CHAPTER 20
From the book: "Beat Depression Quickly and Cheaply:
A psychiatrist tells you how." (Amazon, 2025)

About a "first-aid" medication for intense and painful depression:

Show this chapter to your doctor.

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About: Rapid response of depressive symptoms to quetiapine XR (extended release)

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Dear colleague (GP, FP, specialist):

You are already an expert in the use of antidepressant medications.

Here is more information which is still not widely known among physicians:

The extended-release form of Quetiapine (Quetiapine XR or Seroquel XR) can often bring some rapid improvement for depression. Certain studies indicate that results can be significant even within 3 days.

This is to the point that you may wish to give Quetiapine XR, immediately on seeing the patient, along with an antidepressant of your choice.

I have used quetiapine XR if I feel that the patient's depressive suffering is intense. In such a case, I want to see a rapid improvement to the point that suicide is much less likely.

Also, Quetiapine XR can be a judicious choice, as add-on treatment or even as monotherapy, if a patient is bipolar, or if you suspect that the patient may turn out to be bipolar when given antidepressants. This is because Quetiapine XR is also an approved short-term and long-term treatment for mania and bipolar disorder.

The evidence about Quetiapine XR (the extended-release formulation of Quetiapine) is convincing, in my opinion.

(However, in these studies, not every patient benefited from Quetiapine XR. The response rate was generally something like 50 %.)

Here are the highlights:

Quetiapine XR, as monotherapy for major depression, often gives an improvement within the first week (Cutler et al, 2009). On the 60-point MADRS depression scale, the mean improvement was of 8 points in the first week; and by 4 further points in the second week. The comparison antidepressant, duloxetine (Cymbalta), gave no improvement until after 2 weeks. Of course, some patients showed no significant response to Quetiapine XR.

(In the "real world," in the first week, an 8-point reduction could, in some cases, lead to a switch from moderately severe depression, to merely moderate depression.)

A 2014 study (Porcelli et al) looked at bipolar depression. The study concludes that Quetiapine XR "seems to be a fast treatment, acting within the first 3 days. Indeed, during this time window, the mean reduction in HAM-D [Hamilton Rating Scale for Depression] total score was 24.4%, while during the following 4 days, a further improvement of . . . 1.8% was achieved."

A review paper in 2018 (Zuleide) cited 13 studies in which Quetiapine XR monotherapy improved major depression for at least some people.

Quetiapine XR also can give remarkably good results when added on to standard antidepressants, for difficult-to-treat depression. (Nelson, 2009)

SOME DETAILS

Quetiapine is an antipsychotic which has been on the market in the U.S. since 1997. It is available in 2 formats, depending on the coating of the pill.

There is an "immediate release" form, Quetiapine IR, which has a thin coating. The coating dissolves fairly quickly in the stomach and intestine. The effect is felt by the patient in about an hour. This form of Quetiapine is now often used as a sleeping pill (at 25 or 50 mg HS), because it is effective and is not habit-forming.

The other format is Quetiapine XR. The XR stands for "extended release." The coating dissolves more slowly. Consequently, the Quetiapine is released gradually over a period of about 12 hours, typically. The serum concentration is relatively constant over the course of 12 hours, rather than showing a swift onset and offset like Quetiapine IR.

The half-life of Quetiapine, once present in serum, is about 6 hours.

As mentioned, it's the XR version of Quetiapine that has been shown often to reduce depression rapidly over the course of a few days. There's no official explanation about why this happens. Personally, I see all antipsychotics as having an effect of reducing the patient's sensitivity to his own feelings and inner experiences. This may or may not be true about the effect against psychosis. However, my impression is that Quetiapine reduces sensitivity to depressive suffering. If so, this might explain, in part, its rapid action against depression.

In the research, the daily doses of Quetiapine XR commonly tested are 150 mg HS and 300 mg HS. In most studies, Quetiapine XR generally improved depression; and improvement was not much different for the two doses.

(As a comparison, the usual effective daily doses of Quetiapine XR for psychosis are 300 to 600 mg, and in some cases 900 or 1200 mg.)

To put the cited research into context, here are the two research scales mentioned:

The MADRS (Montgomery–Åsberg Depression Rating Scale), has 10 items about depressive symptoms, each scored from zero to 6. The highest score would be 60. The scale's ranges are given as:

- 0–6 – No or minimal depression
- 7–19 – Mild depression
- 20–34 – Moderate depression
- 35 and higher – Severe depression

The Hamilton Rating Scale for Depression ("HAM-D") is a 17-item questionnaire.
Here are the ranges of depression indicated by the HAM-D:

- not depressed – 0-7
- mild (subthreshold) – 8-13
- mild to moderate – 14-18
- moderate to severe – 19-22
- very severe – 23 and higher

The most commonly reported adverse effects of Quetiapine XR are: mild weight gain, dry mouth, and sedation. Constipation may also occur. (Daily docusate is recommended to keep the stool soft until it is passed.)

The mean increases in the QTc interval are similar for Quetiapine and the SSRIs. The increases are generally lower than 10 milliseconds, but *there may be a wide variability*.

In my opinion, it is best practice to measure, and document, the QTc interval before and during treatment.

- After an initial "classical" baseline ECG, personally, I use the Kardia one-lead device, about the size of a large adult thumb, and available inexpensively online.
- Patients touch the flat device with two fingers. The device gives a 30-second tracing (in PDF form) on the physician's mobile phone.
- With this device, the QTc is not computed automatically. One has to measure manually the QT interval, and then convert it to QTc using an online conversion calculator, which can be found by a Google search. The whole process takes 2 minutes to administer with the patient, then about 5 minutes for measuring and calculating afterward. (The method is not of much use if there is an arrhythmia.)
- The advantage is getting an immediate QTc measurement, rather than ordering an ECG, for which the patient must make an appointment; and, of course, the patient might not show up for it.
- I use this routine for patients who might be at risk for QTc prolongation, such as with a bundle branch block or a long baseline QTc, or taking other medications which might prolong the QTc.

As I said earlier, in these studies, not every patient benefited from Quetiapine XR. The response rate was generally something like 50 %

Articles cited:

Cutler AJ, Montgomery SA, Feifel D, et al. Extended release quetiapine fumarate monotherapy in major depressive disorder: a placebo- and duloxetine-controlled study. Journal of Clinical Psychiatry 2009; 70:526-539.

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