

## Drug Therapy for Small Abdominal Aortic Aneurysm

### Dear Editor,

Abdominal aortic aneurysm is often asymptomatic, less recognized, and causes considerable mortality and morbidity, if missed. The incidence varies from country to country and the occurrence is influenced by modifiable (smoking, coronary heart disease, hypertension, dyslipidemia, and prolonged steroid therapy) and non-modifiable risk factors (increasing age, male gender, and positive family history). Most of the patients with such aneurysm do not exhibit symptoms and the diagnosis is made accidentally during routine medical investigations, abdominal ultrasonography, or by an astute surgeon during an abdominal procedure. Sometimes the diagnosis is made in an emergency room, if the attending resident/doctor is aware of it. Despite good diagnosis and effective management, the outcomes of complicated cases are poor and the treatment cost is prohibitive. Hence, we reviewed the literature to find out the pathogenesis of such aneurysms and the usefulness of available drugs in its prevention.

The pathogenesis for the development of abdominal aortic aneurysm is considered under four headings namely, tissue mechanisms, enzymes related, cellular aspects, and infection-inflammation induced. However, one or a combination of these mechanisms might be involved in its pathogenesis. Tissue mechanisms include proliferation of vascular smooth muscles, angiotensin-II mediated atherosclerosis, rupture of plaques, and abnormal matrix by degradation and suppression of tissue repair through C-junction N-terminal kinase.<sup>1-3</sup> Enzymes such as elastase induce changes in vessel wall layer and remodeling.<sup>1</sup> Human T-lymphocytes activation through activator protein-1,<sup>4</sup> mediates changes at cellular level. Angiotensin converting enzyme (ACE) inhibitors,<sup>1,2</sup> or angiotensin-II receptor blockers,<sup>4</sup> can inhibit the vessel wall changes, and statins,<sup>5</sup> can revert atherosclerotic plaques. Statins inhibit aneurysm development by reducing atherogenic lipoproteins and C-reactive proteins. In experimental models, Janus N Kinase inhibitor (SP 600125),<sup>3</sup> was shown to slow down the degradation and suppression of tissue repair in vessel walls through C-Junction N-terminal kinase. Gadowski and co-workers demonstrated that beta blockers reduced the expansion of un-ruptured abdominal aortic aneurysm,<sup>6</sup> however, another study did not confirm this notion.<sup>7</sup> Hence, further evaluation of the usefulness of beta blockers in such aneurysms need to be conducted.

Among drugs currently used in clinical medicine, ACE inhibitors,<sup>1,2</sup> or angiotensin-II receptor blockers were evaluated in abdominal aortic aneurysm.<sup>4</sup> These medications were found to be beneficial by preventing the development and/or retarding the progression of the aneurysm. In addition, patients on long-term steroid therapy should be monitored for abdominal aortic aneurysm and changed over to suitable alternatives, wherever possible. Progression of such aneurysm can be enhanced by secondary infection with *Chlamydia pneumoniae*, because the bacterium promotes the atherosclerosis in the aortic wall.<sup>8</sup> Hence, the macrolides (Roxithromycin 300mg daily for 4 weeks) may reduce the infection/inflammation-induced changes in vessel walls.<sup>9</sup> Additionally, matrix metalloproteinase (MMP) is closely linked to the aneurysm in animal models and human studies.<sup>10</sup> Hence, MMP inhibitors such as tetracyclines, statins, and ACE inhibitors have shown to reduce the expansion of such aneurysms. Tetracyclines suppresses aortic wall MMP activity, elastin degradation, and aneurysm development in elastase-induced abdominal aortic aneurysm in a rat model.<sup>11</sup>

It should be considered that treatment of small abdominal aortic aneurysm (less than 5-5.5 cm) before rupture substantially lowers the mortality and reduces the cost of treatment. However, mechanical intervention is the only treatment shown to be effective in preventing rupture and aneurysm related death. It is reserved for aneurysms  $\geq 5.5$  cm in men and  $\geq 5$  cm in women, and/or aneurysm of rapid expansion. Because the drug therapy has a preventive effect, regular use of the drugs by susceptible population is likely to lower the onset, progression, or complications of the aneurysm in the years to come.

Smoking is the most important and modifiable risk factor contributes to the development of abdominal aortic aneurysm. Clinicians should aim to modify the modifiable risk factors by recommending a healthy life style by considering factors such as diet, regular physical exercise, smoking cessation, and treating co-morbid illnesses including hypertension and dyslipidemia. Likewise, patients at risk of such aneurysm should be screened by ultrasonography in the elder age groups at regular intervals and motivated for regular follow-up.

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