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# Effect of aerobic exercises on nitric oxide after renal transplantation

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**Abstract**
**Objective:** To assess the therapeutic efficacy of aerobic exercises on nitric oxide after renal transplantation.
**Material and Methods:** Thirteen patients (male or female) who had decreased in renal function (dysfunction of nitric oxide) and were selected randomly from any Hospitals in Cairo, and these patients were randomly subdivided into two equal groups; (15 patients for each):
**Group (A) (Study group):** The study group includes 15 patients who had decreased in renal function (dysfunction of nitric oxide) and their ages were ranged from 30 to 45 years. That group was received aerobic exercises in addition to their routine of medications.
**Group (B) (Control group):** The study group includes 15 patients who had decreased in renal function (dysfunction of nitric oxide) and their ages were ranged from 30 to 45 years. That group was received medications only.All patients All patients were suffered from renal complication (decreased NO). Exclusive criteria were subjects who had other co morbidities which affect results.
**Results:** when comparing the two groups (A and B) before treatment, the mean ± SD values were 27.05 ± 3.91 and 28.49 ± 4.88 respectively which indicated no significant difference (p= 0.382), while comparing the two groups after six weeks of treatment, the mean ± SD values were 38.82 ± 3.66 and 34.98 ± 4.75 respectively which indicated a significant difference (p= 0.02) in favor of group A (MD= 3.84) and % of improvement was 9.89 %.
**Conclusion:** It was concluded that Aerobic exercises had significant effect on nitric oxide after renal transplantation.

**Keywords:** renal transplantation, physical therapy program, nitric oxide, aerobic exercises

## Introduction

Renal transplant recipients are at increased risk of cardiovascular (CV) disease because of an increased prevalence of hypertension, hyperlipidemia, and diabetes. Further, CV disease is the principal cause of death in renal transplant patients (Baum, 2001) [1].

Endothelial dysfunction is an early marker of the atherosclerotic process, is associated with CV risk factors, and has been observed in this population (Hausberg *et al*., 1999) [10].

Studies in intact cells as well as in cellular organelles indicate that nitric oxide modulates mitochondrial respiration, membrane transport and cellular ATP generation (Guilivi *et al*., 1998) [9]. (Garvin and Hong, 1999) [7] showed in renal tubules and isolated renal mitochondria that NO inhibited respiration.

Many studies established that intrarenal NO regulates macrovascular and microvascular including glomerular hemodynamics in the kidney. NOS inhibition decreases basal renal blood flow although preserving auto-regulatory responses (Majid and Navar, 2001) [16].

The protective role of constitutive NO in transplanted kidneys was well documented in several studies (Ishimura *et al*., 2002) [12]. Deficient NO in transplanted kidneys as a result of genetic deficiency of eNOS or NOS inhibitor therapy is associated with hypertension and graft dysfunction. On the other hand, iNOS mediated NO has dual roles with potential for graft dysfunction in the early post-transplant phase mediated by peroxynitrite formation secondary to NOS co-factor deficiency, while iNOS offers renal graft protection in the later phase by suppressing inflammatory cell recruitment and smooth cell proliferation (Vos *et al*., 2000) [20].

A single bout of exercise increases arterial dilatation in animals. (Cheng *et al*., 1999) [4] Demonstrated that exercise acutely enhances receptor-mediated vasodilatation in rats by up regulating either endothelium receptor number or affinity.

Jen *et al*., 2002 reported similar increases in arterial diameter in rats and pigs immediately after exercise and attributed these findings to increases in acetylcholine and NO release. Data on the acute effects of exercise on endothelial vasoreactivity in humans are sparse. Using pulse–wave velocity measurements, reported enhanced arterial compliance 30 minutes after a bout of 30 minutes of exercise in healthy young men (King well *et al*., 1997) [14].

Gattullo and colleagues, 1999 hypothesized that exercise mitigates the vasoconstrictor effects of cardiac risk factors such as hyperlipidemia by stimulating NO synthesis and release in response to acute increases in shear stress and pulse pressure. Finally, Gaenzer *et al*., 2001 demonstrated reduced endothelium–dependent brachial artery vasodilatation in smokers when compared with healthy nonsmokers after a single bout of exercise. Regular exercise is routinely

recommended for renal transplant patients to reduce their CV disease risk (painter, 1999) [18].

There is increasing evidence that nitric oxide (NO) is an important hemodynamic and metabolic regulator during performance of physical activity Furthermore, there are adaptations in this system as a result of exercise training that are likely to contribute to increased functional capacity and the cardio protective effects associated with higher fitness levels. Exercise has particular efficacy in restoring dysfunction of the vascular endothelial NO system, which is becoming established as a precursor to the atherosclerotic process. Recent data also suggest that this benefit may extend to skeletal muscle NO, which appears *inter alia* to mediate glucose uptake during exercise (Bradley *et al*., 1999) [3].

Aerobic exercise has increased work capacity, improved cardio respiratory fitness, enhanced the immune function and brings favourable changes in body mass and body composition, even without dietary restriction. The aerobic conditioning phase of the exercise sessions utilized several modalities; treadmills, lower-extremity ergometers, arm ergometers, combined upper and lower ergometers, were used. Aerobic exercise therapy consisting of a track or treadmill walking, upright or recumbent cycling, rowing, stair-stepping, elliptical trainer exercise, and arm-ergometer training (Belardinelli *et al*., 2008) [2].

## Material and Methods

This study took place at Faculty of Physical Therapy, Cairo University, Cairo, Egypt and during the period between May 2016 to 2017.

### Data Collection

Thirteen patients (male or female) who had decreased in renal function (dysfunction of nitric oxide) and were selected randomly from any Hospitals in Cairo, and these patients were randomly subdivided into two equal groups; (15 patients for each):

**Group (A) (Study group):** The study group includes 15 patients who had decreased in renal function (dysfunction of nitric oxide) and their ages were ranged from 30 to 45 years. That group was received aerobic exercises in addition to their routine of medications.

**Group (B) (Control group):** The study group includes 15 patients who had decreased in renal function (dysfunction of nitric oxide) and their ages were ranged from 30 to 45 years. That group was received medications only.

All patients all patients were suffered from renal complication (decreased NO). Exclusive criteria were subjects who had other co morbidities which affect results. The study was approved by the Institutional Ethics Committee of the Faculty of Physical Therapy, Cairo University, Egypt, and all subjects signed a consent form.

### Instrumentation

**(A) Evaluative equipment**

Blood serum analysis (nitric oxide).

### Therapeutic equipment

Aerobic exercises (electric treadmill).

### Statistical analysis

In this study, the obtained data was recorded on the evaluation sheet. These data was transferred into IBM card using IBM personal computer with statistical program to obtain the following statistical tools:

- **Descriptive statistics**

In this study, the descriptive statistics inform of mean, and standard deviation was calculated for all patients in the three groups of the study to determine the homogeneity and central deviation.

- **Analytic statistics**

In this study, the mean, standard deviation and standard error was calculated for all variables in both groups.

Independent "T" test was used also to compare between pre test and post test in each group.

Comparison was applied by student T test to compare between the independent means.

A value of $p<0.05$ was considered statistically significant

## Results

when comparing the two groups (A and B) before treatment, the mean ± SD values were 27.05 ± 3.91 and 28.49 ± 4.88 respectively which indicated no significant difference (p= 0.382), while comparing the two groups after six weeks of treatment, the mean ± SD values were 38.82 ± 3.66 and 34.98 ± 4.75 respectively which indicated a significant difference (p= 0.02) in favor of group A (MD= 3.84) and % of improvement was 9.89 %.

**Table 1:** Comparing between pre and post treatment mean values of nitric oxide (µmol/L) between the two groups.

| Two Groups | Nitric oxide (µmol/L) | | | |
|---|---|---|---|---|
| | Pre- treatment | | Post- treatment | |
| | Group (A) | Group (B) | Group (A) | Group (B) |
| Mean ± SD | 27.05 ± 3.91 | 28.49 ± 4.88 | 38.82 ± 3.66 | 34.98 ± 4.75 |
| MD | 1.44 | | 3.84 | |
| t-value | 0.89 | | 2.48 | |
| p-value | 0.382 | | 0.02 | |
| Level of Significant | NS | | S | |

Pre: Before application of treatment Post: After six weeks of treatment.

SD: Standard Deviation. MD: Mean Difference.

% of improvement: Percentage of improvement.

T-value: Paired and Un-paired t- test value. P-value: Probability value.

S: Significant NS: Non-Significant.

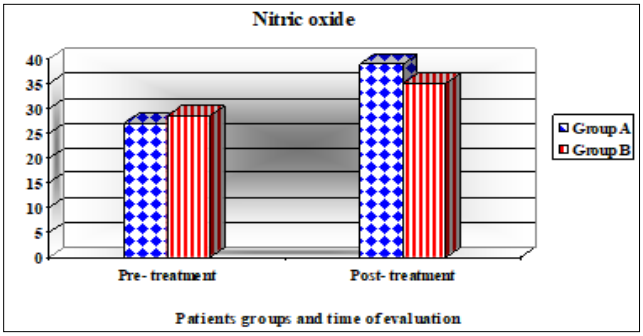

**Fig 1:** Pre and post treatment mean values of nitric oxide (µmol/L) between the two groups.

## Discussion

Renal transplant recipients are at increased risk of cardiovascular (CV) disease because of an increased prevalence of hypertension, hyperlipidemia, and diabetes. Further, CV disease is the principal cause of death in renal transplant patients (Baum, 2001) [1].

Many studies established that intrarenal NO regulates macrovascular and microvascular including glomerular hemodynamics in the kidney. NOS inhibition decreases basal renal blood flow although preserving auto-regulatory responses (Majid and Navar, 2001) [16].

The protective role of constitutive NO in transplanted kidneys was well documented in several studies (Ishimura *et al*., 2002) [12]. Deficient NO in transplanted kidneys as a result of genetic deficiency of eNOS or NOS inhibitor therapy is associated with hypertension and graft dysfunction. On the other hand, iNOS mediated NO has dual roles with potential for graft dysfunction in the early post-transplant phase mediated by peroxynitrite formation secondary to NOS co-factor deficiency, while iNOS offers renal graft protection in the later phase by suppressing inflammatory cell recruitment and smooth cell proliferation (Vos *et al*., 2000) [20].

Physical exercise is another physiological inductor of NO production. During exercise, the increase in shear stress caused by increasing blood flow and muscle contraction-induced distortion of resistance vessels stimulates eNOS and nNOS (Mc Conell *et al*., 2007) [17].

Even though several studies have demonstrated the importance of NO in exercise physiology, none have evaluated its central participation. Furthermore, a study would be important that evaluated the involvement of this neurotransmitter in the antinociceptive effect induced by exercise at the central level, whereas NO is released in different areas of the brain and spinal cord (Forstermann and Sessa, 2012) [5].

Thirteen patients (male or female) who had decreased in renal function (dysfunction of nitric oxide) and were selected randomly from any Hospitals in Cairo, and these patients were randomly subdivided into two equal groups; (15 patients for each):

### Group (A) (Study group)

The study group includes 15 patients who had decreased in renal function (dysfunction of nitric oxide) and their ages were ranged from 30 to 45 years. That group was received aerobic exercises in addition to their routine of medications.

### Group (B) (Control group)

The study group includes 15 patients who had decreased in renal function (dysfunction of nitric oxide) and their ages were ranged from 30 to 45 years. That group was received medications only.

The aim of this study was to investigate the effect of aerobic exercises on nitric oxide after renal transplantation.

The results of present study was agreed with Jen *et al*., 2002 reported similar increases in arterial diameter in rats and pigs immediately after exercise and attributed these findings to increases in acetylcholine and NO release.

The results of present study was agreed with (Bradley *et al*.,

1999) [3] that exercise has particular efficacy in restoring dysfunction of the vascular endothelial NO system, which is becoming established as a precursor to the atherosclerotic process. Recent data also suggest that this benefit may extend to skeletal muscle NO, which appears *inter alia* to mediate glucose uptake during exercise.

There is increasing evidence that nitric oxide (NO) is an important hemodynamic and metabolic regulator during performance of physical activity Furthermore, there are adaptations in this system as a result of exercise training that are likely to contribute to increased functional capacity and the cardio protective effects associated with higher fitness levels (Bradley *et al*., 1999) [3].

The results of present study was agreed with Gattullo and colleagues, 1999 hypothesized that exercise mitigates the vasoconstrictor effects of cardiac risk factors such as hyperlipidemia by stimulating NO synthesis and release in response to acute increases in shear stress and pulse pressure.

The results of present study was agreed with (Husain *et al*., 2002) [11] even though several studies have evidenced that exercise lowers high blood pressure induced by nitric oxide synthase (NOS) inhibition, the effects of chronic exercise on renal HSP70 level, oxidative stress, and antioxidant enzyme activity in a pathological condition similar to compromised endothelium-dependent Furthermore, it has been reported that intense aerobic exercise training is associated with improved NO bioavailability in elderly athletes. In this study, the plasma NOx concentration in the older women increased significantly after the mild exercise training. Thus, it is considered that even mild exercise training could alter the endothelial function in previously sedentary older humans (Taddei *et al*., 2000) [19]. Kingwell *et al*., 1997 [14] showed that 4 weeks of cycle training increased the plasma NOx concentration in humans. Therefore, it is possible that the plasma concentrations of NOx and cGMP are elevated early in the exercise training. However, it is unclear whether the plasma concentrations of NOx and cGMP were increased early in the exercise training in the present study, because plasma NOx and cGMP concentrations may be affected the intensity and/or time of exercise, and/or the age of subjects. The duration of exercise training needed to induce significant alterations of plasma NOx and cGMP concentrations by mild exercise in the elderly remains to be elucidated.

In contrast to short to moderate periods of exercise training, studies over a longer duration have not consistently shown augmented NO-related endothelial function. NO-dependent vasodilatation was unaltered after 16–20 weeks of training in pigs and 16 weeks in rats despite improved arterial compliance (Kingwell *et al.* 1997) [14].

NO-related endothelial function is impaired in these conditions and it is therefore probable that depressed endothelial function is more capable of augmentation by moderate exercise training than is the well preserved function of healthy subjects, which may, however, be improved by more intense training. This theory is supported by findings that regular physical activity may partially reduce the age-related decline in NO-related endothelial function, possibly by reducing the impact of oxidative stress (Taddei *et al.* 2000) [19].

## Conclusion

Finally it was concluded that aerobic exercises had significant effect on nitric oxide after renal transplantation patients.

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