Prescribing antidepressants post Cipriani et al.

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Many of you will have seen the recent paper in the *Lancet* in which a sophisticated meta-analysis of the relative efficacy and acceptability of new antidepressants was conducted (Cipriani et al., 2009). The authors of this paper used a new statistical approach that makes it possible to estimate the relative efficacy of antidepressant drugs even though the majority have not been specifically compared against each other. By comparing the efficacy of different drugs against common comparators, meaningful inferences of relative antidepressant efficacy and acceptability can be made. This new meta-analytical process allowed the authors to rank antidepressants according to these two dimensions as shown in Figure 1. So what are the key messages?

The most obvious ones relate to relative efficacy where mirtazapine escitalopram venlafaxine and sertraline demonstrated significantly greater efficacy than the other drugs [relative odds ratios of about 1.3]; see Figure 1. Reboxetine was significantly less efficacious than the others. The second dimension relates to relative acceptability where escitalopram came top followed by sertraline and bupropion, with venlafaxine and mirtazapine lower down. Based on these two dimensions the authors conclude that escitalopram and sertraline should be the first choice antidepressants with sertraline possibly being preferred on the grounds of lower acquisition costs.

What do these findings mean and what are their implications for clinical practice? From the perspective of the British Association for Psychopharmacology (BAP) the finding that escitalopram and venlafaxine have better efficacy than most other new antidepressants reinforces the message in the recent BAP guidelines on the treatment of depression (Anderson et al., 2008). That escitalopram was among the antidepressants with greatest acceptability was perhaps less obvious given it is the most potent selective serotonin reuptake inhibitor (SSRI). It may reflect some positive benefit of its more prolonged reuptake site kinetics as compared with those of citalopram and other shorter-acting SSRIs such as paroxetine and fluvoxamine. This slow dissociation of escitalopram from the reuptake site appears to be due to its binding to another (the so-called ‘allosteric’) site on the 5HT transporter (Sánchez et al., 2004).

The relatively high efficacy of sertraline was unexpected although its good acceptability and low propensity for drug–drug interactions is well recognised. Whether many psychiatrists will agree with the recommendations of Cipriani et al. (2009) that sertraline should be the first-line antidepressant drug is not known and only time will tell if prescribing practice changes. Currently citalopram and fluoxetine are the most commonly used of the new antidepressants with total script numbers of 7.7 and 5 million, respectively although 30% of citalopram scripts (2.3 million) are for 10 mg tablets which alone would be subtherapeutic. Surprisingly amitriptyline at low dose is also very common with over 6 million scripts for 10 and 25 mg doses but as these are so far below the effective antidepressant dose we presume that they must be being used for other reasons (prescription cost analysis 2008).

The reason for citalopram and fluoxetine being so popular probably reflects the fact they were the first of the SSRIs to become generic. In the NICE (2004) review of antidepressants the ‘considerations’ suggested for the prescribing of SSRIs/serotonin–norepinephrine reuptake inhibitors (SNRIs) were:

- consider generic SSRIs;
- paroxetine, fluvoxamine and fluoxetine are less good due to the potential for drug–drug interactions;
- venlafaxine and duloxetine possibly limited by hypertension/overdose adverse effects.

Although use of generic drugs was only recommended for ‘consideration’, many formulary committees decided to make this a local rule.

Since the last NICE recommendations there has been a move for drug and therapeutic (formulary) committees to recommend SSRIs based on cost, with generic drugs being preferred for this reason. In practice, this has meant fluoxetine and citalopram have become the first-line treatments. One would presume that this would change in light of these new data, indeed the authors of the *Lancet* article themselves suggest that sertraline would be preferred over the other...
generics of similar cost based on their efficacy–acceptability analysis. In terms of pure efficacy, perhaps for patients at the
more severe end of the depression spectrum then escitalopram might be preferred, since although mirtazapine and venlafaxine are now generics, the price differential is slight and the acceptability of escitalopram so good.

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References


