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Increase in deaths in men with type 2 diabetes and testosterone deficiency may be prevented by testosterone replacement

A new study on men with type 2 diabetes shows that those with low levels of testosterone may die sooner unless they are given testosterone replacement therapy. The findings will be presented today at the Society for Endocrinology annual meeting in Birmingham by Professor Hugh Jones (Barnsley Hospital NHS Foundation Trust and the University of Sheffield).

Professor Jones' team conducted a six year study of 587 men with type 2 diabetes, splitting them into three groups: those with normal total testosterone levels (above 10.4nmol/L, n=338), those with low testosterone levels (below 10.4nmol/L) that weren't treated with testosterone replacement therapy (n=182), and those with low testosterone levels treated with testosterone replacement therapy for two years or more during the follow up period (n=58).

The findings show for the first time that low testosterone puts diabetic men at a significantly increased risk of death ($p=0.001$ log rank): 36 of the 182 diabetic men with untreated low testosterone died during the six year study, compared to 31 of the 338 men with normal testosterone levels (20% vs 9%). Furthermore, only 5 of the 58 diabetic men that were given testosterone replacement therapy died during the study (8.6%), meaning they showed significantly better survival compared to the non-treated group ($p=0.049$ log rank).

This is the first study to show testosterone treatment can improve survival in men with type 2 diabetes and testosterone deficiency. Further studies now need to be carried out to fully investigate the potential therapeutic benefit of testosterone replacement in diabetic men with low testosterone.

Professor Hugh Jones, Consultant Endocrinologist and Hon. Professor of Andrology, Barnsley Hospital NHS Foundation Trust and the University of Sheffield, said:

"This is potentially a very exciting finding. Whilst we have shown that low testosterone levels can put diabetic men at greater risk of dying, we have also demonstrated for the first time the potential benefit that testosterone replacement therapy holds for this group of patients.

"It is well known that men with type 2 diabetes often have low testosterone levels, so it is important that we investigate the health implications of this. We now need to carry out a larger clinical trial to confirm these preliminary findings. If confirmed, then many deaths could be prevented every year."

In another study, also presented at this year's Society for Endocrinology meeting, Professor Jones' group found for the first time that low testosterone and severity of erectile dysfunction are independently associated with a reduced health-related quality of life in men with type 2 diabetes. Health-related quality of life questionnaires, such as the one used in this study, measure how a person perceives their own general health in areas such as physical and social functioning, vitality and pain. The questionnaire does not measure how good a person's health actually is; it measures how good a person thinks their health is in daily life.

In the 356 men with type 2 diabetes tested, health related quality of life decreased as testosterone levels decreased ($r=0.353$ $p=0.044$). In the 126 patients who were also assessed for erectile dysfunction, health-related quality of life decreased in the areas including physical functioning ($r=0.5$, $p=0.003$), social functioning ($r=0.445$, $p=0.022$) vitality ($r=0.383$, $p=0.025$) and pain ($r=0.428$, $p=0.012$) as the severity of erectile dysfunction increased. Although severity of erectile dysfunction has been shown to be associated with lower testosterone levels, statistical analysis shows for the first time that these are both independently associated with a reduced health-related quality of life in these men.

Lead researcher Prof Hugh Jones said:

"Our research shows that low testosterone impacts on health-related quality of life in men with type 2 diabetes. This finding supports previous evidence suggesting that erectile dysfunction is a marker of ill health.

"Our next step is to assess whether offering testosterone replacement therapy to diabetic men with testosterone deficiency and erectile dysfunction may help to improve their health related quality of life."

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Notes for editors:

This research will be presented as two posters (P163 and P152) at the Society for Endocrinology BES meeting on Tuesday 12 April 2011 between 1200 and 1400. The abstracts for these posters are reproduced at: <http://www.endocrine-abstracts.org/ea/0025/ea0025p163.htm> (P163) and <http://www.endocrine-abstracts.org/ea/0025/ea0025p152.htm> (P152).

The Society for Endocrinology BES 2011 conference is Britain's biggest scientific meeting on hormones, and is taking place at the Birmingham ICC from 11-14 April 2011. For the full programme, please see <http://www.endocrinology.org/meetings/2011/sfebes2011/prog/prog.aspx>.

Please mention the Society for Endocrinology meeting in any story

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ABSTRACT 1

Low testosterone predicts increased mortality and testosterone replacement therapy improves survival in men with type 2 diabetes

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Background: Low testosterone in men is associated with increase in all-cause and cardiovascular mortality. There is a high prevalence of hypogonadism in men with type 2 diabetes and testosterone replacement therapy (TRT) improves cardiovascular risk. However there is no published data regarding mortality in these patients in relation to testosterone levels, and the long term effect of TRT on mortality.

Aim: We report a 6 year follow-up study examining the effect of baseline testosterone and TRT in hypogonadal men with type 2 diabetes on all-cause mortality.

Methods: 587 patients with type 2 diabetes had total testosterone (TT) performed between 2002 and 2005 and were followed up for 5.8±1.3 years.

Deaths during the first 6 months were excluded. Patients were then analysed in three groups. (1) normal TT (>10.4nmol/l) (2) low TT (≤10.4nmol/L) without TRT.(3) low TT receiving TRT for 2 years or more.

Results: Of 580 patients analysed, 338 had normal TT (58%) and 240 low TT (42%). In the low TT group 58 patients received TRT. Mean age 61±11SD and similarly matched in all three groups. Total deaths 72(12.4%). Mortality rates - low TT without treatment (36/182-20%), normal TT (31/338-9%) and low TT with TRT (5/58-8.6%). Survival was significantly decreased in patients with low TT without TRT (p=0.001 log rank) compared to normal. The treated group had improved survival (p=0.049 log rank). In the Cox Regression model multi-variate (age, weight, HbA1c, pre existing cardiovascular disease, smoking, statin and ACEi/ARB use) adjusted hazard ratio for all-cause mortality was 2.2 (95%CI 1.3-3.7 p=0.001) for low TT.

Conclusions: This study shows that men with type 2 diabetes and low testosterone have a significant increased mortality. TRT improved survival compared to those untreated, recording a similar mortality rate to the normal TT group.

ABSTRACT 2

Low testosterone and severity of erectile dysfunction (ED) are independently associated with poor health related quality of life (HRQoL) in men with type 2 diabetes

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Introduction: Both low testosterone levels and erectile dysfunction (ED) are highly prevalent in men with Type 2 diabetes. Lower testosterone levels are known to be associated with worsening severity of ED as assessed using the International Index of Erectile Function score (IIEF). Testosterone deficiency and erectile dysfunction are both independently correlated with increased risk of cardiovascular disease.

Aim: To investigate the effect of low testosterone and erectile dysfunction on Health-Related Quality of Life (HRQoL) in a cohort of 356 men with Type 2 diabetes.

Method: Total testosterone (TT), bioavailable testosterone (BT) and SHBG levels were analysed from morning blood samples. Free testosterone (cFT) levels were calculated using Vermeulen's equation. SF-36 scores were obtained from 356 patients, of whom 126 completed IIEF questionnaires. Data were analysed using PASW software. Local Ethical Committee approval was obtained.

Results: Mean baseline characteristics were: age 58.5 (± 8.1), TT 12.17nmol/L (± 5.86), BT 3.84nmol/L (± 1.64), cFT 260pmol/L (± 0.14). Mean SF-36 score was 67.7 (± 17.3) and mean IIEF score was 12.16 (± 4.29).

Regression analyses were carried out correcting for age, BMI, HbA_{1c}, smoking, alcohol consumption and cardiovascular disease.

Total testosterone levels significantly correlated with HRQoL scores ($r=0.353$, $p=0.044$, $n=356$) when corrected for SHBG.

In the 126 patients who completed IIEF questionnaires, IIEF scores significantly correlated with total SF-36 scores ($r=0.491$, $p=0.003$). IIEF scores also correlated with SF-36 domains: Physical ($r=0.500$, $p=0.003$), Physical role limitations ($r=0.350$, $p=0.031$), Social ($r=0.445$, $p=0.022$), Vitality ($r=0.383$, $p=0.025$), Pain ($r=0.428$, $p=0.012$), and General health ($r=0.408$, $p=0.001$). IIEF scores significantly correlated with levels of TT ($r=0.546$, $p<0.001$), BT ($r=0.506$, $p=0.004$) and cFT ($r=0.532$, $p<0.001$). TT was corrected for SHBG in addition to the above factors.

Conclusion: This is the first study to report that lower testosterone and severity of erectile dysfunction are both independently associated with reduced quality of life in diabetic men.