KESAN LATIHAN SENAMAN AEROBIK TERHADAP PARAMETER KARDIOVASKULAR, FUNGSI ENDOTELIUM DAN KEROSAKAN DNA DI KALANGAN WANITA PRAHIPERTENSI DAN HIPERTENSI

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TESIS YANG DIKEMUKAKAN UNTUK MEMENUHI SEBAHAGIAN
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PENGAKUAN

Saya akui karya ini adalah hasil kerja saya sendiri kecuali nukilan dan ringkasan yang setiap satunya telah saya jelaskan sumbernya.

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ABSTRAK

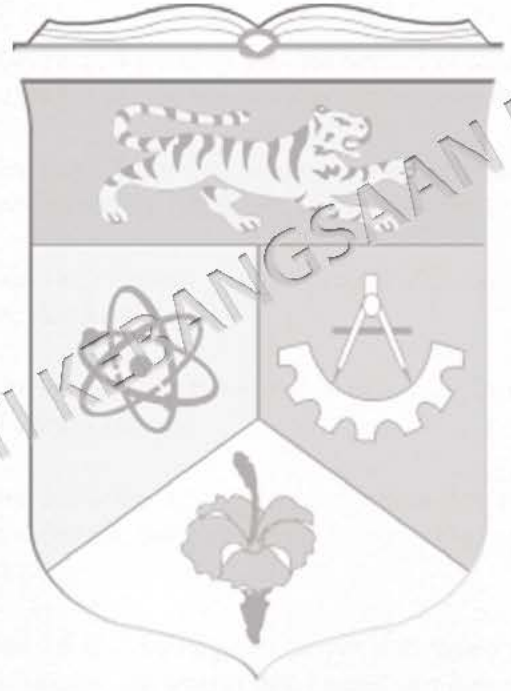
Di Malaysia, prevalens penyakit hipertensi adalah tinggi. Hipertensi mempunyai hubungan yang rapat dengan fungsi endotelium dan tekanan oksidatif. Bagi wanita, risiko untuk mendapat hipertensi adalah lebih tinggi selepas umur 50 tahun. Antara langkah yang berguna dalam perawatan hipertensi adalah senaman aerobik. Kajian ini dijalankan untuk menentukan kesan senaman aerobik terhadap parameter kardiovaskular, fungsi endotelium dan kerosakan DNA di kalangan wanita prahipertensi dan hipertensi yang belum mengambil ubat-ubatan. Seramai 13 orang wanita berumur 35 hingga 60 tahun terlibat dan menjalani pemeriksaan tekanan darah (BP) sewaktu rehat, pemantauan BP selama 24 jam (24-H ABPM), ujian darah untuk menentukan profil lipid dan glukos, ujian urin untuk menentukan paras 8 hidroksi-2'-deoksiguanosin (8-OHdG) sebagai petanda tekanan oksidatif serta ujian kecergasan aerobik, komposisi tubuh dan ultrabunyi dilatasi berasas aliran (FMD). Kumpulan bersenam (n=6) melakukan senaman *treadmill* sekerap tiga kali seminggu pada kadar 50 % kadar jantung simpanan (HRR) selama 30 minit setiap sesi selama empat minggu dan pada kadar 70 % HRR selama 45 minit pada empat minggu seterusnya. Kumpulan kawalan (n=7) diarah supaya terus seperti biasa. Selepas empat minggu, terdapat penurunan yang signifikan pada BP sistole sewaktu rehat pada kedua-dua kumpulan (P<0.05). Dari segi kadar jantung (HR) sewaktu rehat serta HR dan BP sistole sewaktu bersenam submaksimum, terdapat penurunan yang signifikan pada kumpulan bersenam (-4.00 bpm, -6.00 bpm, -17.00 mmHg, P<0.05) manakala kumpulan kawalan mengalami peningkatan (+3.00 bpm, +3.57 bpm, +4.29 mmHg, P>0.05). Selepas lapan minggu, terdapat penurunan yang signifikan pada BP sistole dan HR sewaktu bersenam maksimum pada kedua-dua kumpulan, yang mana kumpulan bersenam mencapainya pada intensiti senaman yang lebih tinggi berbanding dengan kumpulan kawalan (6.05 $\pm$ 1.37 METs lwn. 4.84 $\pm$ 0.65 METs). Selain itu, terdapat penurunan yang signifikan pada urin 8-OHdG pada kumpulan bersenam (sebelum intervensi= 6.58 $\pm$ 2.26, selepas intervensi= 4.33 $\pm$ 0.79 ng/mg kreatinin, P=0.04). Kumpulan bersenam juga dapat mengekalkan tahap kecergasan aerobik dan mengalami peningkatan yang signifikan dari segi tempoh senaman (sebelum intervensi= 13.29 $\pm$ 0.96, selepas intervensi= 14.67 $\pm$ 2.23 minit, P=0.01). Kajian ini mendapati senaman aerobik pada intensiti sedehana, sekerap tiga kali seminggu selama 30 hingga 45 minit setiap sesi menurunkan BP sistole dan HR semasa bersenam, mengurangkan tekanan oksidatif dan mengekalkan kecergasan aerobik wanita prahipertensi dan hipertensi yang tidak mengambil ubat-ubatan.

THE EFFECTS OF AEROBIC EXERCISE TRAINING ON CARDIO-VASCULAR PARAMETERS, ENDOTHELIAL FUNCTION AND DNA DAMAGE IN PREHYPERTENSIVE AND HYPERTENSIVE WOMEN

ABSTRACT

In Malaysia, the prevalence of hypertension is high. Hypertension is closely related to endothelial function and oxidative stress. The risk of hypertension is higher among women after 50 years of age. Aerobic exercise has been recognized as a useful intervention in the treatment of hypertension. This study was done to determine the effects of regular aerobic exercise on cardiovascular parameters, endothelial function and DNA damage in prehypertensive and hypertensive women before commencement of medication. Thirteen women aged 35 to 60 years old were recruited and underwent blood pressure (BP) measurement at rest and during a 24 hour period (24-H ABPM), blood tests for determination of lipid profile and glucose, urine test for measurement of 8-hydroxy-2'-deoxyguanosine (8-OHdG) as an indicator of oxidative stress, aerobic capacity test, body composition and ultrasound Flow Mediated Dilation (FMD). The exercise group (n=6) performed treadmill exercise three times per week at 30 minutes per session at 50 % of heart rate reserve (HRR) for four weeks, which was then increased to 70 % HRR and 45 minutes for another four weeks. The control group (n=7) continued with their usual routine. After four weeks, there was a significant reduction in resting systolic BP in both groups ($P<0.05$). As regards the resting heart rate (HR), submaximal exercise HR and exercise systolic BP, there were significant reduction in the exercise group (-4.00 bpm, -6.00 bpm, -17.00 mmHg, $P<0.05$) while the control group had an increment (+3.00 bpm, +3.57 bpm, +4.29 mmHg, $P>0.05$) respectively. After eight weeks, both groups had significant reduction in maximal exercise HR and systolic BP, with the exercise group achieving it at a higher exercise intensity (6.05 $\pm$ 1.37 METs vs. 4.84 $\pm$ 0.65 METs). In addition, there was a significant reduction in urine 8-OHdG in the exercise group (before intervention= 6.58 $\pm$ 2.26, post intervention= 4.33 $\pm$ 0.79 ng/mg creatinine, $P=0.04$). The exercise group also maintained their aerobic fitness and had significant increment in exercise time (before intervention= 13.29 $\pm$ 0.96, post intervenstion= 14.67 $\pm$ 2.23 minute, $P=0.01$). This study found that aerobic exercise at moderate intensity three times per week with 30 to 45 minutes every session reduced systolic BP and HR during exercise, decreased oxidative stress and maintained aerobic fitness in prehypertensive and hypertensive women who were not on medication.

KANDUNGAN



SENARAI JADUAL

SENARAI ILUSTRASI

SENARAI SINGKATAN

·OH	Ion hidroksil
8-iso-$PGF_{2\alpha}$	8-isoprostaglandin $F_{2\alpha}$
8-OHdG	8-hidroksi-2'-deoksiguanosin
ADMA	Enzim dimetilarginin dimetilaminohidrolase
Ag II	Angiotensin II
APMHR	Kadar jantung maksimum jangkaan umur
ATPase	Adenosin trifosfatase
BMI	Indeks jisim tubuh
BP	Tekanan darah
cGMP	Siklik guanosin monofosfat
CHD	Penyakit jantung koronari
CO	Keluaran jantung
CRP	Protein C reaktif
DBP	BP diastole
DNA	Asid deoksiribonukleik
ECG	Elektrokardiogram
EDD	Dilatasi bergantung endotelium
ELISA	Assai imunosorben hubungan enzim
eNOS	Nitrus oksida sintase endotelium
ESCULA	*European Standards Committee on Urinary (DNA) Lesions*
FMD	Dilatasi berasas aliran
GFR	Kadar penapisan glomerulus
GPX	Glutation peroksidase

GSH	Glutation
GSSG	Glutation teroksida
HR	Kadar jantung
HRR	Kadar jantung simpanan
ICAM-1	Molekul pelekat intersel -1
IL-18	Interleukin-18
IL-6	Interleukin-6
iNOS	Nitrus oksida sintase pencetus
IPAQ	Soal selidik aktiviti fizikal antarabangsa
JNC VII	*Joint National Committee on Prevention, Detection and Treatment of High Blood Pressure*
LDL	Lipoprotein berketumpatan rendah
lwn.	Lawan
MAPK	*Mitogen-activated protein kinases*
MCP-1	Protein penarik kimia monosit -1
MCSF	Faktor pencetus koloni monosit
MDA	Melondialdehid
MLCK	Rantai ringan miosin kinase
NADH DEH	Nikotinamid adenin dinukleotid dehidrogenase
NADPH oksidase	Nikotinamid adenin dinukleotid fosfat oksidase
NCEP ATP III	*National Cholesterol Education Programme Adult Panel Treament III*
NF-κB	*Nuclear Factor kappa light chain enhancer of activated B cells*
NHMS3	National Health And Morbidity Survey III
NO	Nitrus oksida

O_2^-	Ion superoksida
OGG1	Enzim oksoguanin DNA glikosilase
OksiLDL	LDL teroksida
PKG	Protein kinase G
PP	Tekanan denyutan
PWV	Kelajuan gelombang denyutan
RAS	Sistem renin-angiotensin
RER	Kadar pertukaran respiratori
RNS	Spesis reaktif nitrogen
ROS	Spesis reaktif oksigen
SBP	BP sistole
SERCA	Retikulum Sarko/Endoplasmik Ca^{2+}-ATPase
SHRR	Pemulihan kadar jantung yang lambat
SNA	Sistem saraf simpatetik
SOD	Superoksida dismutase
SR	Kadar *shear*
SV	Isipadu sedenyut
TNF-α	Faktor nekrosis tumor alfa
TPR	Rintangan periferi total
VCAM-1	Molekul pelekat vascular-1
VO_2	Penggunaan oksigen
VO_2 max	Penggunaan oksigen maksimum
VO_2 puncak	Penggunaan oksigen puncak

SENARAI SIMBOL

%	peratus
$\%s^{-1}$	peratus per saat
<	kurang daripada
≤	kurang daripada atau sama dengan
>	lebih daripada
≥	lebih daripada atau sama dengan
° C	darjah Celcius
bpm	denyut per minit
cm	sentimeter
kcal/minggu	kilokalori per minggu
kg	kilogram
km/jam	kilometer per jam
METs	metabolik ekuivalens
METs-minit/minggu	metabolik ekuivalens minit per minggu
min/hari	minit per hari
mmHg	millimeter merkuri
mmol/L	milimol per liter
ng/µl	nanogram per mikroliter
nm	nanometer
O_2/kg/min	oksigen per kilogram per minit
rpm	ram per minit
s^{-1}	per saat
µl	mikroliter

BAB I

PENDAHULUAN

1.1 PENGENALAN

Di Malaysia, prevalens penyakit darah tinggi atau hipertensi adalah tinggi dan semakin meningkat. Pada tahun 1996, prevalens hipertensi di kalangan mereka yang berumur melebihi 30 tahun adalah 32.9 peratus dan bertambah kepada 40.5 peratus pada tahun 2004 (Rampal et al. 2008). Hipertensi merupakan salah satu faktor risiko penyakit jantung koronari (CHD), penyakit arteri periferi dan strok. Hipertensi boleh dicegah, dirawat dan dikawal, maka, langkah-langkah awal harus dijalankan oleh semua pihak supaya penyakit ini dapat dibendung sebaik mungkin.

1.2 PERMASALAHAN KAJIAN

Hipertensi telah dikaitkan dengan peningkatan tekanan oksidatif iaitu keadaan di mana berlakunya radikal bebas yang berlebihan atau kekurangan antioksidan (Redon et al. 2003). Selain itu, pesakit hipertensi mempunyai fungsi endotelium yang tidak normal (Benjamin et al. 2004). Kedua-dua keadaan tersebut menyebabkan peningkatan resistan periferi total (TPR) yang seterusnya menyebabkan peningkatan tekanan darah. Disfungsi endotelium juga merupakan prediktor kepada mortaliti akibat penyakit kardiovaskular (Rossi et al. 2008).

Pada wanita, risiko untuk mendapat hipertensi meningkat selepas umur 50 tahun, iaitu apabila seseorang itu mencapai keadaan menopaus (Kannel et al. 1976). Di Malaysia, ini dibuktikan dengan prevalens hipertensi yang menunjukkan dominasi wanita pada golongan umur melebihi 50 tahun (Rampal et al. 2008). Berbanding lelaki, wanita, terutamanya yang menghidap hipertensi, juga mempunyai prognosis

yang lebih teruk apabila mendapat serangan jantung (Gierach et al. 2006). Wanita terutama yang berumur kurang dari 50 tahun dan mendapat serangan jantung mempunyai kadar mortaliti dua kali ganda berbanding lelaki yang sebaya (6.10 % lwn. 2.99 %) (Vaccarino et al. 1999). Wanita juga didapati mempunyai kesan sampingan yang lebih pada ubat antihipertensi berbanding lelaki. Wanita terutama yang tua berbanding lelaki sebaya, mempunyai risiko untuk mendapat hiponatremia dan hipokalemia akibat diuretik (Chapman et al. 2002). Wanita juga mempunyai dua kali ganda risiko untuk mendapat simptom batuk akibat ubat jenis perencat enzim penukar angiotensin berbanding lelaki (Os et al. 1992). Masalah kesan sampingan ini akan menyebabkan pesakit kurang komplians kepada ubat-ubatan.

Antara langkah awal yang dapat diambil untuk mencegah hipertensi adalah dengan perubahan kepada gaya hidup sihat seperti amalan pemakanan yang seimbang dengan pengurangan garam serta gula dan melebihkan sayur-sayuran dan tenusu, bersenam aerobik, tidak merokok, tidak minum alkohol secara berlebihan dan pengurangan tekanan hidup. Bagi pesakit hipertensi pula, amalan gaya hidup adalah penting dan jika tidak dapat dikawal, rawatan ubat antihipertensi adalah perlu (Mancia et al. 2007).

Antara semua gaya hidup sihat yang boleh diamalkan, senaman aerobik secara berkala merupakan langkah yang unik kerana selain daripada kesan menurunkan tekanan darah, ia juga dapat membantu menurunkan faktor-faktor risiko akibat CHD yang lain seperti lipid dalam darah, peratus lemak dalam badan dan meningkatkan tahap kecergasan kardiorespiratori. Senaman aerobik juga dapat mengurangkan tekanan oksidatif dan meningkatkan fungsi endotelium, yang seterusnya dapat mengurangkan TPR dan menurunkan tekanan darah (BP).

Tahap kecergasan kardiorespiratori merupakan antara prediktor utama kepada penyakit kardiovaskular (Kodama et al. 2009; Mora et al. 2003). Senaman aerobik penting untuk meningkatkan tahap kecergasan kardiorespiratori. *American College of Sports Medicine* dan *American Heart Association* telah mencadangkan senaman aerobik yang baik untuk kesihatan adalah bersenam aerobik 5 hari setiap minggu pada intensiti sederhana dengan 30 min setiap sesi (Haskell et al. 2007). Namun, berdasarkan *National Health and Morbidity Survey* III (NHMS3) kadar

aktiviti fizikal dalam masyarakat kita adalah rendah, iaitu sebanyak 40 peratus telah didapati tidak aktif (NHMS3 2006). Mereka yang tidak aktif kebanyakannya adalah wanita, surirumah, penduduk bandar dan orang tua. Memandangkan ramai wanita adalah tidak aktif, dan risiko hipertensi selepas umur 50 tahun, maka adalah penting golongan ini lebih aktif untuk mengelak dari serangan penyakit kardiovaskular.

1.3 TUJUAN KAJIAN

Oleh kerana terdapat kaitan yang rapat antara hipertensi, senaman aerobik dan risiko penyakit kardiovaskular, maka, kajian yang lebih mendalam adalah diperlukan untuk menentukan kesan interaksi antara satu faktor dengan faktor yang lain, terutamanya pada wanita, yang sememangnya kurang mendapat perhatian daripada kajian-kajian sebelum ini berbanding lelaki (Kaplan et al. 1995, Kokkinos et al. 1997, Seals et al. 1997). Kajian ini telah dijalankan untuk menentukan kesan senaman pada parameter kardiovaskular dan fungsi endotelium di kalangan pesakit prahipertensi dan hipertensi wanita. Selain itu, interaksi antara senaman dan tekanan oksidatif juga dikaji, memandangkan tekanan oksidatif merupakan antara faktor utama yang menyebabkan hipertensi dan disfungsi endotelium. Oleh kerana senaman aerobik juga mempunyai kesan terhadap paras lipid darah dan komposisi badan, faktor ini juga akan dikaji. Diharap kajian ini dapat mengurai sedikit sebanyak mekanisme kesan senaman aerobik pada wanita prahipertensi dan hipertensi agar dapat digunapakai dalam kehidupan seharian dalam perawatan hipertensi dan pencegahan serangan jantung.

1.4 OBJEKTIF KAJIAN

1.4.1 Objektif Umum

Menentukan kesan latihan senaman aerobik terhadap parameter kardiovaskular, fungsi endotelium dan kerosakan asid deoksiribonukleik (DNA) pada wanita prahipertensi dan hipertensi.

1.4.2 Objektif Khusus: primer

Menentukan kesan latihan senaman aerobik terhadap parameter kardiovaskular (BP semasa rehat dan bersenam, BP selama 24 jam, kadar jantung semasa rehat dan bersenam) pada wanita prahipertensi dan hipertensi.

1.4.3 Objektif Khusus: sekunder

a) Menentukan kesan latihan senaman aerobik terhadap fungsi endotelium pada wanita prahipertensi dan hipertensi.
b) Menentukan kesan latihan senaman aerobik terhadap kerosakan DNA pada wanita prahipertensi dan hipertensi.
c) Menentukan kesan latihan senaman aerobik terhadap komposisi badan pada wanita prahipertensi dan hipertensi.

1.5 HIPOTESIS KAJIAN

a) Latihan senaman aerobik menurunkan BP semasa rehat, semasa bersenam dan BP 24 jam serta kadar jantung semasa rehat dan bersenam pada wanita prahipertensi dan hipertensi.
b) Latihan senaman aerobik meningkatkan tahap kecergasan aerobik pada wanita prahipertensi dan hipertensi.
c) Latihan senaman aerobik meningkatkan fungsi endotelium pada wanita prahipertensi dan hipertensi.
d) Latihan senaman aerobik mengurangkan kerosakan DNA pada wanita prahipertensi dan hipertensi.
e) Latihan senaman aerobik meningkatkan jisim otot dan mengurangkan jisim lemak tubuh pada wanita prahipertensi dan hipertensi.

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