

Synergistic Effect of Tadalafil and L-arginine in Erectile Dysfunction

Introduction

Although the efficacy of tadalafil has been established in erectile dysfunction (ED), a subgroup of patients is refractory. L-arginine is the only physiological substrate of nitric oxide (NO) synthase required for the generation of NO. Several studies have shown that L-arginine is effective in the treatment of men with mild to moderate ED as increased concentrations of l-arginine leads to higher amount of NO. Both tadalafil and l-arginine have been evaluated in combination therapy with many other drugs. However, there is no study which has studied the synergistic effect of both these drugs.

Aim

The study assesses the efficacy and tolerability of tadalafil 5 mg and l-arginine 2.5 gm in monotherapy and combination therapy in patients affected by varying grades of ED.

Method

Study Design

- Multicenter, randomized, prospective study

Patient Profile

- Confirmed diagnosis of ED based on medical history, laboratory analysis and physical examination

Treatment Strategy

- All the patients completed the International Index of Erectile Function - Erectile Function domain (IIEF-EF) and Sexual Encounter Profile diaries completed at baseline and after treatment.
- Cohort was randomized into 2 groups of 100 men each
- Group A received daily l-arginine 2,500 mg, group B received daily tadalafil 5 mg, and group C received both daily L-Arginine 2,500 mg plus daily tadalafil 5 mg for 12 weeks

Endpoints

- Change in IIEF-EF score from baseline
- Per-patient percentage of "yes" responses to Sexual Encounter Profile (SEP) Question 3 from baseline
- Incidence of treatment emergent adverse events (TEAEs)

Results

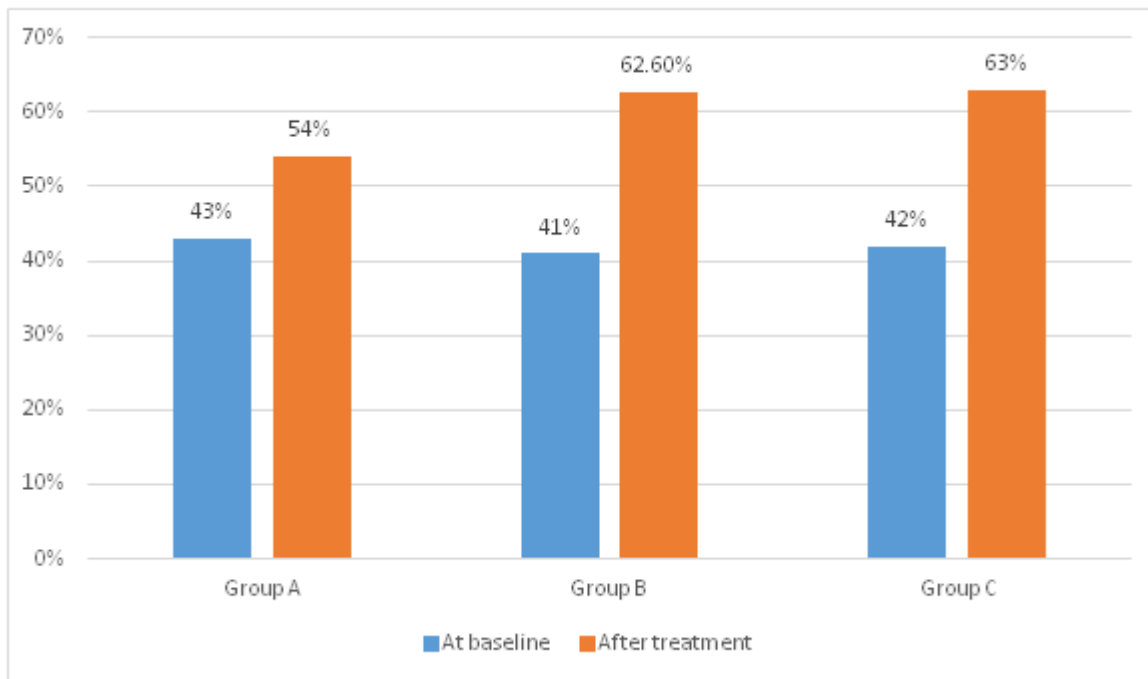
- The patients were graded into mild, moderate and severe ED based on the IIEF-EF score
- The changes in the IIEF-EF scores among the 3 groups are shown in table 1.

Table 1. Overall changes in IIEF -EF scores

	IIEF-EF score at baseline	IIEF-EF score after treatment	Mean change	P value
Overall				
Group A	15±7	18.1±9.2	+3.1	0.0089
Group B	14.8±6.9	20.8±7.3	+6	<0.0001
Group C	14.9±7.1	22±7.5	+7.1	<0.0001
Mild (IIEF-EF score 18- 25)				
Group A	22.1±2.2	27.5±2.3	+5.4	<0.0001
Group B	22.1±2.2	27.8±2	+5.7	<0.001
Group C	22.2±2.2	29.3±0.9	+7.1	<0.0001
Moderate (IIEF-EF score 11-17)				
Group A	13.5±1.9	16±3.1	+2.5	0.001
Group B	13.8±2	20.5±2.2	+6.7	<0.0001
Group C	13.7±2	20.9±3.3	+7.2	<0.0001
Severe (IIEF-EF score 0-10)				
Group A	5.1±2.2	5.2±2.3	+0.1	0.4966
Group B	5.3±2.4	10.2±4.2	+4.9	<0.0001
Group C	5.2±2.3	11.8±3.8	+6.6	<0.0001

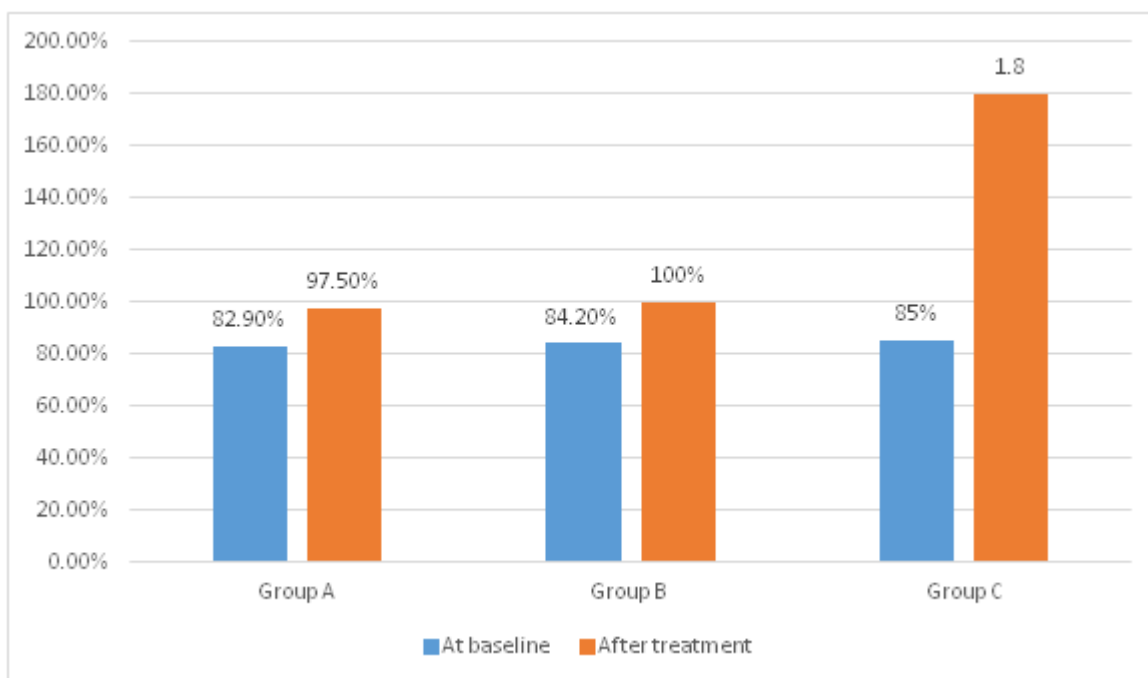
- The percentage of subjects in the overall cohort with 'yes' responses to SEP question 3 are shown in figure 1.

Figure 1. % of patients with 'yes' responses to SEP question 3



- The percentage of patients with mild ED with 'yes' responses to SEP question 3 are shown in figure 2.

Figure 2. % of mild ED patients with 'yes' responses to SEP question 3



- The number of adverse events were 11, 53 and 67 cases in groups A, B and C respectively
- The most common AEs were insomnia in the arginine group with a rate of 5% and dyspepsia in both group B and C reported in the 11% and in the 14% of the survey, respectively.

Conclusion

- The efficacy of l-arginine was comparable to tadalafil in the mild-erectile dysfunction (ED) population with a lower incidence of AEs.

- The patients with moderate ED were benefitted with the addition of arginine. However, arginine did not demonstrate any benefits in severe ED
- Combination therapy with both tadalafil 5 mg and arginine 2.5 grams once a day was superior to monotherapies alone in overall cohort and in patients with mild and severe ED.

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