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LIRAGLUTIDE-DEGLUDEC FIXED DOSE COMBINATION IMPROVES NASH/NAFLD IN PATIENTS WITH UNCONTROLLED TYPE II DIABETES MELLITUS

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Introduction

- Previous studies have demonstrated that standard treatment of diabetes does not cause significant improvement in NAFLD.[1-4]
- GLP-1 analogues improve hepatic insulin signal by acting on adipocytes, muscle, CNS and decreases excessive blood level of FFA (due to adipose tissue insulin resistance).It also decreases apoB-100 synthesis resulting in suppression of VLDL particle production. It also enhances SIRT1-mediated deacetylation of promoter of heat shock protein (HSP) genes, increasing expression of molecular chaperones HSP70 and HSP40 and alleviating hepatic ER stress and lipid accumulation induced by palmitate.[5]
- Therefore, the present study was conducted to evaluate the effects of Liraglutide-Degludec fixed dose combination (FDC) 3.6mg/100 IU on NAFLD with elevated transaminases among patients with type 2 diabetes mellitus (T2DM).

Methodology

- A total of 34 patients (male-13, female-21) with age group of 35-65 years, uncontrolled with oral anti diabetic drugs and basal insulin were included in the study.
- These patients had elevated transaminases and NAFLD.
- Liraglutide-degludec FDC was given along with other oral antidiabetic drugs and standard care.
- Selected clinical and demographic profile and liver fat content were recorded for all patients at both baseline and 24 weeks of treatment.
- The hepatic steatosis was assessed using transient elastography (Fibroscan) as CAP value and MR fat quantification.
- Age, BMI, diabetes duration, FPG, PPG, HbA1c, lipid profile, Microalbuminuria, RFT and LFT were also measured at baseline and every 3 months.
- All adverse events were recorded.
- Statistical Software used: SAS version 9.3 (for windows).

Results

- Total 34 patients data were included in this analysis.
- After a mean study duration of 12 weeks in 34 patients (meeting appropriate preset inclusion criteria), there was significant reduction in weight from 84.3±8.6 kg (Mean ± SD) to 79.1±6.7 kg (reduction of 5.19 ± 6.13; p<0.001), as computed by paired t-test.
- This is accompanied by significant reduction in the liver fat content from a baseline of 346.4±38.2 (Mean ± SD) dB/m to 208.3±24 (a reduction of 138.40 ± 27.8;p<0.001)), as computed by paired t-test.
- There was also significant improvement in glycemic control with reduction in HbA1c from 8.6 ± 0.56% to 7.2 ± 0.34% , p<0.001 as computed by paired t-test.
- The Mc-Nemar's test also demonstrated a significant higher proportion of patients with reversibility of transaminase from baseline to follow-up, p=0.002.

Table 1: Descriptive Statistics

		N	Mean	Std. Deviation	Std. Error Mean	Change
Pair 1	Baseline HbA1c (in %)	34	8.60	.546	.093	-1.4% ± 0.70
	Week 24-HbA1c (in %)	34	7.200	.3490	.059	
Pair 2	Baseline-Liver Fat Content (dB/m)	34	346.70	23.59	4.045	- 138.40 ± 27.8
	Week 24-Liver fat (dB/m)	34	208.30	14.367	2.463	
Pair 3	Baseline Weight (kg)	34	84.30	4.679	.802	- 5.19 ± 6.13
	Week 24-Weight (kg)	34	79.10	4.313	.739	

Table 2: Paired Samples Test Statistics

Change in Study Parameters at the end of Study Period		Paired Differences					t value	df	p. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Baseline HbA1c - Week 24-HbA1c	1.40	0.70	.121	1.153	1.64	11.545	33	<0.001
Pair 2	Baseline-Liver fat Content - Week 24-Liver fat	138.40	27.80	4.76	128.70	148.10	29.027	33	<0.001
Pair 3	Baseline Weight - Week 24-Weight	5.19	6.13	1.05	3.05	7.33	4.938	33	<0.001

	Baseline	Follow-up	Change	P (Mc-Nemar's Test)
Reversibility of Transaminase	34/34	27/34	82%	0.002

Conclusion

1. *Liraglutide-Degludec FDC is effective for reducing hyperglycemia in uncontrolled diabetes.*
2. *It also reduces hepatic steatosis and effectively cause reversal of elevated transaminases as well as weight reduction.*
3. *We recommend liver histology study for efficacy of this FDC in NASH treatment in T2DM.*

References

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