



Diabetes Update

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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"DIABETES UPDATE"** which contains latest and interesting news in the field of Diabetes and Endocrinology.

- Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure: SOLOIST-WHF trial
- SGLT-2 inhibitors and GLP-1 receptor agonists for T2DM: systematic review and network meta-analysis
- Effect of yoga intervention on biochemical, oxidative stress markers, inflammatory markers and sleep quality among subjects with type 2 diabetes

Should you require any specific article or medical information, please feel free to contact us at

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure: SOLOIST-WHF trial

Sodium–glucose cotransporter 2 (SGLT2) inhibitors represent a major therapeutic advance. The safety and potential efficacy of initiating SGLT2 inhibition soon after an episode of decompensated heart failure remain uncertain. Potential safety concerns include the risks of hypotension and precipitation of kidney failure among patients with fluctuating volume status and renal function who are receiving treatment with other drugs that might also affect the glomerular

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filtration rate (GFR). In addition, whether the benefits of SGLT2 inhibition extend to patients with heart failure with preserved ejection fraction remains unknown.

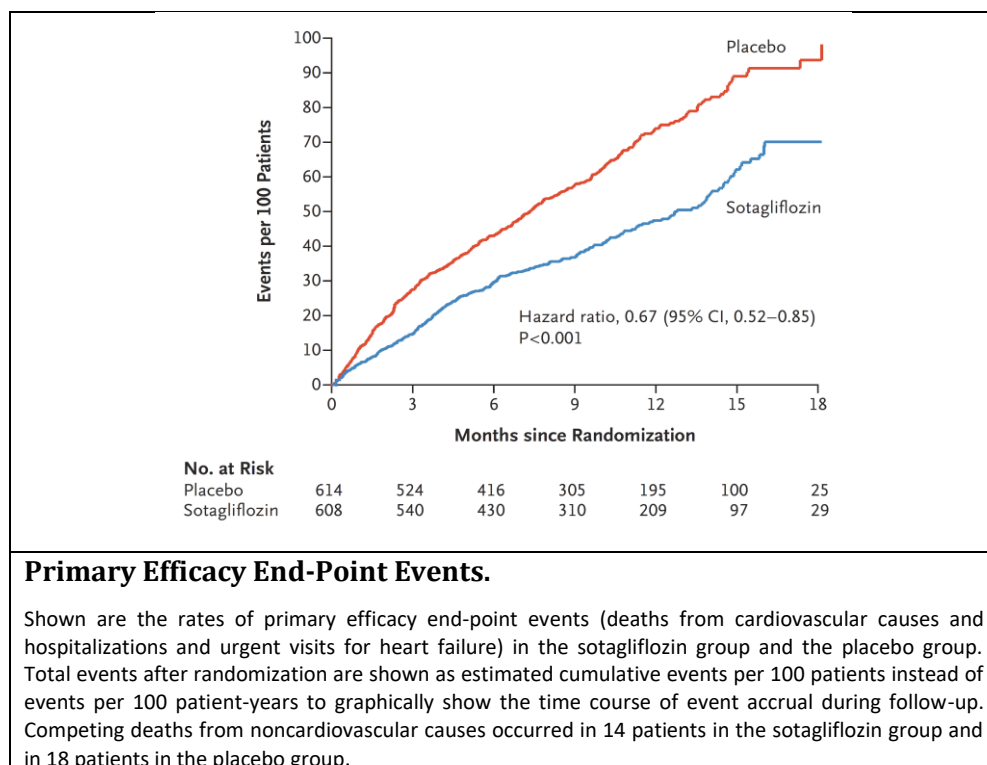
Sotagliflozin on Cardiovascular Events in Patients with Type 2 Diabetes Post Worsening Heart Failure (SOLOIST-WHF) trial was a phase 3, double blind, randomized, placebo-controlled trial in which patients with type 2 diabetes mellitus who were recently hospitalized for worsening heart failure were randomly assigned to receive sotagliflozin or placebo. The primary end point was the total number of deaths from cardiovascular causes and hospitalizations and urgent visits for heart failure (first and subsequent events).

A total of 1222 patients underwent randomization (608 to the sotagliflozin group and 614 to the placebo group) and were followed for a median of 9.0 months; the first dose of sotagliflozin or placebo was administered before discharge in 48.8% and a median of 2 days after discharge in 51.2%. Among these patients, 600 primary end-point events occurred (245 in the sotagliflozin group and 355 in the placebo group). The rate (the number of events per 100 patient-years) of primary end-point events was lower in the sotagliflozin group than in the placebo group (51.0 vs. 76.3; hazard ratio, 0.67; 95% confidence interval [CI], 0.52 to 0.85; $P < 0.001$). The rate of death from cardiovascular causes was 10.6 in the sotagliflozin group and 12.5 in the placebo group (hazard ratio, 0.84; 95% CI, 0.58 to 1.22);

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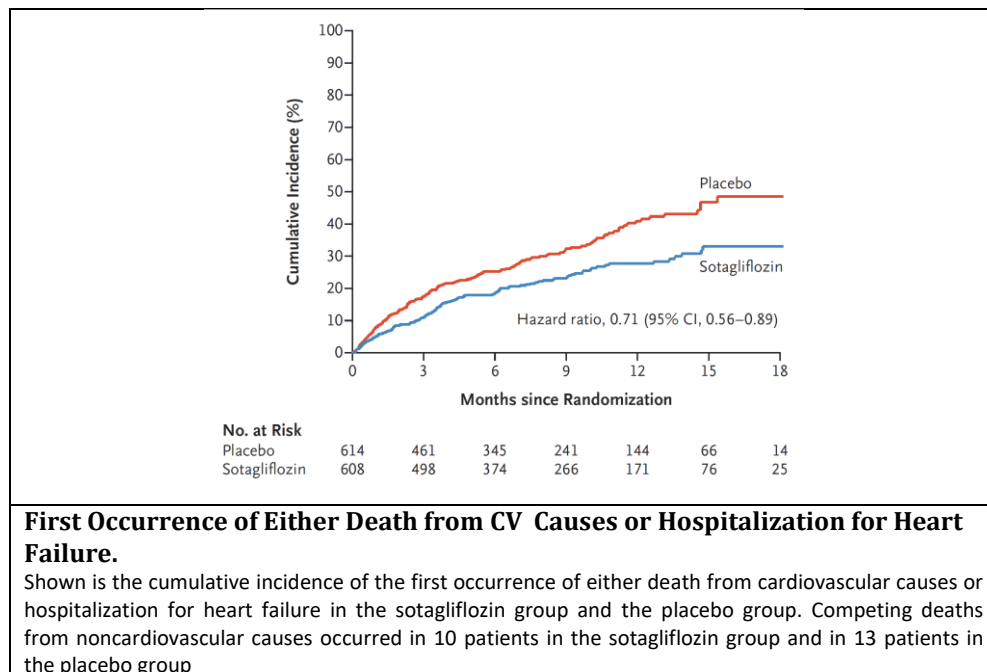
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the rate of death from any cause was 13.5 in the sotagliflozin group and 16.3 in the placebo group (hazard ratio, 0.82; 95% CI, 0.59 to 1.14). Diarrhea was more common with sotagliflozin than with placebo (6.1% vs. 3.4%), as was severe hypoglycemia (1.5% vs. 0.3%). The percentage of patients with hypotension was similar in the sotagliflozin group and the placebo group (6.0% and 4.6%, respectively), as was the percentage with acute kidney injury (4.1% and 4.4%, respectively). The benefits of sotagliflozin were consistent in the prespecified subgroups of patients stratified according to the timing of the first dose.



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Source: Bhatt DL et al. N Engl J Med. 2020 Nov 16. doi: 10.1056/NEJMoa2030183.

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SGLT-2 inhibitors and GLP-1 receptor agonists for T2DM: systematic review and network meta-analysis

Diabetes poses a significant health burden. Recommendations released by the American Diabetes Association include using SGLT-2 inhibitors and GLP-1 receptor agonists in the management of diabetes for people with cardiovascular disease or kidney disease who have not reached their glycaemic target goal.

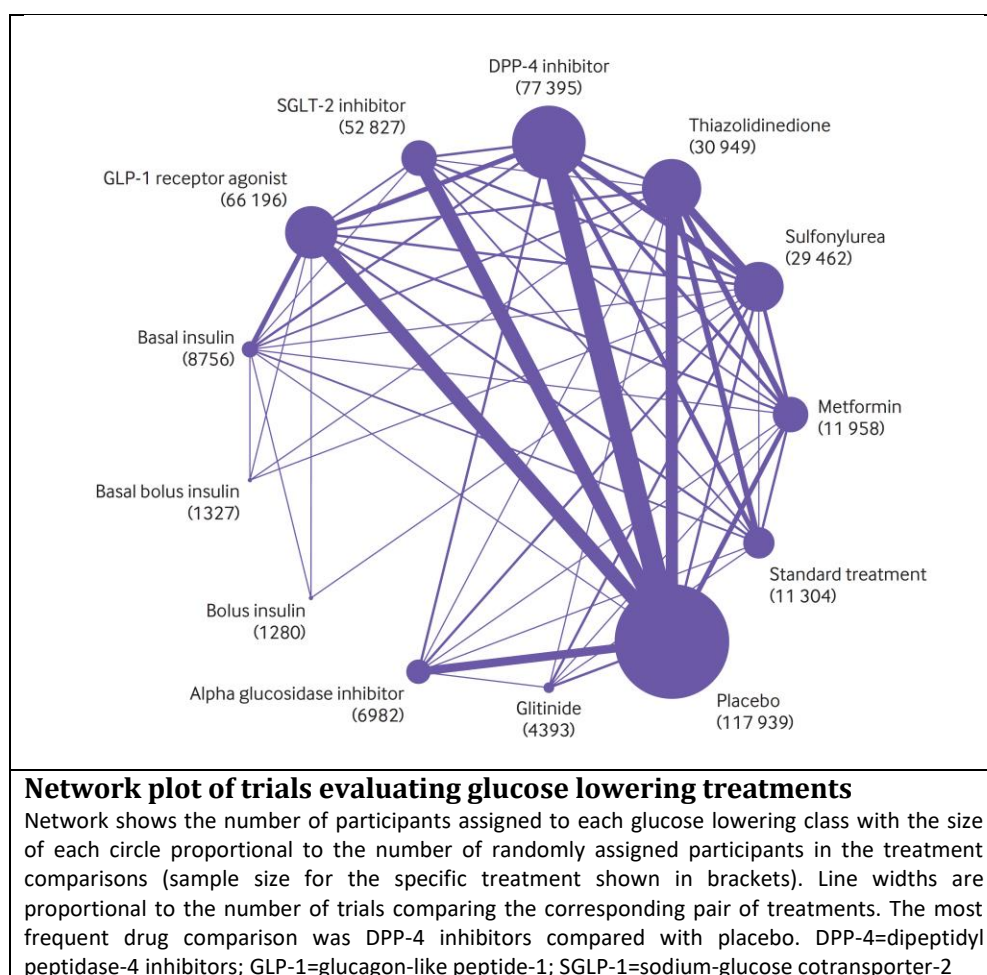
This network meta-analysis evaluate sodium-glucose cotransporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists in patients with type 2 diabetes at varying cardiovascular and renal risk. Randomised controlled trials comparing SGLT-2 inhibitors or GLP-1 receptor agonists with placebo, standard care, or other glucose lowering treatment in adults with type 2 diabetes with follow up of 24 weeks or longer. Studies were screened independently by two reviewers for eligibility, extracted data, and assessed risk of bias.

Frequentist random effects network meta-analysis was carried out and GRADE (grading of recommendations assessment, development, and evaluation) used to assess evidence certainty. Results included estimated absolute effects of treatment per 1000 patients treated for five years for patients at very low risk (no cardiovascular risk factors), low risk (three or more cardiovascular risk factors), moderate risk

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(cardiovascular disease), high risk (chronic kidney disease), and very high risk (cardiovascular disease and kidney disease).



764 trials including 421 346 patients proved eligible. All results refer to the addition of SGLT-2 inhibitors and GLP-1 receptor agonists to existing diabetes treatment. Both classes of drugs lowered all cause

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mortality, cardiovascular mortality, non-fatal myocardial infarction, and kidney failure (high certainty evidence). Notable differences were found between the two agents: SGLT-2 inhibitors reduced mortality and admission to hospital for heart failure more than GLP-1 receptor agonists, and GLP-1 receptor agonists reduced non-fatal stroke more than SGLT-2 inhibitors (which appeared to have no effect). SGLT-2 inhibitors caused genital infection (high certainty), whereas GLP-1 receptor agonists might cause severe gastrointestinal events (low certainty). Low certainty evidence suggested that SGLT-2 inhibitors and GLP-1 receptor agonists might lower body weight. Little or no evidence was found for the effect of SGLT-2 inhibitors or GLP-1 receptor agonists on limb amputation, blindness, eye disease, neuropathic pain, or health related quality of life. The absolute benefits of these drugs vary substantially across patients from low to very high risk of cardiovascular and renal outcomes (eg, SGLT-2 inhibitors resulted in 5 to 48 fewer deaths in 1000 patients over five years).

Six hundred and four trials including 242 745 patients reported glycated haemoglobin A1c during a median follow-up of six months. SGLT-2 inhibitors (mean difference -0.60% (95% confidence interval -0.67 to -0.54); low certainty) and GLP-1 receptor agonists (-0.89% (-0.95 to -0.82); low certainty) might lower glycated haemoglobin A1c levels more than placebo (low certainty). GLP-1 receptor agonists

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reduced glycated haemoglobin A1c levels to a greater extent than SGLT-2 inhibitors (mean difference -0.28% (95% CI -0.37 to -0.19); high certainty).

Comparison	Relative effect (odds ratio (95% CI))
SGLT-2 inhibitor vs placebo	0.77 (0.71 to 0.83)
GLP-1 receptor agonist vs placebo	0.88 (0.83 to 0.94)
SGLT-2 inhibitor v GLP-1 receptor agonist	0.88 (0.79 to 0.98)

Summary of anticipated absolute differences comparing GLP-1 receptor agonist treatment with placebo treatment per 1000 patients with diabetes type 2 and with very low to very high CV risk, treated for five years

Risk*	All cause mortality	Cardiovascular mortality	Non-fatal myocardial infarction	Non-fatal stroke	Kidney failure	Hospital admission for heart failure	Body weight	Diabetic ketoacidosis	Serious hyperglycaemia	Genital infection
Very low	2 fewer (4 fewer to 1 fewer) ⊕⊕⊕	0 fewer (2 fewer to 1 more) ⊕⊕⊕	1 fewer (4 fewer to 2 more) ⊕⊕⊕	5 more (1 more to 10 more) ⊕⊕⊕	0 (1 fewer to 0) ⊕⊕	1 fewer (2 fewer to 1 fewer) ⊕⊕⊕				
Low	7 fewer (12 fewer to 2 fewer) ⊕⊕⊕⊕	2 fewer (6 fewer to 4 more) ⊕⊕⊕⊕	3 fewer (8 fewer to 4 more) ⊕⊕⊕⊕	9 more (1 more to 19 more) ⊕⊕⊕⊕	1 fewer (2 fewer to 2 more) ⊕⊕⊕	7 fewer (10 fewer to 4 fewer) ⊕⊕⊕⊕				
Moderate	12 fewer (21 fewer to 3 fewer) ⊕⊕⊕⊕	3 fewer (11 fewer to 6 more) ⊕⊕⊕⊕	5 fewer (15 fewer to 7 more) ⊕⊕⊕⊕	16 more (2 more to 33 more) ⊕⊕⊕⊕	1 fewer (5 fewer to 3 more) ⊕⊕⊕	18 fewer (25 fewer to 11 fewer) ⊕⊕⊕⊕	0.47 kg lower (0.09 lower to 0.85 lower) over 6 months ⊕⊕⊕	1 more (0 to 3 more) ⊕⊕⊕	5 more (2 fewer to 19 more) ⊕⊕⊕	158 more (64 more to 299 more) ⊕⊕⊕⊕
High	16 fewer (28 fewer to 4 fewer) ⊕⊕⊕⊕	4 fewer (15 fewer to 8 more) ⊕⊕⊕⊕	5 fewer (16 fewer to 8 more) ⊕⊕⊕⊕	18 more (3 more to 36 more) ⊕⊕⊕⊕	6 fewer (21 fewer to 13 more) ⊕⊕⊕	24 fewer (32 fewer to 13 fewer) ⊕⊕⊕⊕				
Very high	23 fewer (40 fewer to 6 fewer) ⊕⊕⊕⊕	5 fewer (22 fewer to 12 more) ⊕⊕⊕⊕	7 fewer (24 fewer to 11 more) ⊕⊕⊕⊕	27 more (4 more to 53 more) ⊕⊕⊕⊕	10 fewer (34 fewer to 20 more) ⊕⊕⊕⊕	48 fewer (66 fewer to 27 fewer) ⊕⊕⊕⊕				

*Risk categories represent the following patient populations: very low=no or less than three cardiovascular risk factors; low=three or more cardiovascular risk factors; moderate=cardiovascular disease; high=chronic kidney disease (reduced glomerular filtration rate or macroalbuminuria); very high=cardiovascular disease and chronic kidney disease. Certainty of the evidence for each estimate is shown: high certainty ⊕⊕⊕⊕; moderate certainty ⊕⊕⊕⊕; low certainty ⊕⊕; very low certainty ⊕.

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This network meta-analysis provides evidence of the absolute benefits and harms of SGLT-2 inhibitors and GLP-1 receptor agonists. The balance of benefits and harms depends on individual risk profiles of patients, and thus the results support a risk stratified approach for provision of SGLT-2 inhibitors and GLP-1 receptor agonists to patients with type 2 diabetes.

Source: Palmer SC et al.. BMJ. 2021 Jan 13;372:m4573. doi: 10.1136/bmj.m4573.

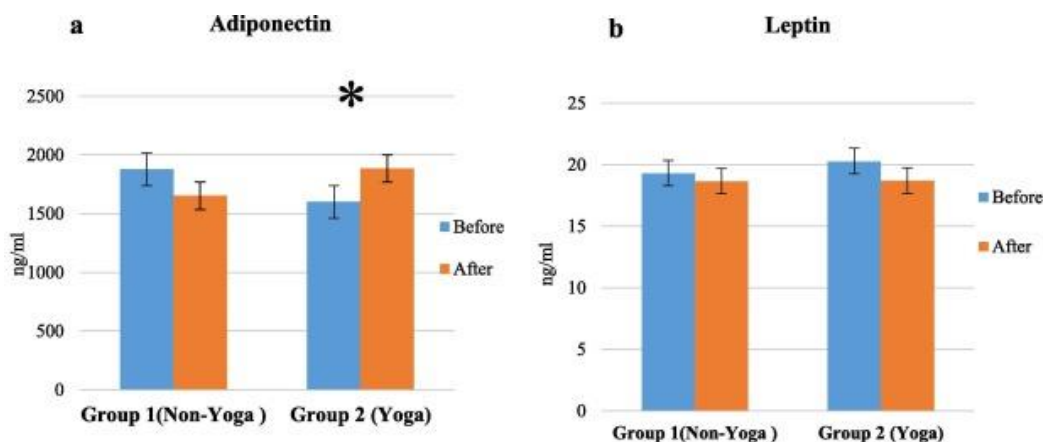
Effect of yoga intervention on biochemical, oxidative stress markers, inflammatory markers and sleep quality among subjects with type 2 diabetes

An increasing number of people have been diagnosed with type 2 diabetes mellitus (T2DM) with social and economic development. scientific evidence suggests the potential role of yoga-based lifestyle modifications in the management of type 2 diabetes and its associated risk factors. It is suggested that psychoneuro-endocrine and immune mechanisms have holistic effects in diabetes control.

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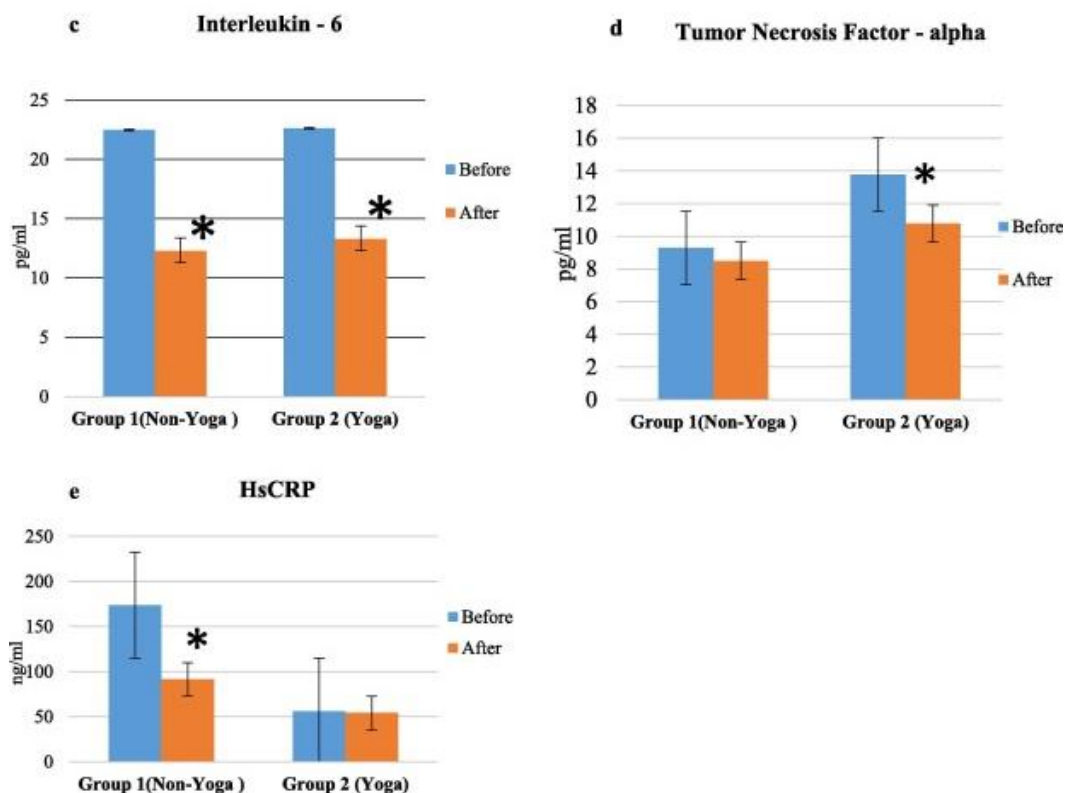
The aim of this study was to investigate the effect of yoga intervention on the biochemical, oxidative stress markers and inflammatory markers and sleep quality among subjects with type 2 diabetes. Subjects with type 2 diabetes attending a tertiary care centre for diabetes during Feb 2017 to Oct 2019 were randomly assigned to two different groups. Group1(non-Yoga) (n = 150) was advised on simple physical exercises whereas group2 (Yoga) (n = 150) was trained and advised to do yogasanas with static loosening exercises for 50 min for 5 days in a week. Both the groups were followed up for a period of 3 months. Anthropometric, biochemical, oxidative stress markers, inflammatory markers and sleep quality were assessed at baseline and after follow up.



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There was a significant reduction in BMI, blood glucose levels, HbA1c, lipid levels, IL6, TNF α and TBARS in Yoga group as compared to non-Yoga group. There was marked improvement in the levels of Adiponectin, PTGIS and sleep quality among subjects practising yogasanas.



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Yoga practices such as cleansing processes, asanas, pranayama, mudras, bandha, meditation, mindfulness, and relaxation are known to reduce blood glucose levels and to help in the management of comorbid disease conditions associated with type 2 diabetes mellitus, resulting in significant positive clinical outcomes. This study also emphasized that regular practice of yogasanas improved glycaemic control, oxidative stress, inflammatory response and sleep quality among subjects with type 2 diabetes. Hence, Yogasanas can be used as an adjuvant therapy for managing type 2 diabetes.

Source: Viswanathan V et al. Diabetes Res Clin Prac. 2021 Feb. 172: 108644



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