Serum thyroid hormones and TSH concentrations in amiodarone treated rabbits

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This study aimed at investigation of the influence of amiodarone hydrochlaride on the serum **T_3**, **T_4** *and TSH values in rabbits. Ten male and ten female totally 20 New Zetland Albino rabbits were treated with daily 10 mg/kg amiodarone hydrochloride added to their drinking water.* **T_3** *concentration on 30th day was markedly and significantly (P<0.001) higher than the mean basal value. In contrast the values on 45th and 60th days were significantly (P<0.001) lower than the basal value. Decrements in* **T_4** *level in first week and on 15th and 60th days were markedly and statistically significant (p<0.001) when they were compared to the basal value and TSH values in first week, and* **T_4** *level at the 60th day of the treatment were significantly (P<0.001) lower than the basal level. In conclusion, amiodarone is very effective drug for changes in serum thyroid hormones and TSH concentrations. Individual variations and gender and time related fluctuations require further work such as histopathological and immunological evaluations in animal models.*
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Key Words: Amiodarone, **T3, T4**, TSH, Rabbits

Amiodarone causes increases in serum total **T4** and **T3** with a concamitant decrease in **T3** by inhibiting the peripheral conversion of **T4** to **T3** (1). Amiodarone also stimulates TSH release from cultured rat anterior pituitary cells by direct effect of amiodarone on the thyrotroph cell mediated via nuclear **T3** receptor binding (2) However, a slight reduction of serum TSH in amiodarone treated fisher rats has been reported (3). In addition, measurement of thyrotrophin in plasma by an ultrasensitive immunoradiometric assay demonstrated that a normal TSH value in euthyroid patients or a decreased TSH value in subclinic hyperthyroidism could be evaluated in amiodarone taken patients (4).

There is some consistency about amiodarone effect on thyroid hormones but additional studies are needed to solve time-and model-related variations.

MATERIALS AND METHODS

In this study, 10 male and female, totally 20 New Zelland albino rabbits have been studied. Their weights were between 1600-2500 grams (averaged: 2554±371 grams). The animals have been treated with daily 10 mg/kg amiodarone hydrochloride during a period that covered 45 days by specially prepared drinking water containing above mentioned amount amiodarone hydrochloride.

Blood samples were taken before amiodarone administration and 7th, 15th, 30th, 45th, 60th days of treatment via IV catheter inserted in ear veins. Specimens were centrifuged and separated promptly and then stored at -20°C until the time of the RIA for TSH, **T3, T4**. Hormon assay was carried out using Amerlite RIA kits. All the measurements have been done at the same time and bench.

For comparison within groups, the student's -t test for paired groups was used P<0.01 has been statistically meaningful.

RESULTS

Changes in serum **T3** level: The mean basal **T3** concentration was 0.689±0.584 nmol/lt. The mean values have been changed in consequitive days (1.092±1.141 nmol/lt in first week 1.950±2.198 nmol/lt on 15th day 2.008±0.965 nmol/lt on 30 day).

There were statistically significant increments on 30th day and decrements on 45th and 60th days com-

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Table 1. Serum T3, T4 and TSH values in amiodarone treated rabbits

		DAYS					
		Basal	7	15	30	45	60
T3		0.689	1.092	1.95	2.008	0.228	0.125
		±	±	±	±	±	±
	nmol/lt	+0.534	±1.141	±2.198	+0.965*	±0.125*	±0.249*
T_4		39.3	21.645	19.146	30.711	30.533	17.153
		±	±	±	±	±	±
	nmol/lt	±15.883	±12.539*	±12.264*	±15.66	±12.152	±8.458*
TSH		0.217	0.113	0.14	0.16	0.206	0.207
		±	±	±	±	±	±
	mIU/lt	±0.14	±0.016*	±0.07	+0.123	±0.259	±0.035*

*-P<0.001

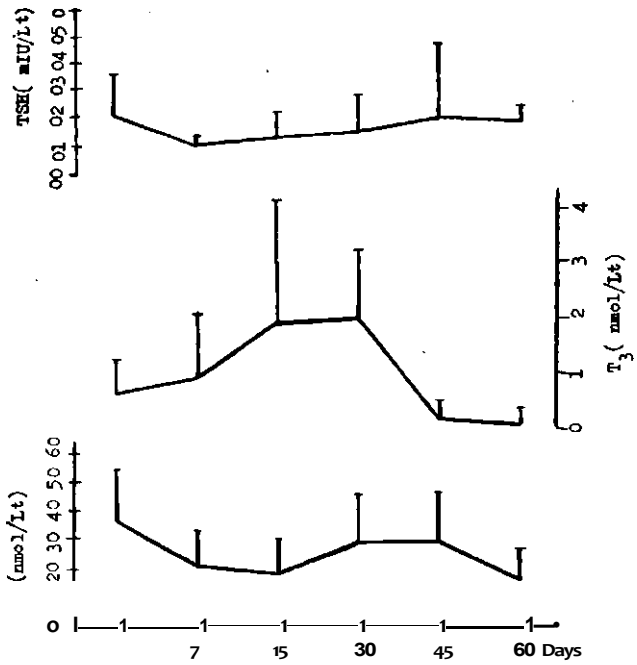

Figure 1. Alterations in ?> \i •• „ TSH values following amiodarone administration

pared to the mean basal value (P n 001). All of the hormones values are given in Table 1.

Changes in serum T4 level: The mean serum T4 concentrations in the first week, on 15th and on 60th days (21.645±12.535 nmol/lt, 19.146±12.264 nmol/lt, 17.153±8.458 nmol/lt respectively) were significantly (p<0.001) lower than the mean basal value (39.300+15.883 nmol/lt). Time related changes in serum total T4 value were shown in Figure 1.

Changes in serum TSH level: All the TSH values, as seen in Table 1, tended to be lower following amiodarone administration. The mean values in first week and on 60th day of the treatment were significantly lower than the mean basal value (0.113±0.016 mIU/lt, 0.207±0.035 mIU/lt, 0.217±0.14 mIU/lt P<0.001 respectively).

DISCUSSION

The changes in serum TSH, T3 and T4 levels were different in the first and second month of the treatment. Amiodarone induced an increment in serum T3 on 30th day of administration but it significantly reduced T3 concentrations on 45th and 60th days. All of these values were significantly different from the mean basal value (P<0.001). In another study, it has been reported that amiodarone had no effect on the T3 value in the rats. It has been noted that amiodarone caused increases in serum thyroxin and reverse T3 and concomitant decreases in T3 by inhibition of peripheral deiodination of T4 (5). These results are not compatible with our data which is evaluated in the early phase of the study but similar decreases in T3 value on 45th and 60th days are prominent. Elevated T3 value in the early phase of the experiment as shown in figure I might be related to the acute injuries effected by amiodarone on the thyroid tissue.

Elevated TSH values caused by direct effect of amiodarone on pituitary gland in human beings, and reduced TSH values in the rats were reported (3-5). Findings in this study showed that TSH values decreased at the beginning of experiments as demonstrated in rat models. Slightly elevated T3 value in the early phase of the treatment might be responsible for changes in TSH concentrations and compatible changes in T4 values with previous works are considered to be changed in the future. Significantly reduced T4 value on 7th, 15th and 60th days could be due to thyroid inhibition by iodine content of amiodarone.

Amiodaron uygulanan tavşanlarda serum tiroid hormonları ve TSH konsantrasyonları

Bu çalışmanın amacı tavşanlarda amiodaron hidroklorürün, serum T3, T4 ve TSH değerlerine etkisini araştırmaktır. On erkek ve 10 dişiden oluşan toplam 20 Yeni Zellanda albino tavşanına günde 10 mg/kg ölçüsünde amlodarone hidroklorür içme

sularına katılarak verildi. Otuzuncu gündeki T3 konsantrasyonu, bazal değer ortalamalarından anlamlı olarak yüksektir (P<0.001). Aksine 45 ve 60.gündeki değerler, bazal değerlerden anlamlı ölçüde daha düşüktür (P<0.001). 1.hafta, 15.günve 60.günlerdeki 14 düzeyindeki düşmeler, bazal değerlere bakışla belirgin ve istatistiksel ölçüde anlamlıdır (P<0.001). 1.hafta ve tedavinin 60.günündeki TSH değerleri bazal değerlerden anlamlı ölçüde daha düşüktür (P<0.001). Sonuç olarak; amiodaron, serum tiroid hormon ve TSH konsantrasyon değişimleri üzerine çok etkili bir ilaçtır. Bireysel farklılıklar, cinsiyet ve zamana ilişkin değişimler; hayvan örneklerinde histopatolojik ve immünolojik değerlendirmeler gibi daha ileri düzeyde çalışmaları gerektirmektedir. [Türk J Med Res 1994; 12(6): 229-231]

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