

The Effects of High Dose of Sodium Selenite Injection on Thyroid Hormones in Horses

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Abstract: Iodothyronine deiodinases contains Selenium that controls the synthesis and degradation of the biologically active thyroid hormone T3. Some practitioners believe that thyroid dysfunction are responsible for variety of the clinical signs in horses but many of studies on this issue, were carried out on human and rats and there is not enough information on horse. Therefore our study was designed to monitor the effects of high dose of selenium on thyroid hormones (T4 ; T3 ; FT4 and FT3) in 7 adult male horses. All horses were under close observation for 50 days. During the first 25 days, blood samples were taken on days 0, 5, 10, 15, 20 and 25 and were assigned as control. During the next 25 days, all horses received of sodium selenite (30µg/kg bw, selenium content is about 13.5µg) daily, which is several times more than basic needs according to the literature and blood samples were taken on the same days as done in control period. Serum thyroid hormones were measured by Radioimmunoassay. No significant hormonal changes on thyroid hormones were observed during the experiment in comparison with control stage (p>0.01).

Key words: Selenium • Thyroid Hormone • Horse • Radioimmunoassay

INTRODUCTION

One well-cited assertion in the literature is that selenium is an integral part of normal body function and selenium deficiency in different animals results in lower level of Triiodothyronine (T3) and higher level of thyroxine(T4) in comparison to the control group [1-3].

Despite plenty information on different species, few reports exist on effects of sodium selenite on thyroid hormones in horses. So, definitive diagnosis of any dysfunction of this gland is often difficult in horse [4].

Previous studies showed that selenium is important in antioxidant defense, immune function, has very basic and important role in metabolic regulation by thyroid hormones and has possible anticarcinogenic effects [5]. Previous study conducted on rats, suggested a relationship between selenium deficiency and thyroid

function[5].Also evidence suggests that iodothyronine deiodinases have sites for selenium and have very important role in regulation of T3 [6]. In conclusion selenium has a role in some enzymes construction including deiodinase and glutathion peroxidase[7].

The research discussed above suggests, at the least, investigation on the effect of selenium as supplement on T3, T4, free iodothyronine FT3 and free T4 (FT4) especially in horses.

FT3 and FT4 are believed to be responsible for the biological action. For this reason the measurement of FT3 and FT4 concentrations are better indicator of patient thyroid status than T4 and T3 levels. To test the hypothesis that sodium selenite has effect on thyroid hormones and discusse the issue in more details, the present study was conducted on horses' blood T3, T4, FT3 and FT4 level before and 25 days after treatments with sodium selenite by Radioimmunoassay.

MATERIALS AND METHODS

An experimental study was designed in that seven healthy adult male horses with five years old averagely were randomly selected and observed for two periods (25-days each). During the first 25 days, all horses were considered as control group and in the next 25 days, the horses were assigned as experimental group. They did not receive any drugs one month before the start of the study and all of them were clinically healthy based on physical examination.

In the first stage, all horses were given 0.9% NaCl solution subcutaneously with dose of 1 ml/100 kg body weight with considering of least stress. During the next 25 days, all horses received 30 µg /kg/day of sodium selenite (it is about 13.5 µg selenium) subcutaneously. Although little information is available on the need of horses for selenium but the optimum intake is 6 mg/week or 2.4 µg/kg BW daily [5]. The dose we used was several times more than those suggested in literature. To prepare this combination 3 gram of sodium selenite powder was dissolved in 100 ml of sterile water. The horses housed in stable with adlib access to food and water during experiment. Daily ration of them includes Alfa Alfa hay. Following, blood sampling in whole period of experiment were done on days 0, 5, 10, 15, 20, 25, 30, 35, 40, 45 and 50 in the morning and stored in tube without any coagulant material. Prior to injection, body temperature, heart rate and respiratory rate were monitored and registered. Serum was harvested and frozen in -20 °C. In whole of second stage, the horses were considered closely for clinical signs of poisoning by selenium and no sign was observed. Serum thyroid hormones (T_4 and T_3) were measured by Radioimmunoassay (RIA) using commercially available kits (Orion spectria) via Gamma counter. To Measure Free-triiodothyronine (FT3) and Free-thyroxine (FT4) comparative Elisa kit of Monobind Company was used. The value of the hormones calculated automatically in 450 nm for reading absorption level and according to the standard curve. The data were analyzed using Repeated Measure ANOVA and turkey's test (SPSS 15), the mean value of the control and the experimental data on days of 5, 10, 15, 20 and 25 after sodium selenite injection, were compared statistically.

RESULTS

In this study the mean and Standard Error (SE) of T_3 and T_4 before and after sodium selenite injections in all horses were analyzed. The results are shown in Table 1. Those values of FT₃ and FT₄ can be seen also in Table 2.

Table 1: Mean and Standard Error (S.E) of T_3 and T_4 values before and after sodium selenite injections

Hormone level	Day	T_4 (nmol/L)	T_3 (nmol/L)
Before sodium selenite injection	Average of 0-25	14.673 ± 1.412	0.709 ± 0.111
Following sodium selenite injection	5	14.989 ± 1.330	0.650 ± 0.129
	10	14.347 ± 1.230	0.700 ± 0.098
	15	15.238 ± 1.135	0.707 ± 0.123
	20	14.567 ± 1.201	0.679 ± 0.109
	25	14.567 ± 1.201	0.651 ± 0.873

*The mean of T_3 , T_4 , FT₃ and FT₄ in first 25 days considered as

Table 2: Mean and Standard Error (S.E) of FT3 and FT4 values before and after sodium selenite injections

Hormone level	Day	FT ₄ (pmol/L)	FT ₃ (pmol/L)
Before sodium selenite injection	Average of 0-25	12.345 ± 1.256	7.913 ± 0.513
Following sodium selenite injection	5	12.341 ± 1.209	7.201 ± 0.498
	10	12.348 ± 1.205	7.129 ± 0.529
	15	12.348 ± 1.205	7.129 ± 0.529
	20	11.375 ± 1.291	7.437 ± 0.420
	25	11.012 ± 1.309	7.21 ± 0.694

*The mean of T_3 , T_4 , FT₃ and FT₄ in first 25 days considered as control.

In this survey, there was significant positive correlation between mean values of T_3 and T_4 ($r=0.83$, $P<0.05$), T_4 and FT₄ ($r=0.98$, $P<0.01$), T_3 and FT₄ ($r=0.98$, $P<0.01$), FT₃ and FT₄ ($r=0.92$, $P<0.05$) and T_3 and T_4 ($r=0.923$, $P<0.01$) from day 0 to 25 after sodium selenite injection

No significant changes were observed in T_3 , T_4 , FT₃ and FT₄ following the sodium selenite injection in stallions ($P>0.01$).

DISCUSSION

The purpose of the study was to compare changes in the mean of T_3 , T_4 , FT₃ and FT₄ before and after high dose of sodium selenite injections in all horses.

The data indicate that following sodium selenite injections, there were no significant changes observed in thyroid hormones values ($P>0.01$).

One possible explanation for this result is that it seems type I iodothyronine de-iodinase activity (the enzyme that converts T_4 to T_3) is affected by Vitamin E more than selenium. In current study the horses were fed with alfa alfa hay that has enough amount of this nutrient. Behne *et al.* [6] declare that excess selenium in food has no and sometimes reverse effect on type I iodothyronine de-iodinase activity. Overly activity of this enzyme doesn't need high level of selenium in food and required amount of it provides by food.

Selenium deficiency in different species result in lower T3 and upper T4 in compare to those receive selenium supplementation [1-3, 9]. Chanoine *et al.* [2] suggested that increased T4 is as a result of reduced activity of type I iodothyronine de-iodinase. Thyroid gland has many roles in fetal development especially in neural segment, growth, bone development, behavior, metabolism, reproduction, etc in both rats and humans [19].

Eayrs [20] showed that thyroid hormone deficiency requires early remediation for normal development in the rat. Study of utero-effects of thyroid hormones on growth in a thyroidectomized lamb model, was demonstrated by Hopkins and Thorburn [21].

Selenium is an essential component of many selenoproteins that regulate thyroid hormone synthesis, preserve thyroid integrity in conditions of marked oxidative stress and control hormone metabolism in nonthyroidal tissues such as liver and kidney where T4 is converted to biologically active T3 or its inactive isomer reverse-tri-iodothyronine [7, 22-24].

Our results support those studies in human, sheep and rats [9-11]. The serum changes of FT4, FT3 and Thyroid-stimulating hormone (TSH) were seen in normal range in mothers who live in the area with high level of selenium in soil [10].

Thomson [12] showed, following the consuming of high amount of selenium by human, T4 level in plasma reduces, but this was not significant.

Yet, our results provide no evidence for those of Arthur and Goeffrey [13] studies that claim selenium could affect thyroid hormone metabolism provided by observing of increased T4 and decreased T3 concentrations in plasma in selenium deficient rats and cattle. These changes were associated with considerable decreases in hepatic and renal type I iodothyronine de-iodinase activity which converts T4 to T3.

It was observed that a concurrent deficiency of selenium and iodine in rats lead to significant reduction in hepatic T₄, thyroid T₃ and T₄ and plasma T₄. But plasma and hepatic T₃ had no notable change. Beckett *et al.* [14] suggested that selenium deficiency is able to exaggerate hypothyroidism observed in iodine deficiency.

However, our results are also in disagreement with those of different results about T₃ changes following selenium supplementation. Olivieri *et al.* [15] declared that selenium supplementation decreased plasma T₄, but plasma T₃ and TSH concentrations were unaffected by selenium status and treatment.

One possible explanation for this discrepancy is that existing of correlation ships among thyroid hormones observed in this study, are perhaps as a result of converting these hormones to each other.

Selenium is essential for iodothyronine deiodinases that control the synthesis and degradation of the biologically active thyroid hormone T3 [3]. But iodothyronine deiodinase enzyme does not need high amount of selenium for activity and required selenium supplies from routine daily ration. By the way increased production of iodothyronine deiodinase enzymes induced by high level of selenium in body system don't necessarily indicate their increased activities [16, 17]. It means though increased production of these enzymes, they stored in hepatic microsomes because there is no need to them.

In other hand, Beech *et al.* [18] suggested TSH is more essential for serum T3 adjunction than sodium selenite. In this survey, as values of T3 and T4 had no significant change, so TSH secretion from hypophysis presumably didn't change.

One limitation for this study was that little information is available on the need of horses for selenium.

We recommend:

1. To test this level of selenium compound on the experimental deficient horse in selenium also to see the curing signs as well
2. To investigate type I iodothyronine de-iodinase activity following injection of high dose of selenium as were done in other species.
3. To investigate effects of vitamin E solely and concurrent with selenium on thyroid hormones.
4. It is better to evaluate TSH as the same time as thyroid hormones.

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