Abstract
This study is aimed to determine the correlation between fasting glucose level, erectile dysfunction, and lower urinary tract symptoms (LUTS) in patients diagnosed with benign prostatic hyperplasia (BPH). We enrolled patients with BPH-related LUTS aged over 50 years old. LUTS and erectile dysfunction (ED) were evaluated using International Prostate Symptom Score (IPSS) and International Index of Erectile Function-5 (IIEF-5). Diabetes mellitus was established if fasting glucose level was above 126mg/dL. Forty-two patients were enrolled in this study from outpatient clinic in Kardinah Hospital, Tegal during January–March 2015. Patients' mean age was 68.8±8.6 years old with most of them suffered from ED (83.3%) and also suffered from severe LUTS (80.96%). Mean fasting glucose level was 108.3±21.1 mg/dl. However, diabetes mellitus was observed in 26.2% subjects with mean fasting glucose level was 136.8±7.8mg/dl. IPSS score was correlated with fasting glucose level (r=0.879, p<0.001) and IIEF-5 score (r=-0.346, p=0.025). IIEF-5 score showed negative correlation with age (r=-0.31, p=0.046) and fasting glucose level (r=-0.305, p=0.049). Higher fasting glucose level in a man older than 50 years with BPH would increase severity of LUTS and ED.

Keywords: Diabetes mellitus; lower urinary tract symptoms; erectile dysfunction

Korelasi antara Glukosa Darah Puasa, Disfungsi Ereksi, dan Gejala Saluran Kemih Bagian Bawah pada Pasien Benign Prostatic Hyperplasia

Abstrak
Penelitian ini bertujuan untuk mengetahui hubungan antara nilai glukosa darah puasa, disfungsi ereksi (DE), dan gejala saluran kemih bagian bawah (LUTS) pada pasien dengan pembesaran prostate jinak/benign prostatic hyperplasia (BPH). Subjek adalah pasien berusia lebih dari 50 tahun dengan pembesaran prostat jinak di RS Kardinah, Tegal pada bulan Januari-Maret 2015. LUTS dan DE dievaluasi dengan menggunakan International Prostate Symptom Score (IPSS) dan International Index of Erectile Function-5 (IIEF-5). Diabetes mellitus ditegakkan jika gula darah puasa lebih dari 126mg/dL. Terdapat 42 pasien yang dilibatkan dalam penelitian ini dengan usia rata-rata pasien 68,8±8,6 tahun, mayoritas menderita DE (83,3%) dan LUTS (80,96%). Rata-rata gula darah puasa 108,3±21,1mg/dl. Diabetes mellitus ditemukan pada 26,2% pasien dengan rata-rata nilai gula darah puasa 136,8±7,8mg/dl. Nilai IPSS berhubungan dengan nilai gula darah puasa (r=0,879, p<0,001) dan nilai IIEF-5 (r=-0,346, p=0,025). Nilai IIEF-5 menunjukkan hubungan negatif dengan usia (r=-0,31, p=0,046) dan gula darah puasa (r=-0,305, p=0,049). Disimpulkan peningkatan kadar gula darah puasa pada laki-laki dengan BPH berusia 50 tahun ke atas meningkatkan derajat keparahan dari LUTS dan DE.

Kata kunci: Diabetes mellitus; gejala saluran kemih bagian bawah; disfungsi ereksi
Introduction

The increased life expectancy in developing countries leads to increased number of age-related diseases in geriatric population. One of age-related diseases that decrease patients’ quality of life is benign prostatic hyperplasia (BPH). It is accompanied with urinary symptoms known as lower urinary tract symptoms (LUTS). Prostate enlargement is not only causing discomfort due to urinary problems, but also establish a vicious circle of quality of life due to anxiety, mental stress, and interpersonal issues related to LUTS and erectile dysfunction (ED).1,2 Beside positive correlation between the manifestation of LUTS and ED, diabetes mellitus also believed to have correlation to the occurrence of LUTS and ED.3

The exact pathogenesis about the correlation between LUTS and ED is not fully understood. However, there are some theories such as; 1) change in nitric oxide (NO)-cyclic guanosine monophosphate (cGMP) pathways, 2) RhoA-Rho-kinase (ROCK) signal enhancement, 3) autonomic hyperactivity, and 4) pelvic atherosclerosis.4 However, it is believed that any pathologic condition in blood vessels and neurological defect that are related to disruption of NO production will lead to the occurrence of LUTS and ED.5

As men grow older, the prevalence of LUTS and ED are increasing about 31.2% and 51.1% respectively. The increased of their prevalence are believed to be related to multifactorial condition caused by degeneration process such as metabolic syndromes, diabetes, and hypogonadism. However, type 2 diabetes alone is associated with LUTS and ED in men aged less than 45 years old.5,4

Our study aimed to discover the correlation between fasting glucose level, erectile dysfunction, and LUTS in patients diagnosed with benign prostatic hyperplasia (BPH).

Methods

A total of 42 patients aged over 50 years old who were admitted to outpatient clinic in Kardinah Hospital, Tegal due to BPH-related LUTS were enrolled in this study from January – March 2015. The inclusion criteria were men aged 50 years or above with LUTS due to BPH. We excluded patients with a history of treatment for LUTS and/or ED, genital defect, psychological issues, history of major surgical intervention in pelvic region, and non-BPH LUTS. Written informed consents were obtained from all participants and study protocols were approved by ethics committee of Kardinah Hospital, Tegal.

All patients who fulfilled the inclusion and exclusion criteria were included in the study. Body height, weight, blood pressure, and fasting blood glucose level of all the participants were measured and recorded. LUTS and ED were evaluated with International Prostate Symptom Score (IPSS) and International Index of Erectile Function-5 (IIEF-5). The diagnosis of diabetes mellitus was established if patient's fasting glucose level was above 126mg/dL. LUTS was classified into 3 groups; mild, moderate, and severe LUTS with the IPSS of 0-7, 8-19, and >19 respectively and ED was classified into 2 groups; ED positive and ED negative with the IIEF-5 score of 5-21 and >21 respectively.

Statistical analysis was performed using IBM SPSS® version 22 software. Pearson and spearman correlation coefficients were used to analyze the correlation between fasting glucose level, IPSS, and IIEF-5. Statistical significance was stated as p<0.05.

Results

Demographic and Characteristics of the Participants

Mean age of all participants was 68.8±8.6 years old with the average of body mass index (BMI) was 20±3kg/m² and mean prostate volume of 44.3±14.7mL. Half of the participants were suffering from hypertension. Most patients were suffering from severe LUTS (81%) followed by moderate LUTS (19%) with the mean of IPSS was 24.5±6.1. ED was observed in 83.3% with the mean IIEF-5 score was 14.8±6.7. Diabetes mellitus was observed in 26.2% of the participants with the mean fasting glucose level was 108.3±21.1mg/dL. (Table 1)

| Parameter                                      | (n=42) |
|-----------------------------------------------|--------|
| Age (year)                                    | 68.8±8.6 |
| Body mass index (kg/m²)                       | 20±3   |
| Mean fasting glucose level (mg/dL)            | 136.8±7.8 |
| Prostate volume (mL)                          | 44.3±14.7 |
| Hypertension                                  |        |
| Yes                                           | 21 (50%) |
| No                                            | 21 (50%) |
| LUTS                                          |        |
| Mean IPSS                                     | 24.5±6.1 |
| Mild                                          |        |
| Moderate                                      | 8 (19%) |
| Severe                                        | 34 (81%) |
| Erectile Dysfunction                          |        |
| Mean IIEF-5 Score                             | 14.8±6.7 |
| Yes                                           | 35 (83.3%) |
| No                                            | 7 (16.7%) |
| Diabetes Mellitus                             |        |
| Mean fasting glucose level (mg/dL)            | 108.3±21.1 |
| Yes                                           | 11 (26.2%) |
| No                                            | 31 (73.8%) |
Correlation between LUTS, ED, Fasting Glucose Level, and Age

IPSS significantly correlated with fasting glucose level \((r=0.879, p<0.001)\) and IIEF-5 score \((r=-0.346, p=0.025)\). This condition showed that the higher fasting glucose level of a man aged 50 years or above with BPH, the more severe his LUTS would be. As his LUTS became more severe, his IIEF-5 score became lower or in other word, his ED became worsen (Table 2). IIEF-5 score showed significant negative correlation with age \((r=-0.31, p=0.046)\) and fasting glucose level \((r=-0.305, p=0.049)\). This condition showed that with increasing age and fasting blood glucose of a BPH man above 50 years old, ED worsens.

Table 2. Correlation between IPSS, IIEF-5, Fasting Glucose Level, and Age

|          | Age  | BMI   | Systolic | Diastolic | Fasting Glucose Level | IIEF   |
|----------|------|-------|----------|-----------|-----------------------|--------|
| IPSS     | -0.47| 0.212 | 0.127    | -0.036    | 0.879                 | -0.346 |
|          | (0.769)| (0.179) | (0.422) | (0.821)    | (<0.001)              | (0.025) |
| IIEF     | -0.31| 0.051 | -0.253   | -0.003    | -0.305                |        |
|          | (0.046)| (0.749) | (0.106) | (0.983)    | (0.049)               |        |

Discussion

In this study, 80.9% of participants suffered from severe LUTS (IPSS>19), with the mean age of 69 years old. Similar study in Turkey, with the mean age of 62 years old, showed that most of them suffered from mild-moderate LUTS (62.8%).

This discrepancy could be caused by the difference of mean age of the participants. Increasing age of BPH patients may correlate with higher IPSS. The occurrence of ED in men with BPH in our study was 83.3%. A study in Turkey revealed that the prevalence of ED on BPH man was 70.5%. Higher number in our study could be caused by higher result in IPSS. A study in Iran showed that there was strong relationship between IIEF score and the severity of LUTS, irrespective of other comorbidities.

Our study showed that fasting glucose level was positively correlated with IPSS. This condition showed that the higher fasting glucose level of a man aged 50 years or above in BPH, the more severe his LUTS would be. A study in Taiwanese men with diabetes mellitus showed that patients with diabetes mellitus had significantly higher IPSS compared to control. Fasting glucose level also showed negative correlation with IIEF score in our study. This condition showed that increasing age and higher fasting blood glucose of a BPH patient above 50 years old tend to decrease IIEF-5 score or in other word worsened ED. A study in Taiwanese man with diabetes mellitus showed that control group had significantly higher IIEF score. From this study we could conclude that higher fasting blood glucose level would lead to more severe LUTS and ED. A study done in Korean men aged more than 40 years old showed that diabetic men with severe LUTS tend to have more severe ED.

Our study also showed negative correlation between IIEF score with age and IPSS. This condition showed that older and worse LUTS may indicate more severe ED. Similar study in Turkey showed that increasing age in men with BPH was related to lower IIEF score. Other study done in Korea showed significantly negative correlation between IIEF score and the age of participants. A cross-sectional study done in Beijing showed that there was negative correlation between aging and ED. A cross-sectional study done in Hong Kong also showed negative correlation between IPSS and IIEF score. A study done in Beijing with 1644 men aged more than 50 years old showed negative correlation between LUTS and IIEF score. A large-scale prospective study held in America with more than 50.000 respondents also showed that the occurrence of ED was related to the severity of LUTS. A multinational study in Asia also showed that there was direct correlation between LUTS and the severity of ED.

We acknowledge some limitations in our study, such as limited participants and low educational status of the participants. These led to difficulties in understanding IPSS and IIEF questionnaire and poor data distribution. We recommend using HbA1c as an additional diagnostic method however HbA1c is not widely used in developing country due to cost and standardization problem.

Conclusions

Increasing fasting glucose level in a man diagnosed with BPH and age older than 50
years would increase his LUTS and ED severity. Increasing age and severity of LUTS in a man older than 50 years with BPH would increase the severity of ED.

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