Public release date: 1-Aug-2005

Contact: Margaret Willson
m.willson@mwcommunications.org.uk
44-153-677-2181
European Society of Cardiology

Women missing out in heart treatment – more needed in clinical trials

The designers of heart disease trials should ensure that they recruit enough women to reveal reliably whether they are responding to the drugs in a different way from men, according to research published on line (Tuesday, 2 August) in Europe's leading cardiology journal, the *European Heart Journal*[1].

Women are under represented in most clinical studies, so the data and the results are less well documented for them, according to Dr Verena Stangl, senior author of the paper, who is from the Charité Hospital, Humboldt-University Berlin, Germany.

Dr Stangl, who is Professor of Cardiology (Molecular Atherosclerosis) at the hospital's Department of Cardiology, Angiology and Pneumology, said that although the percentage of women in studies of coronary heart disease had risen since the mid 1980s to reflect the prevalence of CHD in women, they were still under represented in trials involving coronary artery disease, arterial hypertension and heart failure.

She said: "It is essential that trials are designed to provide the necessary data so that researchers know from the outset that they will be able to analyse factors that could contribute to different outcomes for men and women, such as hormonal aspects, possible effects of drug dosage and known differences in biochemical and physiological responses between men and women."

Currently, conclusions for women were mostly reached retrospectively via subgroup, post hoc or meta-analyses, which was unacceptable, she said.

Dr Stangl and her team reached their findings after an extensive review of articles on female-specific aspects of drug therapy for chronic cardiovascular diseases.

Although they concluded that there are only slight differences in implications for treatment, they highlighted several key examples of differing response between men and women, or of situations where evidence is unclear. For example:

- Women developed adverse drug reactions, such as the cough associated with ace-inhibitors, twice as frequently as men, probably due to higher levels of the drug in the blood plasma;
- Potentially life-threatening heart rhythm disorders occur significantly more often in women, so they need closer monitoring when undergoing antiarrhythmic treatment;
- Aspirin is proven as a primary preventive for heart attack in males, but questionable for women. The reasons it appears not to be effective in primary heart attack prevention are unclear as yet;
- Digitalis is associated with higher mortality in female patients.

"Because too few women participate in heart disease trials we are not sure whether they really benefit from some therapeutic strategies that have shown clinical benefit in trials conducted predominantly in men. So, we prescribe drugs to women adapted from evidence-based data obtained from studies conducted mainly in men and we do not really know whether we help or harm the female patients. Take one example: as we have no prospective data for digitalis in female patients, it's unclear whether it is really linked to increased mortality among women or whether this increase is an effect only of an overdose, and therefore whether they would benefit from lower doses adapted to their weight."

Dr Stangl said women have historically been under-represented in trials. The main reason was probably because cardiovascular diseases have erroneously been perceived as 'male' diseases. As most cardiovascular diseases tend to occur later in women, co-existing health problems and age limitations on trials have worked against their inclusion. Late diagnosis due to different and more ambiguous symptoms was another reason and, for women of child-bearing age, the risks of damaging a foetus if a woman became pregnant, led to exclusion.

Dr Stangl's call for increasing the numbers of women in heart trials is backed in an editorial also published in EHJ on line [2] by specialists from the University of Pavia in Italy.

Senior author Dr Silvia Priori, Associate Professor of Cardiology at the University of Pavia, said that research published this year showed that of 300 new drug applications to the US Food and Drug Administration (FDA) between 1995 and 2000 only 163 included an analysis according to gender. Yet 11 of the drugs involved showed a difference in the way a woman's body dealt with the drugs compared with a man's (the pharmacokinetics).

"These differences underlie the importance of studying women as well as men in major cardiovascular trials. Most of the progress in this direction has occurred in the USA as a direct consequence of the commitment of funding agencies that have provided economic support only when a balanced gender presence was assured in the design of a trial," said Dr Priori.

She urged scientific societies to play a major role in ensuring trials investigate gender-specific response to therapy. The Europe Society of Cardiology (ESC), which publishes the European Heart Journal, recently developed the 'Women at Heart' programme to organise initiatives targeted at promoting research and education in cardiovascular disease in women.

The ESC Congress in Stockholm (3-7 September) will focus specially on women and cardiovascular diseases, said Dr Priori, and the ESC is to perform gender-based analyses of data in the Euro Heart Survey – the programme that monitors clinical practice in Europe. She added that, in future, the ESC will work to promote a larger representation of women in clinical trials to provide missing data on gender differences in response to drug therapy.

###

[1] Female-specific aspects in the pharmacotherapy of chronic cardiovascular diseases. European Heart Journal. doi: 101093/eurheartj/ehi397.

[2] Gender-specific prescription for cardiovascular diseases? European Heart Journal. doi: 10.1093/eurheartj/ehi428.

Contact: (media inquiries only)
Margaret Willson:
Tel: 44-153-677-2181
Mobile: 44-797-385-3347
Email: m.willson@mwcommunications.org.uk
PDF of paper available on request.

ESC Press & PR Office (for independent comment):
Gina Dellios:
Tel: +33 (0)4 92 94 86 27
Fax: +33 (0)4 92 94 86 69
Email: gdellios@escardio.org