循征医学报告

同济大学医学院 08 级研究生

朱 芸

0820110144

2008 年 12 月 25 日
一、疾病案例

患者男性，65岁，退休工人。3年前无明显诱因突发胸痛、心悸，舌下含服硝酸甘油可缓解。之后多次无明显诱因出现胸痛、心悸，舌下含服硝酸甘油后可缓解，心电图示：V2-V5ST段压低0.10～0.15mV。超声心动图：左室射血分数45%。冠脉造影提示：左回旋支前降支85%狭窄，确诊为冠状动脉粥样硬化性心脏病。既往患有“原发性高血压”，血压最高时达190/100mmHg，曾服用“阿替洛尔、双氢克尿塞”降压药治疗，血压控制在140/80mmHg左右。现服用“维拉帕米、群多普利”降压治疗，血压仍控制在140/80mmHg左右。

二、提出问题

该患者为冠心病合并高血压患者，采用“阿替洛尔+双氢克尿塞”方案降压与采用“维拉帕米+群多普利”方案降压效果有差别吗？

三、证据检索与评价

（一）证据检索


2. 关键词和主题词

（1）关键词：高血压（Hypertension）、冠心病（Coronary heart disease）、治疗（Therapy or treatment）、目标血压（Target blood pressure）、主题词：hypertension、coronary disease、therapeutics、Meta-Analysis、Randomized Controlled Trials、Practice Guideline

3. 检索结果：

PubMed-Clinical Queries

检索词组合：(Hypertension) AND ((Coronary heart disease) AND (Target blood pressure)) AND (therapeutics)

（1）Meta分析：3篇

1.Hypertension, hypertensive heart disease and perioperative cardiac risk.
2.Ongoing trials: what should we expect after ALLHAT?
3.Identification of risk factors in hypertensive patients: contribution of randomized controlled trials through an individual patient database.

（2）Practice Guideline：6篇

3.What do international guidelines say about therapy?
5.Guidelines for management of hypertension: report of the third working party of the
British Hypertension Society.

(3) Randomized Controlled Trials: 19篇
2. Obesity paradox in patients with hypertension and coronary artery disease.
3. Long-term trandolapril treatment is associated with reduced aortic stiffness: the prevention of events with angiotensin-converting enzyme inhibition hemodynamic substudy.
4. Angioplasty and STent for Renal Artery Lesions (ASTRAL trial): rationale, methods and results so far.
5. [Evaluation of hypotensive and antiischemic effects of a combination of dihydropyridine and non-dihydropyridine calcium antagonists in patients suffering from coronary artery disease with arterial hypertension]
6. [Depression in cardiological practice: pilot results from a multicenter clinico-epidemiological trial in hypertensive patients with ischemic heart disease (koordinata)]
7. Impact of a structured intensive follow-up program on the control of hypertension in coronary patients--a randomized trial.
8. Treating to hypertension targets.
9. [Clinical study of the month. Which initial antihypertensive? Results from the ALLHAT trial]
11. [Effect of intensive antihypertensive treatment and of aspirin in a low dose in the hypertensive. The HOT (Hypertension Optimal Treatment) study]
12. Study population and treatment titration in the International Nifedipine GITS Study: Intervention as a Goal in Hypertension Treatment (INSIGHT).
13. Rationale and design of the International Verapamil SR/Trandolapril Study (INVEST): an Internet-based randomized trial in coronary artery disease patients with hypertension.
14. Effects of 2,000 kcal per week of walking and stair climbing on physical fitness and risk factors for coronary heart disease.
15. The renin-angiotensin system as a target for therapeutic intervention.
17. Acebutolol effects on lipid profile.
18. Effect of antihypertensive therapy on plasma lipids and lipoproteins in mild hypertension.

Cochrane 图书馆 13篇


3. [Depression in cardiological practice: pilot results from a multicenter clinico-epidemiological trial in hypertensive patients with ischemic heart disease (koordinata)] Chazov EI, Oganov RG, Pogosova GV, Shal'nova SA, Romasenko LV, Shchurov DV Year: 2006


（二）评价证据


OBJECTIVE: To compare the effects of two antihypertensive treatment strategies for the prevention of coronary heart disease and other cardiovascular events in the large subpopulation (n=5137) with diabetes mellitus in the blood pressure-lowering arm of the Anglo-Scandinavian Cardiac Outcomes Trial. METHODS: Patients had either untreated hypertension or treated hypertension. For those with type II diabetes mellitus, inclusion criteria required at least two additional risk factors. Patients were randomized to amlodipine with addition of perindopril as required (amlodipine-based) or atenolol with addition of thiazide as required (atenolol-based). Therapy was titrated to achieve a target blood pressure of less than 130/80 mmHg. RESULTS: The trial was terminated early due to significant benefits on mortality and stroke associated with the amlodipine-based regimen. In patients with diabetes mellitus, the amlodipine-based treatment reduced the incidence of the composite endpoint--total cardiovascular events and procedures--compared with the atenolol-based regimen (hazard ratio 0.86, confidence interval 0.76-0.98, P=0.026). Fatal and nonfatal strokes
were reduced by 25% (P=0.017), peripheral arterial disease by 48% (P=0.004) and noncoronary revascularization procedures by 57% (P<0.001). For the other endpoints included in the composite, the endpoint differences were less clear including coronary heart disease deaths and nonfatal myocardial infarctions (the primary endpoint), which were reduced nonsignificantly by 8% (hazard ratio 0.92, confidence interval 0.74-1.15). CONCLUSION: In the large diabetic subgroup in the blood pressure-lowering arm of the Anglo-Scandinavian Cardiac Outcomes Trial, the benefits of amlodipine-based treatment, compared with atenolol-based treatment, on the incidence of total cardiovascular events and procedures was significant (14% reduction) and similar to that observed in the total trial population (16% reduction).

证据级别：I级

2. 冠心病患者钙拮抗剂与非钙拮抗剂降压治疗策略：国际维拉帕米与群多普利随机对照试验
   The Journal of the American Medical Association (Chinese Edition) 2005年 24卷 3期 起止页码：131-137
目的：在采用钙拮抗剂治疗方案(calcium antagonist strategy, CAS)或非钙拮抗剂治疗方案(non—calcium antagonist strategy, NCAS)的高血压CAD患者中进行比较。
设计、地点和参试者：随机、开标(open—label)、盲法终点研究。研究于1997年9月至2003年2月在14个国家的862家单位的22576例高血压CAD患者中进行。患者年龄>50岁。
干预：患者随机接受CAS(盐酸维拉帕米缓释剂)或NCAS(阿替洛尔)。两种治疗均有详细的剂量及用药方案。
主要观察指标：全因死亡，首发非致死性心肌梗死或非致死性脑卒中；心血管残废、心绞痛、不良事件、住院以及24个月时血压控制情况。
结果：在24个月时，CAS组有6391例(81.5%)服用维拉帕米缓释剂；4934例(62.9%)服用群多普利；3430例(43.7%)服用双氢克尿塞。NCAS组有6083例(77.5%)服用阿替洛尔；4733例(60.3%)服用双氢克尿塞；4113例(52.4%)服用群多普利。在61 835病人一年随访之后(每例平均2.7年)，2 269例患者发生主要结局事件，两种治疗方案无统计学显著差异(CAS为9.93%，NCAS为10.17%；相对危险度(relative risk, RR)，0.98；95%可信区间[confidence interval,CI]，0.90～1.06]。两组两年内血压控制情况相似。CAS组达到INC VH目标血压者分别为65.0%(收缩压)和88.5%(舒张压)，NCAS组为64.0%(收缩压)和88.1%(舒张压)。CAS组总共有71.7%而NCAS有70.7%的患者达到收缩压<140 mmHg、舒张压<90 mmHg的水平。
结论：对高血压CAD患者而言，以维拉帕米+群多普利为基础的治疗方案与以阿替洛尔+双氢克尿塞为基础的方案一样有效。
证据级别：I级

3. Study population and treatment titration in the International Nifedipine GITS Study: Intervention as a Goal in Hypertension Treatment (INSIGHT).


OBJECTIVES: To ascertain the baseline characteristics of the high-risk hypertensive patients entering the International Nifedipine GITS Study: Intervention as a Goal in Hypertension Treatment (INSIGHT). To determine the success of single and combination therapy in achieving target blood pressures in such a population.

DESIGN: INSIGHT is a double-blind, prospective outcome trial comparing the efficacy of the calcium channel blocker, nifedipine GITS, and the thiazide, co-amilozide, in preventing myocardial infarction and stroke. We recruited 2996 men and 3454 women, aged 55-80 years, with blood pressure during placebo run-in >150/95 mmHg or isolated systolic blood pressure >160 mmHg from nine countries. Treatment allocation to nifedipine GITS 30 mg daily or co-amilozide (hydrochlorothiazide 25 mg/amiloride 5 mg) once daily was performed by minimization rather than randomization to balance additional risk factors. This was followed by four optional increases in treatment: dose-doubling of the primary drug, addition of atenolol 25/50 mg or enalapril 5/10 mg, and then any other hypotensive drug excluding calcium blockers or diuretics. Target blood pressure was 140/90 mmHg or a fall > or = 20/10 mmHg. RESULTS: Blood pressure at randomization was 172+/−15 / 99+/−9 mmHg. Thirteen per cent of the patients were previously untreated. The proportions of each additional risk factors were: smoking > 10/day, 29%; cholesterol > 6.43 mmol/l, 52%; family history of premature myocardial infarction or stroke, 21%; diabetes mellitus 20%; left ventricular hypertrophy, 10%; previous myocardial infarction, other presentations of coronary heart disease, and peripheral vascular disease, each 6%; proteinuria, 3%. Fifty-five per cent of patients had one additional risk factor, whereas 33%, 9% and 3% had two, three or more additional risk factors, respectively. The blood pressure (and falls in blood pressure) at the end of titration and at 1 year after minimization was 139+/−12 / 82+/−7 mmHg (33+/−15 / 17+/−9) in the 5226 patients still on randomized treatment. The numbers requiring the four treatment increments were, respectively, 1591, 780, 597 and 294, meaning that almost 70% of patients on randomized treatment in INSIGHT are receiving only the primary drug. At one year, 69% of patients had a blood pressure < or = 140/90 mmHg. CONCLUSION: INSIGHT is one of the first double-blind comparisons of active antihypertensive treatments, requiring high-risk patients to achieve sufficient power. Despite this requirement, it is possible to achieve good blood pressure control in most patients without the addition of multiple additional treatments that may dilute any differences between the primary agents.

证据级别：I级

总结：随着冠心病(coronary artery disease，CAD)主要危险因素(血压高、年龄大、糖尿病、肥胖和不好运动)的增加，冠心病的发生率不断增加。血压对CAD的进展具有重要作用。

1997年9月至2003年2月在14个国家的862家单位的22576例高血压CAD患者中进行。患者年龄大于等于50岁。患者随机接受CAS组(维拉帕米缓释剂加群多普利)或NCAS组(阿替洛尔加双氢克尿塞)治疗。最终的研究结果表明，两组患者收缩压和舒张压降低幅度达到的水平相似。
大多数INVEST患者均达到JNC VI的血压控制目标。CAD患者的这些结果扩展了LIFE和ALLHAT的发现，证实可以通过更积极的治疗使血压达到更低的水平。然而，ALLHAT既未检验β受体阻滞剂也未证实血管紧张素Ⅱ活性制剂对糖尿病、肾功能不全或心力衰竭患者的脏器保护作用。所以，INVEST研究在老年CAD人群通过纳入一种以β受体阻滞剂为基础的方案脏器保护的结果补充了ALLHAT的不足。INVEST数据还证实并扩展了其他研究，提示单药治疗对高血压理想治疗是不够的。总之，两个治疗组报告的不良事件均很少，而且发生率相似。交叉率的差异可能反映了联合应用阿替洛尔加双氢克尿塞(NCAS组)不良事件(呼吸困难、头晕、症状性心动过缓和喘息)与维拉帕米缓释剂加群多普利(CAS组)不良事件(便秘和咳嗽)相互比较的结果。阿替洛尔组交叉率更高，可能与患者既往不耐受或者医生对β受体阻滞剂存在偏见有关。特别是最近服用β受体阻滞剂的患者从试验中排除。另一种可能性是CAS(维拉帕米缓释剂加群多普利)或NCAS(阿替洛尔加双氢克尿塞)的不同药物组成可能有控制血压之外的益处。联合应用维拉帕米缓释剂和群多普利可能较少发生代谢并发症，例如观察显示新诊断的糖尿病减少。预计NCAS方案可能对既有心肌梗死和冠状动脉重建的患者有益，然而，观察两组结果相似。另一方面，对于既往有心力衰竭的患者，我们的结果数据与最近的试验一致，这些试验证实β受体阻滞剂加用利尿剂和血管紧张素转换酶抑制剂的益处，但是在这些试验中并非所有患者均有高血压。根据我们的报告，高血压治疗必须关注患者的危险因素和整体治疗方案而不是单一药物。

综上所述，采用多种药物联合治疗方案可将合并高血压的CAD患者的血压控制在更低水平。CAS方案和NCAS方案在预防死亡、心肌梗死或卒中方面的临床效果相同，在需控制血压的临床稳定的CAD患者中可应用其中任何一种方案。对于特殊患者，用药种类应该根据其他因素(包括不良事件、心力衰竭病史、糖尿病危险性)以及医生的最佳判断确定。

四、实施决策

经过前述的严格的证据评价，本例患者为冠心病合并高血压患者，无其他危重疾病，目前病情相对稳定，采用“阿替洛尔+双氢克尿塞”方案降压与采用“维拉帕米+群多普利”方案降压效果没有太大的差异，两个方法都可以采用。现已继续予以“维拉帕米+群多普利”方案降压治疗。

五、后效评估

在对患者进行治疗后，还应该对患者进行长期随访，了解治疗效果、药物不良反应、患者满意度等，以进一步提高循证治病的效果。此处因条件有限，暂缺。

六、参考文献
1、叶任高主编. 内科学. 第六版.北京：人民卫生出版社，2006. 335-338.
2、The Anglo-Scandinavian Cardiac Outcomes Trial: blood pressure-lowering limb: effects in patients with type II diabetes.


3. 冠心病患者钙拮抗剂与非钙拮抗剂降压治疗策略: 国际维拉帕米与群多普利随机对照试验
   The Journal of the American Medical Association (Chinese Edition) 2005 年 24 卷 3 期
   起止页码: 131-137

4. Study population and treatment titration in the International Nifedipine GITS Study: Intervention as a Goal in Hypertension Treatment (INSIGHT).