Review Article

Potential Benefits of Selenium Supplementation in Patients with Kidney Disease

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ABSTRACT

Trace element deficiency is common among patients with end-stage renal disease (ESRD); the reason is that since these patients undergo dialysis, they lose these elements more than healthy people, and also the use of trace elements is restricted due to loss of appetite. Selenium (Se) is a trace element that is essential for the oxidative stress defense system. Se deficiency leads to some complications similar to those often seen in ESRD patients, such as all-cause mortality due to cardiovascular diseases, bone loss, uric acid elevation, and anemia. This article aims to review the evidence on consequences of Se deficiency in ESRD patients, as well as effects of Se supplementation in hemodialysis patients. Multiple databases were searched to summarize the available evidence on selenium's role in kidney diseases. Since the complications of ESRD and those of Se deficiency are mostly similar, this triggers the idea that Se deficiency may be considered as a cause of these problems, but it needs to be more assessed that Se deficiency is a single factor or there are other factors participated in. Also the role of Se supplementation on resolving the mentioned complications, needs to be more studied through well-designed clinical studies.

KEYWORDS: *Hemodialysis, kidney disease, peritoneal dialysis, Selenium supplementation*

INTRODUCTION

Chronic kidney disease (CKD) is an umbrella term for several conditions that affect the kidneys, but it generally means permanent and usually progressive damage to the kidneys caused by a variety of conditions.[1] End-stage renal disease (ESRD) is a terminal illness defined as having a glomerular filtration rate of <15 mL/min. The most common cause of ESRD in the US is diabetic nephropathy, followed by hypertension. Despite extensive advancements over the past years in kidney transplantation and dialysis as well as novel methods of pharmacotherapy, death is still quite high among dialysis patients compared to a normal population.[2]

Cachexia and protein loss during hemodialysis are two key factors that lead to an oxidative stress situation and loss of essential amino acids and trace elements, which act as positive feedback and worsen patients' health. Because of the loss of proteins and low intake of proteins and amino acids secondary to loss of appetite, wasting plays a crucial role in oxidative stress. Because of oxidative stress, there is a risk of cardiovascular diseases (CVDs) 10-to-30-fold higher than normal people; also, the condition of the kidneys worsens.

Low intake and extended loss of selenium in ESRD patients result in weakened defense against oxidative stress secondary to impaired GPx activity.[3,4] The use of selenium in ESRD patients either orally or parenterally increases selenium levels.[5-7] Accordingly, in this paper, first we will become more familiar with Se, Se in the human body and its intake criteria, then review the

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effect of selenium deficiency on ESRD patients and finally review studies that intervened to recompense selenium deficiency in ESRD patients (also with respect to animal studies).[8]

Methods

Data for this review were identified by searching Medline, PubMed, Scopus, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews. Keywords used as search terms were "selenium," "chronic kidney diseases," "kidney disease," "hemodialysis," and "peritoneal dialysis." This search was performed without time limitations. Major well-designed studies which used selenium supplementation as an intervention in patients with kidney disease were included.

Results

The most common cause of ESRD in the US is diabetic nephropathy, followed by hypertension. Other etiologies can include glomerulonephritis, cystic kidney disease, recurrent kidney infection, chronic obstruction, etc., The symptoms of the disease may include nausea, vomiting, metabolic, hematologic, electrolyte derangements, seizures, coma, bleeding diathesis, refractory fluid overload, and hypertension unresponsive to pharmacotherapy, uremic pericarditis, etc., Vigilant monitoring of glomerular filtration rate (GFR) and proteinuria in diabetics and nondiabetics is essential to managing disease progression in patients with CKD.[9] Early referral to specialists is necessary for timely dialysis or renal transplant planning.[10,11]

According to the United States Renal Data System, in 2015, there were 124,411 new ESRD diagnoses, reflecting an increasing burden of kidney failure. The disease prevalence has been steadily increasing at a rate of around 20,000 cases each year.[12,13]

Coronary heart disease is a significant complication of CKD and is the most common cause of death in this population. Patients on dialysis have a 10-to-30-fold higher risk of cardiovascular mortality compared to the general population.[8] Peripheral vascular disease is also commonly seen in these patients.[14]

Common complications of progressive renal failure are as follows: hypertension, mineral and bone disorders (secondary to hyperparathyroidism and Vitamin D deficiency), hyperuricemia, metabolic acidosis, hyperphosphatemia, hypoalbuminemia, and anemia.[10]

Selenium is a chemical element with atomic number 34. It is a nonmetal element (rarely considered a metalloid) with properties that are intermediate between the elements above and below in the periodic table, sulfur, and tellurium; also, it has similarities to arsenic. Selenium was discovered in 1817 by Jöns Jacob Berzelius.[15]

A history of the important discoveries of the biological processes that selenium participates in, and a point-by-point comparison of the chemistry of selenium with the atom it replaces in biology, sulfur; shows that redox chemistry is the largest chemical difference between the two chalcogens. This difference is significant for both one-electron and two-electron redox reactions; it is mostly due to the inability of selenium to form π bonds of all types. The outer valence electrons of selenium are also more loosely held than those of sulfur. As a result, selenium is a better nucleophile and reacts with reactive oxygen species faster than sulfur, but the resulting lack of the π-bond character in the Se–O bond means that the Se-oxide can be much more readily reduced compared to S-oxides. The combination of these properties means that replacement of sulfur with selenium in nature results in a selenium-containing biomolecule that resists permanent oxidation.[16]

Selenium is an essential component of several major metabolic pathways, including thyroid hormone metabolism, antioxidant defense systems, and immune function.[17]

There is also evidence that selenium has a protective effect against some types of cancer; also, it may enhance male fertility, decrease CVD mortality, and regulate the inflammatory mediators in asthma.[17]

Selenium is incorporated into proteins as selenocysteine. Selenium mainly acts through these selenoproteins. In the human genome, 25 genes for selenoproteins have been identified.[18] Among enzymatically active selenoproteins, selenocysteine is a central component of the active center and is directly involved in redox reactions. Glutathione peroxidase (GPx), thioredoxin reductase (TrxR), and deiodinases are among the group of well-characterized selenoproteins. The five human selenium-containing GPx, catalyze the reduction of hydroperoxides.[19] Selenoprotein *P* (SePP) is essential for the distribution and transportation of selenium, in particular to the brain and testicles.[20]

Criteria for the assessment of selenium supply

The following parameters are used as biomarkers for selenium supply: The concentration of selenium in plasma or serum, along with the GPx activity in plasma (GPx3), erythrocytes (GPx1), thrombocytes (GPx1), or whole blood (GPx3 and GPx1), as well as the concentration of SePP in plasma or serum. In general, the measurement

of selenoproteins reflects the functional selenium pool bound to selenoproteins, while the total selenium content also includes selenomethionine that is nonspecifically incorporated into proteins.

Most reference values are based on the measurement of GPx activity in plasma. However, the SePP concentration in plasma is deemed to be the most conclusive marker to determine the optimum supply of selenium.[21-23] The SePP concentration does not indicate a maximum level until a plasma selenium concentration of 100 μg/L to 120 μg/L is reached, while GPx activity in plasma reaches its optimum at a lower level of approximately 90 μg/L.[24,25] In addition, nowadays, there are improved analysis methods that allow the determination of SePP. Based on human intervention studies, it is assumed that any further increase in selenium supply above a plasma selenium concentration of 120 μg/L will not lead to any further increase in selenoprotein expression.[26]

Similar complications in ESRD and Se deficiency

Physiologically, high selenium levels are associated with a decreased risk of CVD incidence and mortality.[27] Some studies have analyzed the effect of selenium on all-caused CVD mortality among patients. A meta-analysis study showed that participants with the highest selenium concentration had a lower risk for all-cause CVD mortality.[28] Another systematic review and meta-analysis of randomized controlled trials showed that a decreased risk with antioxidant mixtures was seen for CVD mortality when selenium was part of the mixture with no association when selenium was absent. Similarly, when selenium was part of the antioxidant mixture, a decreased risk was seen for all-cause mortality. It is concluded that the addition of selenium should be considered for supplements containing antioxidant mixtures if they are associated with CVD and all-cause mortality risk reduction.[29]

It is worth mentioning that most of these studies have been conducted on cases with normal kidney function, or at least the chief complaint of patients has not been associated with altered function of the kidneys.

Although some studies have concluded that low selenium content might be a risk factor for the development of hypertension,[30] recent studies have shown that high serum selenium concentrations are associated with a higher prevalence of hypertension;[31] for instance, a study showed that even in a population with very low serum selenium concentrations, higher serum selenium concentrations were associated with higher blood pressure levels and a higher prevalence of hypertension.[32] A positive association was found between serum selenium and hypertension, irrespective of age or antihypertensive medication intake.[33] Another study proved that long-term excessive selenium supplementation induced hypertension in rats.[34] It is important to closely monitor the amount of selenium intake and control its range, which could have adverse effects.

Emerging evidence supports the view that selenoproteins are essential for maintaining bone health. Antioxidant selenoproteins, including GPx and TrxR, as a whole, play a pivotal role in maintaining bone homeostasis and protecting against bone loss. GPx1, a major antioxidant enzyme in osteoclasts, is upregulated by estrogen, an endogenous inhibitor of osteoclastogenesis. TrxR1 is an immediate-early gene in response to 1α, 25-dihydroxyvitamin D3, an osteoblastic differentiation agent. The combination of 1α, 25-dihydroxyvitamin D3, and selenium generates a synergistic elevation of TrxR activity in Se-deficient osteoblasts. Of particular concern, pleiotropic TrxR1 is implicated in promoting nuclear factor-κB activation. Coincidentally, TrxR inhibitors (such as curcumin and gold compounds) exhibit potent osteoclastogenesis inhibitory activity. Studies in patients with mutations of selenocysteine insertion sequence-binding protein 2, a key trans-acting factor for the co-translational insertion of selenocysteine into selenoproteins, have clearly established a causal link of selenoproteins in bone development. Selenium transport to bone relies on SePP. Plasma SePP concentrations have been found to be positively correlated with bone mineral density in elderly women.[35]

Uric acid (UA) is the end product of purine metabolism in humans. UA has powerful antioxidant properties as ascorbic acid and accounts for nearly half of the antioxidant capacity in plasma. However, it can be deleterious pro-oxidant as well, resulting in vascular smooth muscle cell proliferation and endothelial dysfunction.[36] Excessive UA production or reduced urate excretion leads to hyperuricemia and gout. Furthermore, hyperuricemia plays a crucial role in the development and prognosis of hypertension, hyperlipidemia, insulin resistance, and other CVDs.[37] It was found that urinary selenium concentrations were inversely associated with serum UA (SUA) levels in males. In addition, under the exposure of vanadium and arsenic, only if high selenium content existed, no significantly increased SUA levels and hyperuricemia risk in both sexes can be found.[38]

Low serum selenium is associated with anemia among older adults in the US. Serum selenium levels were lower in anemic adults compared with nonanemic adults. The prevalence of anemia was high in the lowest quartile and low in the highest quartile of serum selenium.[39]

Nonclinical studies on the use of Selenium

Some studies have shown the antioxidant effect of selenium in animals such as goose, sheep, and acute heat stress-exposed quails. The antioxidant effect of selenium increases the protective effect of neutrophils, has a positive effect on cellular immunity, and finally increases the activity of the immune system. This increase in the immune system, in addition to the antioxidant effect of selenium, has been proven to increase the serum concentration of total immunoglobulins and circulatory immune complexes and had significantly heavier spleen and bursa in broilers. However, it was found in this study that Vitamin E has a synergistic effect with selenium.[40]

Furthermore, this increase in the immune system has been observed in newborn calves, and even studies conducted by Liu. on pigs showed that selenium deficiency had negative effects on cell-dependent immunity.[41,42] Another well-documented benefit of selenium is its ability to decrease oxidative stress. This benefit in animals, such as sheep, was associated with improved spermatogenesis. Improvement of semen with selenium in chicken was seen as a marked increase in the concentration of total lipids and phospholipids in the seminal plasma from the control group. Improvement of spermatogenesis was also demonstrated in sheep. Table 1 summarizes some nonclinical studies on the use of selenium.

Clinical trials on the use of Selenium in hemodialysis patients

Based on clinical trials in hemodialysis or peritoneal dialysis patients, selenium increased plasma concentration of selenium and red blood cell GPx (RBC GSH-Pxs) activities. Although it is debatable whether selenium supplementation can increase plasma GPx activity, some studies have shown that plasma GPx activity can be increased by selenium supplementation in combination with one or two more components, such as erythropoietin. Table 2 summarizes some clinical trials on the use of selenium in dialysis patients or patients with altered renal function.

Discussion

Figure 1 demonstrates the concept for Se role in CKD, especially ESRD. It is clear that loss of appetite has a direct relation with decrease of GFR. Hence, with CKD progression and consequently loss of appetite, the intake of trace elements and particularly Se decrease. Of course, patients with early CKD have restricted diets and by disease progression, it gets worsen. On the other hand, by starting dialysis, the loss of proteins, amino acids, nutrients, and trace elements increase. While trace element deficiency occurs, the body radical scavenging system weakens so it could not fight against oxidative stress efficiently. In addition, loss of proteins and low intake of them results in wasting, which increases the extent of oxidative stress. Moreover, in the end, we know that oxidative stress has a main role in increase the risk of CVD, anemia, bone disorders, and other complications that ESRD patients face with.

It seems that selenium supplementation in ESRD patients can be beneficial and improve the radical scavenging system. However, further studies are needed to determine if selenium supplementation alone can reduce oxidative stress in patients with impaired renal function.

Conclusion

In summary, a total of 20 animal studies, 8 randomized controlled trials on a variety of kidney diseases, especially HD patients have been reviewed. The most results from most of these studies consistently demonstrate the effect of selenium supplementation on increasing selenium levels in plasma, which Se deficiency is proved among them.

It can be accepted that Se supplementation is beneficial in reaching Se optimum plasma concentration in either those healthier ones or CKD patients. Furthermore, it should keep in mind that increase in Se plasma concentration more than optimum will result in side effects like blood hypertension. On the other hand, there are controversial results that compensation of Se deficiency may not affect ESRD patients. There is the point here that there needs a short period to achieve optimum Se plasma concentration, but the beginning of effect of this intervention is not clear; for example, the effect of Se supplementation in the elderly was assessed during 5 years and in this time course its advantages became obvious. Hence, there should be studies that assess the beginning of Se compensation effect in ESRD patients.

In the study of Omrani *et al*., it was seen that the serum level of selenium in dialysis patients who received selenium supplements was significantly different from the control group. In that study, they claimed that taking (400 mg) twice a week for 2 months improved the oxygen radical scavenging system, increased plasma and red blood cell selenium concentrations, and increased selenium-dependent GPx activity; however taking selenium supplements in hemodialysis patients does not help much to reduce the harmful level of blood lipids, although lowering low-density lipoprotein-C and cholesterol and the contradictory results of other research studies show that more similar studies are needed in a larger population.

Table 1: Nonclinical use of Selenium

Study	Year	Animal models	Administration plan	Study period	Beneficial effects of Se	Reference
Feldmann *et al*.	1998	Newborn calves	0.2 mg Se and 60 mg Vitamin E per kg body weight	Fourth week of life	The application of Se and Vitamin E seemed to improve the status of health in the Se-deficient calves, although the results could not be assured statistically	[42]
Malbe *et al*.	2003	Cows	0.2 ppm organic Se in the form of Se yeast	8 week	Se supplementation in cows with low GPx activity seems to support udder defense mechanisms that favor reduction of the incidence of new mastitis cases	[43]
Contreras *et al*.	2005	Cows	1 mg Se/kg bodyweight subcutaneously, as barium selenate	60 days	Serum T3 concentrations decreased during early lactation in unsupplemented cows grazing pastures low in Se (0.03-0.04 ppm) and both serum T3 and erythrocyte GSHPx activities were consistently lower throughout lactation compared with Se-supplemented cows. Se supplementation had no effect on serum T4 concentrations	[44]
Biswas *et al*.	2006	Japanese quail	0.5 and 1.0 mg Se/kg	6 weeks	Supplementing the diet with Se has a beneficial effect on immune responses but does not affect production performance in growing Japanese quail	[45]
Dimitrov *et al*.	2007	Turkey	0.3 ppm organic Se in the form Sel-Plex	30 days	The positive effect of Se supplementation was observed on the lipid composition of stored semen: The concentration of the total lipids and phospholipids in the seminal plasma from the control group significantly increased, while in the experimental group remained constant. Better semen integrity in the experimental group was associated with an improved fertilizing ability of spermatozoa: the fertility rate of stored spermatozoa in the control group was 88%, while in the experimental group was 90.5%	[46]
Hall *et al*.	2009	Sheep	5 mg injection	5 months	Se administration may positively affect the immune system and, therefore, the sheep's ability to resist diseases such as footrot. Use of oral supplementation would eliminate the need for repeated Se injections	[47]
Baowei *et al*.	2011	Goose	Diets supplemented with 0, 0.10, 0.30, 0.50 mg/kg YS (on Se basis)	63 days	Yeast supplementation had no effect on the growth performance of goose, but significantly improved the meat quality and Se eposition in goose. Dietar yeast Se significantly stimulated the organ immunity and cell immunity of the geese, but showed no effect on the humoral immunity. The Se content of 0.3 mg/kg in the diet is the optimum concentration from the perspective of meat quality, antioxidant capacity, and immunity function	[48]
Ceballos-Marquez *et al*.	2010	Heifers	Subcutaneous injection of Se (1 mg/kg) fed Se yeast (3 mg/heifer/d)		Se supplementation did not result in a reduction of the incidence of new IMI or clinical mastitis or in decreased SCC during the balance of the first month of lactation. However, in pasture-based heifers injected with barium selenate before calving, and fed diets with 1.3 and 2.5 mg of Se/d precalving and during lactation respectively, no cases of clinical mastitis were observed in the first month of lactation	[49]
Leal *et al*.	2010	Lambs experimentally infected with *H. contortus*	0.2 mg/kg of LW SS by IM		Supplementation with Se provided greater antioxidant protection against oxidative stress generated from experimental infection of lambs with *H. contortus*	[50]
Speight *et al*.	2012	Boars	0.3 mg/kg		The results of this study suggest that there are positive effects of dietary supplementation with Sel-Plex on boar semen characteristics and that organic Se supplementation may help ameliorate the negative effects of semen storage on characteristics of sperm motility	[51]

Contd...

Table 1: Contd...

Study	Year	Animal models	Administration plan	Study period	Beneficial effects of Se	Reference
Ren *et al*.	2011	Goats	0.5, 2 and 4 mg kg^{-1} DM Se	174 days	Maternal and dietary Se-induced oxidative stress can modulate the mRNA and protein expression of the cell cycle-related genes (p34cdc2 and CyclinB1) in the testis of their offspring. In addition, Se deficiency and Se excess could prevent the completion of the cell cycle	[52]
Alhidary *et al*.	2012	Sheeps	0.5, and 5 mg of sodium selenate injection (5 mg/mL Se)	On days 1, 8, and 15 of exposure to heat stress	The 5 mg Se treatment decreased RT by 0.3°C (P=0.02) and BW loss by 4.5% (P<0.05) and increased eosinophil count (P<0.05). There were no differences (P>0.05) between treatments in RR and DMI, serum concentrations of glucose, total protein, cholesterol, and NEFA or in blood hematology variables	[53]
Brummer *et al*.	2013	Horses	0.06 mg/kg DM 0.12 mg/kg DM	35 weeks	Although the OVA and influenza vaccination responses were unaffected by Se status, other measures of immune function did indicate that low Se status could adversely affect cell-mediated immunity	[54]
Shi *et al*.	2014	Roosters	0.5, 1.0 or 2.0 mg Se/kg DM (from SS)		These data suggest that dietary Se can influence the population of SSCs of roosters during spermatogenesis and that oxidative stress can modulate SSCs behavior through regulating some key factors during spermatogenesis	[55]
Wang *et al*.	2016	Broilers	+0.05, 0.15 or 0.25 mg/kg Seas SS	42 days	dl-Se-Met is more effective than SS in increasing immunity and promoting conversion of T4-T3 , thus providing an effective way to improve the growth performance of broilers. Besides, based on a consideration of all experiment indices, 0.15 mg Se/kg was suggested to be the optimal level of Se supplementation under the conditions of this study	[40]
Del Vesco *et al*.	2017	Acute heat stress-exposed quails	0.33 mg/kg, nutritional demand for Se (SS)	7 days	Animals subjected to HS and fed with Se supplemented diet showed better results regarding gene expression and, thus, better results for the activities of enzymes used as stress markers, which could be due to the higher antioxidant capacity provided by the action of the studied genes	[56]
White and Warren	2017	Young equine athletes	0.1 or 0.3 mg Se/kg DM	14 weeks	Results indicate that exercise training lessens muscle damage and improves antioxidant defense following an acute bout of prolonged exercise and was not further enhanced by feeding Se above the NRC requirement	[57]
Elgendy *et al*.	2016	Sheeps	0.40 mg Se/d, SS 1.45 mg Se/d as Sel-Plex	4 weeks	Overall, from a global gene expression (whole-transcriptome) point of view, short-term supplementation of a high dietary organic Se to Se-nondeficient sheep results in a transcriptomic signature that mainly reflects an induced immune system and a modulation of transcription effect. Also, the present study provides a custom whole-transcriptome microarray platform that can be used in further global gene expression studies in the ovine species	[58]
Wang *et al*.	2016	Chicken	5-15 mg/kg	45 days	The excessive Se could result in a decrease in immunity, an increase in oxidative damage, and a series of clinical pathology changes, such as cortex drop, incrassation of the medulla, and degeneration of the reticular cells	[59]
Liu *et al*.	2018	Pigs	0.20 ppm Se 1.0 ppm Se yeast	2 weeks	HS induced oxidative stress and attenuated lipid mobilization in pigs. The short-term supranutritional Se supplementation alleviated hyperthermia but did not protect against oxidative stress in heat-stressed pigs	[41]

H. contortus=*Haemonchus contortus*, LW=Live weight, IM=Intramuscular injection, GPx=Glutathione peroxidase, dl-Se-Met=dl-selenomethionine, Se=Selenium, SS=Sodium selenite, DM=Dry matter, GSH-Px=Glutathione peroxidase, BW=Body weight, IMI= intramammary infection, SCC=somatic cell count, RR=respiration rate, DMI=dry matter intake, NEFA=nonesterified fatty acid, OVA=ovalbumin, SSCs= spermatogonial stem cells, HS=heat stress, NRC=National Research Council

Table 2: Selenium supplementation in clinical trials

Author	Year	Subjects	Patients number	Treatment plan	Control group	Follow up period	Outcome	Reference
Temple *et al*.	2000	Hemodialysis patients	79	28 µg daily	7 µg daily Se served as placebo	14 days	The results of this study indicate that a liquid formula supplemented with Se as selenate is successful at maintaining Se concentrations within normal range, as well as significantly increasing plasma Se levels compared with nonsupplementation	[6]
Zachara *et al*.	2001	Hemodialysis patients	58	300 µg 3 times a week	Placebo	3 months	Se supplementation increased se concentration and GSH-Px activity in blood components. The weak or absence of response in plasma GSH-Px activity to Se supply indicates that the impaired kidney of uremic HD patients has reduced possibilities to synthesize this enzyme	[60]
Zachara *et al*.	2011	Hemodialysis patients	42	200 µg daily	Placebo	3 months	This study shows that in CKD patients on HD, DNA damage in white blood cells is higher than in healthy controls, and Se supplementation prevents the damage of DNA	[61]
Salehi *et al*.	2012	Hemodialysis patients	80	200 µg daily	Placebo	3 month	This study shows that Se may be an effective complementary supplement for reducing the severity of malnutrition in HD patients through alleviating oxidative stress and inflammation	[5]
Sedighi *et al*.	2014	CKD patients	45	200 µg daily	Before intervention patient status	3 months	Plasma Se concentration and RBC GSH-Pxs activity increased significantly in all groups of patients with CKD	[62]
Tonelli *et al*.	2015	Hemodialysis patients	150	50 (low dose) and 75 (medium dose) µg daily	Healthy volunteers	6 months	Supplementation with low or medium doses of zinc and Se did not correct low zinc or Se status in hemodialysis patients	[63]
Omrani *et al*.	2016	Hemodialysis patients	84	Se capsule	Placebo	3 months	Se supplementation had no beneficial effect on lipid profile in hemodialysis patients	[64]
Alehagen *et al*.	2020	Elderly people	589	200 µg daily	Placebo	5 years	Low Se status is related to impaired renal function, and thus supplementation with Se and coenzyme Q10 results in significantly improved renal function	[65]

CKD=Chronic kidney disease, HD=Chronic hemodialysis, RBC=Red blood cell, GSH-Px=Glutathione peroxidase, Se=Selenium

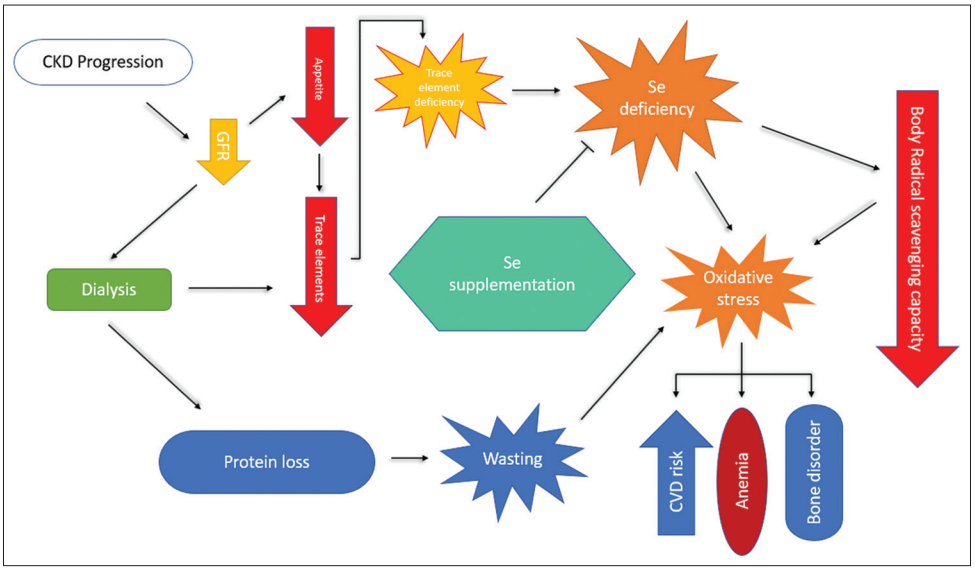

Figure 1: A summary of the role of Se and Se supplementation

Since the complications of ESRD and those of Se deficiency are mostly similar, this triggers the idea that Se deficiency may be considered as a cause of these problems, but it needs to be more assessed that Se deficiency is a single factor or there are other factors participate in.

Hence, strong interventional studies are still necessary to determine whether plasma selenium depletion has adverse effects in CKD patients. Finally, differences in effectiveness between different augmentation therapies have not been compared in the literature.

Authors' Contribution

S. Badri, S. Vahdat, S. Seirafian, and M. Pourfarzam developed the idea of research and criticized the findings. S. Assarzadeh, and S. Ataei searched and recruited the studies. All authors contributed in manuscript preparation and revision.

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Conflicts of interest

There are no conflicts of interest.

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