Why similar meta-analyses addressing the same topic reach different conclusions!

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Data from IVF cycles irrespective of the indication for IVF are not in concordance on which type of gonadotrophin to be used. How to explain this conflict?! According to EBM, we should search for the best evidence in meta-analysis. The results of a meta-analysis usually reflect a wide range of clinical settings and patient characteristics; thus, the results can be broadly generalized among typical patients. (Collins, 2003)

However, results of meta-analyses can be very misleading if suitable attention has not been given to formulating the review question; specifying inclusion criteria; identifying, selecting and critically appraising studies; collecting appropriate data; and deciding what would be meaningful to analyse.

Two previous meta-analyses compared uFSH with hMG (Daya 1995; Agrawal 2000) regarding clinical pregnancy rate. Daya 1995 showed favorable outcome for uFSH over hMG. On the contrary, Pooling the trials included in Agrawal et al, 2000 that differentiated between different GnRHa protocols and found no significant difference between urinary FSH and hMG. When used the long protocol, it resulted in an odds ratio for clinical pregnancy rate per woman of 0.88 (95% CI: 0.65-1.19). The meta-analysis of Daya did not differentiate between the GnRHa protocols used.

Three meta-analyses studying recombinant FSH reached different conclusions. Recombinant FSH was found to yield higher pregnancy rates and the total gonadotropin dose required was lower (Daya, 2002). In this meta-analysis Daya concluded that for every 19 patients treated one additional patient would conceive when treated with recombinant FSH. Spontaneous abortion, multiple pregnancy, and OHSS rates were similar for both gonadotropins. However, Al-Inany et al. found no evidence of increased clinical pregnancy rates when recombinant FSH was compared with urinary FSH (Al-Inany et al., 2003). Another recent meta analysis concluded that urinary HMG was associated with higher clinical pregnancy rates in cycles down regulated by GnRH agonists (van Wely et al. 2003).

Does this means that in patients undergoing IVF firm conclusions cannot be reached regarding the choice of gonadotrophin!!!!! Daya meta-analysis did not compare to hMG but compared recombinant to purified and highly purified FSH (both have been withdrawn from the market). Van Wely compared recombinant FSH to hMG included only five trials (true and quasi-randomised RCTs) while Al-Inany et al meta-analysis has included more truly RCTs with 2031 IVF/ICSI cycles and showed no statistically significant difference between both drugs regarding live birth rate. Subgroup analysis was done including only women down regulated with long protocol. There was statistically significant difference in favor of hMG over recombinant FSH O.R.: 1.27 (95% CI 1.00-1.62). The number needed to treat was calculated and found to be 23. Thus, it would require 23 cycles of ART treatment to achieve a single additional clinical pregnancy with hMG treatment compared with recombinant FSH. A large treatment effect leads to a small NNT and vice versa. NNTs for treatment should be small. It should be noted that NNT for Van Wely
meta-analysis was 18 while in ours is 23 (with more trials included). This figure could be even increased with more trials.

In conclusion, There is actually no conflict in conclusions reached by different meta-analyses, but the difference between them come from the search date and methodology design of each meta-analysis.

REFERENCES