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Depression is disabling a growing proportion of children, but evidence on treatment is disputed. **Andrew Cotgrove** believes drugs are a vital part of the armoury but **Sami Timimi** is unconvinced that they are helpful or safe

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Sami Timimi consultant child and adolescent psychiatrist, Lincolnshire Partnership NHS Trust, Sleaford, Lincolnshire NG34 8QA stimimi@talk21.com

The medical profession had endorsed the use of selective serotonin reuptake inhibitors (SSRIs) well before any of the big studies in children were published.[1] Now that studies have been done, the evidence is clear: the drugs are not effective in young people and can increase suicidal behaviour. Continuing to use SSRIs in young people is not good value for money, dangerous, and ethically unsound.

It is well established that tricyclic antidepressants are not effective for childhood depression.[2] The evidence suggests SSRIs are no better. None of the studies on SSRIs for childhood depression have, on outcome measures reported by patients or parents, showed significant advantage over placebo.[3] No data regarding rates of self harm, presentations to emergency or mental health services, or school attendance were presented in any of the studies, leading the reviewers to conclude that investigators exaggerated the benefits and downplayed the dangers of SSRIs for children. A subsequent systematic review found that unpublished trials showed that newer antidepressants were even less effective and more harmful for children than suggested by the published trials.[4]

Despite this, one antidepressant, fluoxetine, was spared. National guidelines concluded that it was the only antidepressant with a favourable balance of benefit over risk.[5] Given its similar pharmacological properties, there is no theoretical reason why fluoxetine should have a significantly different profile from other SSRIs; and indeed it doesn't. The treatment of adolescent depression study (TADS)[6] is the most influential study backing fluoxetine and provides a good example of how the publicity does not match the published findings.

The investigators claimed to show an advantage for fluoxetine, especially when combined with cognitive behaviour therapy. However, the way they reported their data was flawed.[7] The study included a double blind comparison of fluoxetine against placebo and an unblinded comparison between cognitive behaviour therapy alone and fluoxetine with cognitive behaviour therapy. The lack of patient blinding and placebo control in the last two groups is likely to exaggerate the benefit seen in participants receiving fluoxetine with cognitive behaviour therapy because they had more face to face contact and knew (as did their doctors) that they were not receiving placebo. Furthermore, the poor response in the group receiving only cognitive behaviour therapy is inconsistent with other published studies, raising questions about the quality of the psychotherapeutic intervention in this study.

Comparing results across all four groups is therefore misleading. The valid finding from the study is the lack of a statistical advantage for fluoxetine over placebo on the primary end point, the children's depression rating scale. Despite the exclusion of known suicidal behaviour, the study found a trend to more suicidal behaviour (six attempts in the fluoxetine groups versus one in the no fluoxetine groups). This result is consistent with that of other trials of SSRIs. Putting together that result with the lack of clinically important advantage over placebo on most measures and similar findings in the previous studies comparing fluoxetine and placebo,[8] the profile for fluoxetine is similar to that of all other SSRIs—it has little efficacy and is potentially dangerous.

However, we should spare a thought for the beleaguered doctor. Given the high placebo response, many doctors will see improvements after prescribing an antidepressant for a young person in distress and subsequently attribute improvements to the drug. This high placebo response may thus reinforce prescribing, and it has been difficult for many doctors faced with a distressed young person to accept that SSRIs may be ineffective.

Distorted reporting hasn't helped this situation. Major medical journals have published papers on antidepressants for children in which the message (affirmations of efficacy and safety) is at odds with the reported outcomes (of no statistical significance, dubious clinical importance, and increased rates of suicidal behaviour). Thus many of the abstracts do not mention lack of significance on the primary measures. Others such as the recent adolescent depression antidepressant and psychotherapy trial (ADAPT)[9] didn't even include a placebo arm, giving the (false) impression that SSRIs have already been shown to be more effective than placebo.

Thus marketing spin has taken precedence over scientific accuracy. One reason for doing the studies in the first place was to justify well established prescribing patterns. It created a trend which has become difficult to reverse despite the evidence. But reverse it we must, as it is neither value for money nor clinically useful, may have resulted in a small but tragic number of avoidable suicides, and contributed to a trend of inappropriately medicalising common emotional states and experiences.[10] Most states of childhood distress are self limiting and do not require extensive intervention, but when intervention is necessary psychotherapy has a well established record of effectiveness.[11]

Competing interests: None declared.

References are on bmj.com