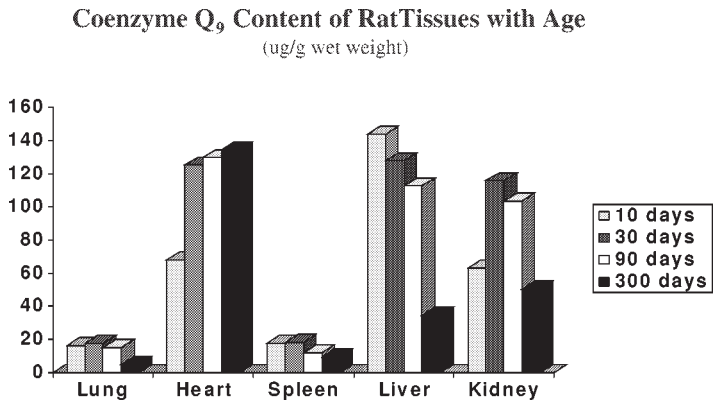

Fig. 2. Effect of age on tissue content of coenzyme Q_9 in rats.

Figure 3 shows that CoQ declines substantially in human tissues with age from a high in early adulthood. The tissue levels of CoQ in 77–81 year olds declined 48.3% in lung, 57.1% in heart, 60.1% in spleen, 17.0% in liver and 34.7% in kidney from the levels found in 19–21 year olds.

Similarly, Kant et al. [3] have shown that indicators of vitamin B_6 status also decline with age (Fig. 4). The mean plasma PLP for the 25–35 year age group was 76 $\pm$ 6 nmol/l as compared to 42 $\pm$ 6 nmol/l for the 65–75 year group. This represents a decrease of 44.7%.

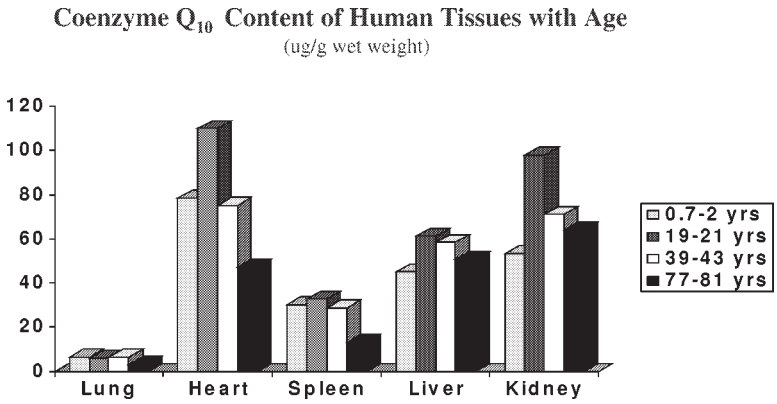

Fig. 3. Effect of age on tissue content of coenzyme Q_9 in humans.

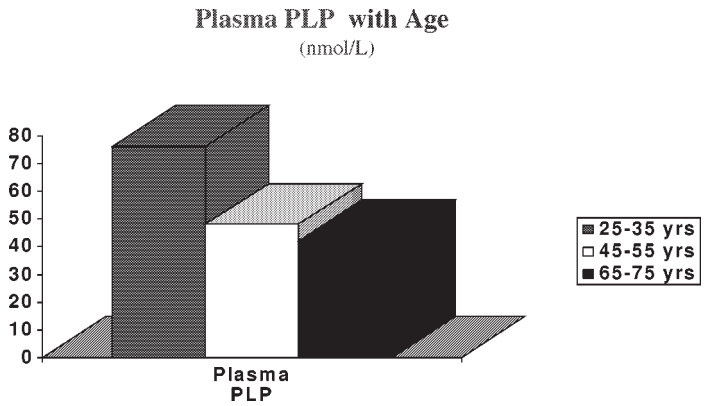

Fig. 4. Effect of age on human plasma PLP concentrations.

The Food and Nutrition Board of the US National Academy of Sciences also reports [4] a decline in dietary intakes of vitamin B_6 with advancing age. The Recommended Dietary Allowance (RDA) for vitamin B_6 is 1.0 mg for young children, 2.0 mg for adult men and 1.6 mg for adult women. The Food and Nutrition Board reports that, on the average, young children exceed the RDA at 1.2 mg/day while adults fall short of the RDA at 1.9 mg for men and 1.2 mg for women.

As an added concern, the US intake of protein is substantially higher than the Recommended Dietary Allowance at every age group. This increases the need for vitamin B_6 even further. Average protein intakes in the US are 50 g/day in young children, 110 g/day in men and 70 g/day in women as compared to the RDAs of 24 g/day, 58 g/day, and 44 g/day, respectively.

Since both CoQ_{10} levels and vitamin B_6 levels are known to decrease with age and since vitamin B_6 is essential for the biosynthesis of CoQ_{10}, it is possible that the age related decline in CoQ_{10} levels is due, at least in part, to poor vitamin B_6 status. Alternatively, it is possible that the age related declines of the two substances are merely coincidental and not directly related to one another. As an initial step in defining the nature of the relationship, a study was undertaken to determine if there was a correlation between blood levels of CoQ_{10} and vitamin B_6 status in a group of patients and healthy subjects submitting samples to our laboratory. If a correlation is found to exist, further studies would be warranted.

Table 1
Mean CoQ_{10} and vitamin B_6 levels

Coenzyme Q_{10}	EGOT		
μg/ml	$-$PLP s.a.	$+$PLP s.a.	% Saturation
1.1 ± 0.3	0.30 ± 0.13	0.37 ± 0.12	78.9 ± 13.9

s.a. units = μmol pyruvate/hr/10^8 erythrocytes.

Table 2
Correlation between CoQ_{10} and EGOT

	Specific activity	Percent saturation
Correlation coefficient	0.5787	0.4174
$p<$	0.001	0.025

2. Methods

Blood samples were collected from 29 patients and healthy subjects. None of the participants were receiving supplements of either CoQ_{10} or vitamin B_6 at the time of blood collection. Samples were analyzed for CoQ_{10} by HPLC using a slight modification of the procedure of Lang et al. [5]. Vitamin B_6 status was estimated as specific activity of erythrocyte glutamic-oxaloacetic transaminase (EGOT) by the procedure of Kishi and Folkers [6]. Data analyses were performed using SPSS for the Macintosh [7].

3. Results and discussion

Blood samples from 29 patients and healthy volunteers were analyzed for their content of CoQ_{10} and for specific activities of EGOT, an indicator of vitamin B_6 status. Subjects ranged in age from 23 to 66 years. None of the subjects was currently receiving either vitamin B_6 or CoQ_{10} supplements. The results are displayed in Table 1. As can be seen, the mean CoQ_{10} level (1.1 ± 0.3 μg/ml) was within the expected normal range. The mean specific activity ($-$PLP) for EGOT was 0.30 ± 0.13 μmol pyruvate/hr/10^8 erythrocytes which is at the lower end of the normal range. The mean specific activity after addition of PLP ($+$PLP) was 0.37 μmol pyruvate/hr/10^8 erythrocytes indicating that the system was 78.9% saturated. EGOT is an inducible enzyme. With vitamin B_6 supplementation, specific activities of 0.70 are often seen with 100% saturation.

Correlational analyses revealed a strong positive correlation between blood levels of CoQ_{10} and the specific activity of EGOT ($r = 0.5787$, $p < 0.001$) and between CoQ_{10} and the percent saturation of EGOT with PLP ($r = 0.4174$, $p < 0.025$). The finding may be of clinical importance. If, as the biochemistry of the synthetic pathway suggests, a person's vitamin B_6 nutriture affects the endogenous biosynthesis of CoQ_{10} then both a possible mechanism for lowered CoQ_{10} levels in blood and tissue of some patients and a mechanism for improving these levels may exist.

4. Conclusions

Studies are currently in progress in our laboratories to determine the effect of supplementation with vitamin B_6 of blood CoQ_{10} levels. Until those results are available, it appears prudent to recommend that patients receiving supplemental CoQ_{10} be concurrently supplemented with vitamin B_6 to potentially provide for better endogenous synthesis of CoQ_{10} along with the exogenous CoQ_{10}.

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