

# THE EFFECT OF EXENATIDE TREATMENT ON SERUM GHRELIN LEVELS IN PATIENTS WITH TYPE 2 DIABETES.

Figen TOPYILDIZ\*, Sinem KIYICI\*, Zulfiye GUL\*\*, Deniz SIGIRLI\*\*\*, Metin GUCLU\*, Gurcan KISAKOL\*, Sinan CAVUN\*\*

\*Sevket Yilmaz Education and Research Hospital, Department of Internal Medicine, Bursa, Turkey.

\*\*Uludag University Medical Faculty, Department of Pharmacology, Bursa, Turkey.

\*\*\*Uludag University Medical Faculty, Department of Bio-Statistics, Bursa, Turkey.

## OBJECTIVES

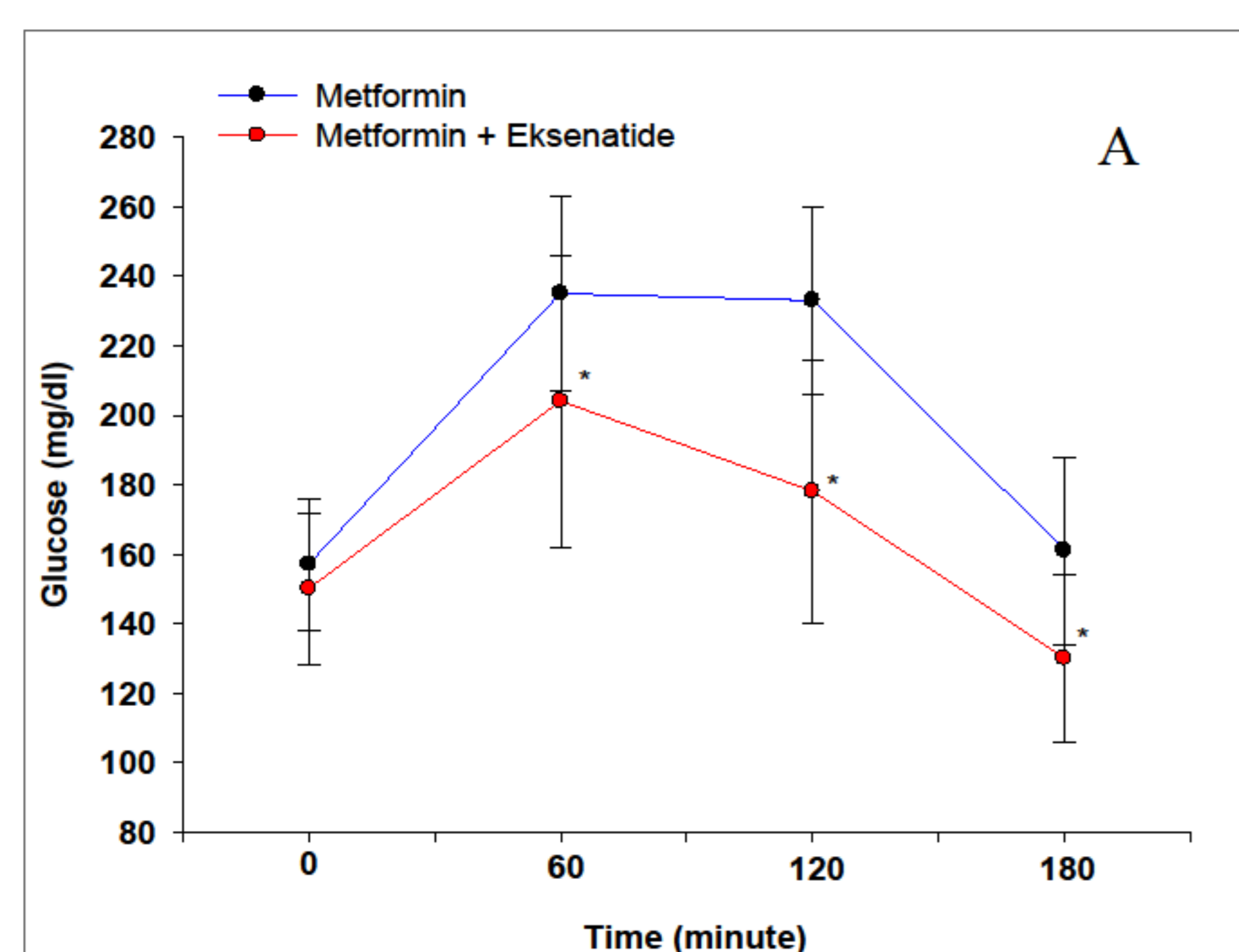
Ghrelin, an orexigenic peptide mainly produced in the stomach, play also an important role in stimulation of food intake and long-term regulation of body weight (1). Exenatide is an agonist of GLP-1 receptor which is being used in the treatment of type 2 diabetes and promotes weight loss as well as glycemic control (2). How exenatide promotes weight loss is not clearly understood. In present study we aimed to investigate the effect of exenatide treatment on serum ghrelin levels in patients with type 2 diabetes.

## METHODS

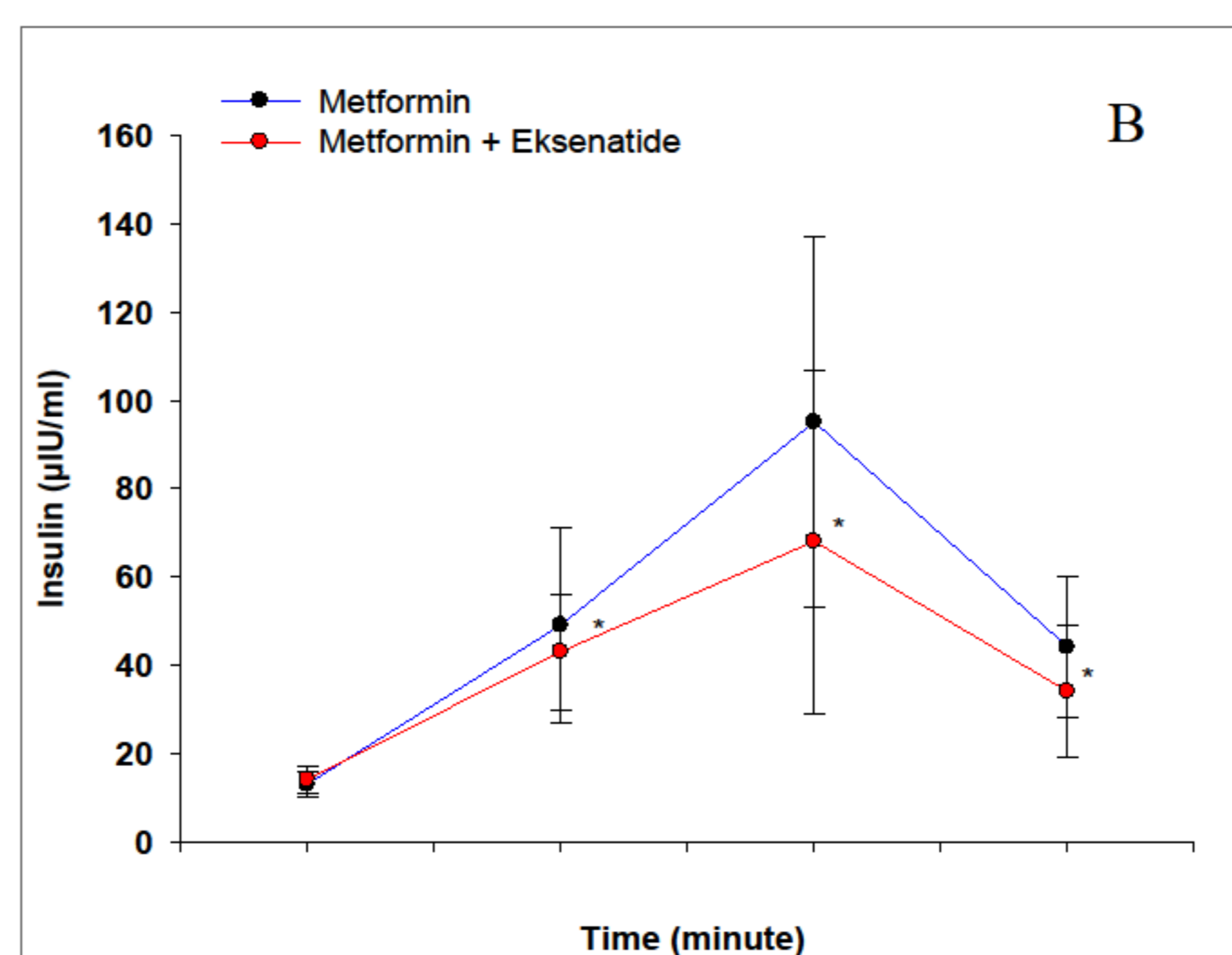
Fourteen women patients with type 2 diabetes treated with metformin and exenatide were enrolled in the study. A mixed meal test was applied to the patients after a 8-12 hour fasting period while they are using their daily medications. Venous blood samples were taken before (0<sup>th</sup> minute) and 60<sup>th</sup>, 120<sup>th</sup> and 180<sup>th</sup> minutes after mixed meal test for the measurement of serum total ghrelin, glucose and insulin levels. On the following week exenatide treatment of the patients was paused 24 hours and same experimental procedures were repeated.

## RESULTS

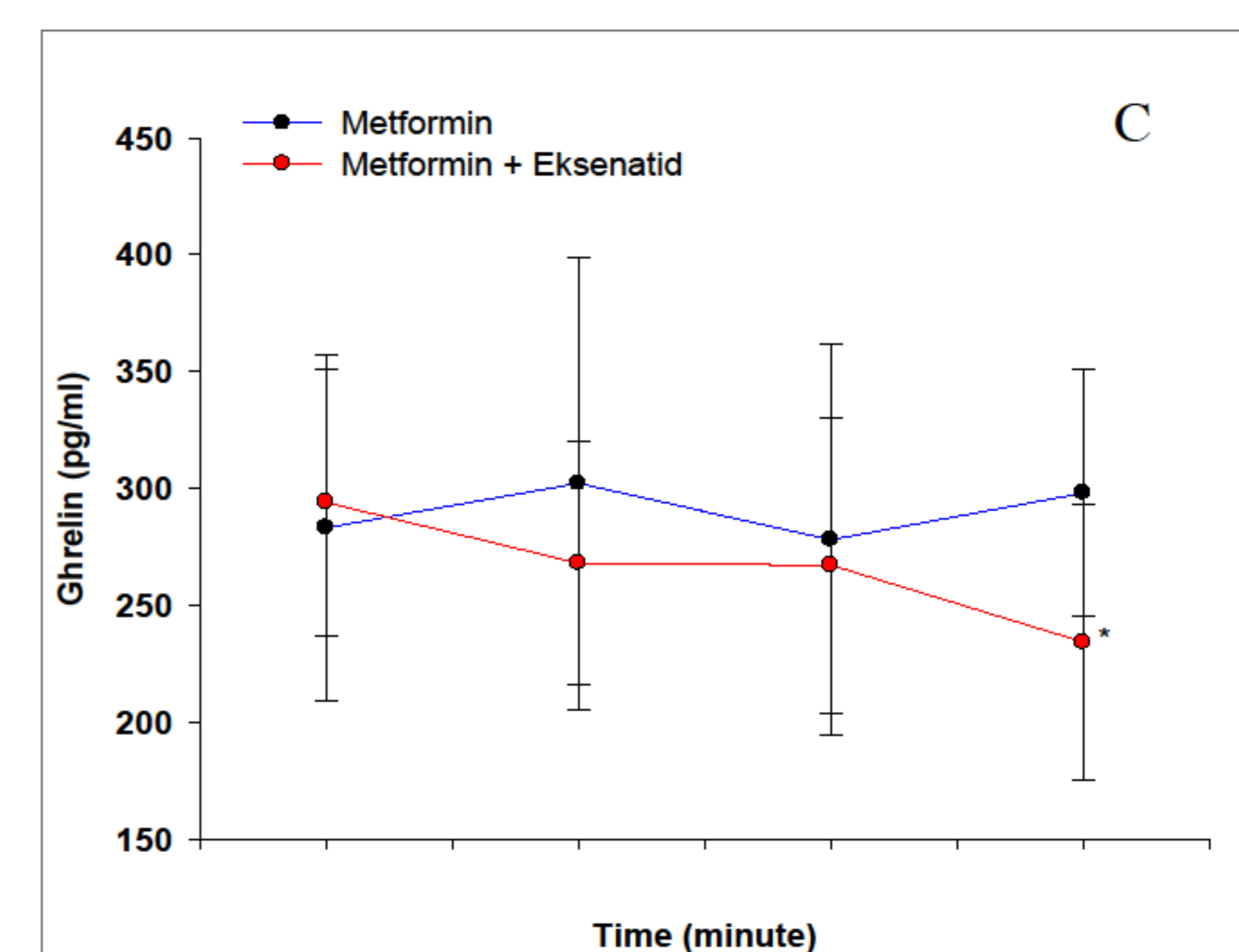
Percentage change in serum glucose and insulin levels after the mixed meal test were found significantly suppressed with exenatide treatment while compared with the skipped exenatide treatment (figure A and B;  $p < 0.05$ ). Serum ghrelin levels were found suppressed significantly at the 60<sup>th</sup> and 180<sup>th</sup> minutes compared with baseline values after mixed meal test with exenatide treatment ( $p = 0.042$  and  $p = 0.000$ ; respectively). While percentage change in serum ghrelin levels after mix meal tests with and without exenatide usage were compared, no significant difference was found at the 60<sup>th</sup> and 120<sup>th</sup> minutes. But percent changes in serum ghrelin levels at the 180<sup>th</sup> minute was statistically significant ( $p = 0.001$ ) (figure C).



**Figure A:** Serum glucose levels with and without exenatide treatment after the mixed meal test. \*=  $p < 0.05$  when the two groups were compared



**Figure B:** Serum insulin levels with and without exenatide treatment after the mixed meal test. \*=  $p < 0.05$  when the two groups were compared



**Figure C:** Serum ghrelin levels with and without exenatide treatment after the mixed meal test. \*=  $p < 0.05$  when the two groups were compared

## CONCLUSIONS

In present study we found that exenatide treatment suppresses serum ghrelin levels for longer time compared with the results of skipped exenatide treatment. These results suggest that the effect of exenatide on weight loss may be related with prolonged suppression of serum ghrelin levels, which is an orexigenic peptide.

## References

1. Nakazato M, Murakami N, Date Y, Kojima M, Matsuo H, Kangawa K, Matsukura S. A role for ghrelin in the central regulation of feeding. *Nature* 2001;409(6817):194-8.
2. DeFronzo RA, Ratner RE, Han J, Kim DD, Fineman MS, Baron AD. Effects of exenatide (exendin-4) on glycemic control and weight over 30 weeks in metformin-treated patients with type 2 diabetes. *Diabetes Care*; 28(5):1092-100.

