Treatment of sub/infertility is normally a stepwise procedure. Even if the procedure is initiated after 1 year of ‘failure to conceive’, patients are only rarely referred directly to IVF treatment. Depending upon a number of factors, including age of the women and previous medical history, couples with no ‘severe or absolute causes’ are often advised to either continue trying to conceive at home or start in an IUI program an option unfortunately not included in the model. Last year as many IUI cycles as ART cycles were performed in Denmark. Or for some patients, a diagnostic program is initiated. No matter what initial decision is taken, the consequence often is that even if a couple consults a doctor immediately after 1 year of failed conception, IVF treatment will not be initiated until many months later. Even in a country with free access to ART such as Denmark.

A model as presented by Habibema et al. (2009) is interesting from a theoretical perspective. However, we see a very different picture in the fertility clinic. In real life, couples are not having IVF after 1-year unprotected sex.

In a prospective longitudinal cohort study on cumulative 5-year delivery and adoption rates among 1338 consecutive couples initiating treatment at a specialized fertility clinic in Denmark, the mean duration of infertility was 4.1 year before starting at a fertility clinic (Pinborg et al., 2009). This is in a system with free access to treatment. Other examples could be the large trial conducted by the pharmaceutical industry—normally conducted on good prognosis patients. In the MERIT trial, the included patients had a mean duration of infertility of 3.9 years (Andersen et al., 2006). In the Bravelle study, the patients had a mean duration of infertility of 2.8 years (Andersen et al., 2008).

It is therefore important—also in order to be able to initiate low-technology treatments as IUI—that the couples do not wait too long before contacting a doctor.

In conclusion, we fully agree with te Velde and colleagues that subfertile/infertile couples should have access to free ART. However, we believe that we have a long way to go before this is reality on a European level.

The barrier to accessibility to fertility treatment experienced in most countries must be addressed by governments. In Europe, this not only means providing financial assistance to couples undergoing ART but also that ARTs provided are of the highest quality and based on the best available science. This will to reduce the emotional and psychological burden suffered by infertile couples and the demographic challenges we are faced with.

References


Søren Ziebe1,3 and Paul Devroey2
1The Fertility Clinic, Rigshospitalet, University Hospital of Copenhagen
2Center for Reproductive Medicine of the Vrije Universiteit Brussel, Brussels, Belgium
3Correspondence address. E-mail: ziebes@rh.dk
doi:10.1093/humupd/dmp041
Advanced Access publication on October 1, 2009

Effects of soy protein and isoflavones on circulating hormone concentrations in pre- and post-menopausal women: a systematic review and meta-analysis

Sir,

We greatly appreciate the meta-analysis by Hooper et al. (2009) which found that there were minor changes in circulating reproductive hormone levels in pre- and post-menopausal women in response to isoflavone exposure from soyfoods and isoflavone supplements. However, we are troubled by the author’s concern that the small (~14%) non-statistically significant increase in circulating estradiol concentrations in post-menopausal women might represent an increased breast cancer risk. Hooper et al. (2009) cite a meta-analysis by Key et al. (2002) that included nine studies that showed being in the top quintile of total circulating estradiol levels was associated with a doubling of breast cancer risk when compared with the bottom quintile. Not mentioned, however, is that in the same analysis higher estrone and estrone sulfate levels were also associated with increases in breast cancer risk, similar to those reported for estradiol (Key et al., 2002). Other investigators have also identified higher post-menopausal estrone levels as a risk factor for breast cancer (Gruber et al., 2002; Kaaks et al., 2005; Neilson et al., 2009); elevated estrone levels are also associated with an increase of mammographic breast density (Crandall et al., 2008)—a parameter considered to be a better predictor of breast cancer than serum estradiol levels (Cummins et al., 2009).

These estrone levels are important because in the meta-analysis of Hooper et al. (2009), there was a decline in estrone levels in response to soy, although also non-significant and based on smaller subject numbers, that paralleled the increase in estradiol levels. Thus, when considering both estrone and estradiol, the small and non-significant changes in opposite directions are in fact not suggestive of an increased breast cancer risk.
Furthermore, there is considerable question as to whether estrogen therapy alone increases breast cancer risk (Conner et al., 2008). In the Women’s Health Initiative trial, the combination of conjugated equine estrogens (CEE) plus the progestin medroxyprogesterone acetate increased breast cancer risk (Rossouw et al., 2002), whereas the opposite was the case for CEE-only therapy (Anderson et al., 2004; Stefaniak et al., 2006). This finding suggests that exposure to isoflavones, which are considered to be mixed estrogen agonists/antagonists, is very unlikely to increase breast cancer risk. This conclusion is supported by the lack of effects of isoflavones observed in clinical studies on markers of breast cancer risk including breast tissue density and breast cell proliferation (Verheus et al., 2007, 2008; Marinì et al., 2008; Messina and Wood, 2008; Maskarinec et al., 2009). Furthermore, recent epidemiological data indicate that isoflavone exposure after a diagnosis of breast cancer may actually improve prognosis (Guha et al., 2009; Messina et al., 2009). Thus, the evidence indicates that isoflavones will not increase breast cancer risk in healthy women or worsen the survival of breast cancer patients.

References


Johannes Huber1, Martin Imhof1,2,4 and Mathias Schmidt1

1Department of Gynecologic Endocrinology and Reproductive Medicine, Medical University Vienna, Vienna, Austria
2Department of Gynecology and Obstetrics, Teaching Hospital, Korneuburg, Austria
3Isoflavone Research Initiative, Wartbergweg 15, D-86874 Mattstetten, Germany
4Correspondence address. E-mail: martin.imhof@meduniwien.ac.at doi:10.1093/humupd/dmp040

Advanced Access publication on October 8, 2009

Reply: Effects of soy protein and isoflavones on circulating hormone concentrations in pre- and post-menopausal women: a systematic review and meta-analysis

Sir,

Thank you for your interest in our systematic review (Hooper et al., 2009) and for raising some important points in relation to the complex dataset we reviewed. As we stated in the review, the effects for post-menopausal women for both estrone and estradiol were not statistically significant, suggesting that soy isoflavones may not cause clinically relevant changes in the hormone levels of post-menopausal women. However, given that the 2.76 pmol/l (95% CI 0.37 to 5.90) (or 0.75 pg/ml) increase in estradiol was close to statistical significance (P = 0.07), whereas the 5.33 pmol/l (95% CI 11.56 to 0.90) decrease in estrone was not (P = 0.26), we...