"Tapering of antidepressant medication – trials and tribulations"

Day: | Time: | Track:
Thursday 12th July 2018 | 3:30 – 4:45 pm | Clinical Applications

The first presenter is Anders Sørensen. He will discuss a Cochrane review to describe the efficacy of any intervention aiming at stopping treatment with an antidepressant drug.

The second presenter is Alice Tickell. She will discuss emerging findings of a qualitative analysis of process data during mindfulness-based cognitive therapy combined with support to taper or discontinue anti-depressant medication (MBCT-TS). Results focussed on people's experiences over time as they tried to taper/discontinue medication and use skills learnt in MBCT-TS, will be presented.

Carolien Wentink is the third presenter, she will discuss facilitators and barriers in the process of discontinuation of anti-depressant medication in patients with recurrent depression after Mindfulness-Based Cognitive Therapy.

Finally, Claudi Bockting will present a study with two primary objectives 1) to compare antidepressants (AD) to Preventive Cognitive Therapy (PCT) while tapering AD (PCT/-AD), and 2) assess the added value of PCT to AD (PCT+AD) in terms of relapse/recurrence.

Symposium overview

Presenter 1   **Anders Sørensen** - Cochrane Review of psychopharmacological withdrawal

Presenter 2   **Alice Tickell** - Experiences of tapering antidepressants in the context of Mindfulness-Based Cognitive Therapy: Findings from the PREVENT trial.

Presenter 3   **Carolien Wentink** - An Exploration of the Facilitators and Barriers of Discontinuation of Antidepressant Medication after Mindfulness-Based Cognitive Therapy in Patients with Recurrent Depression.

Presenter 4   **Claudi Bockting** - Preventive cognitive therapy compared to medication for relapse prevention in depression (DRD study): a three-arm randomised controlled trial.

Chair: *Zindel Segal*

Cochrane Review of psychopharmacological withdrawal

Anders Sørensen

Nordic Cochrane Centre, Denmark

BACKGROUND: There is no doubt that withdrawing from antidepressant drugs can be beneficial for the patients, as the scientific literature on long-term use is replete with arguments against. Coming off the drugs is a highly desired goal for many patients. However, the transition from being medicated to medicine-free can be challenging both emotionally and physically, especially if done unsupervised and rapidly. The primary reason for having difficulties coming off antidepressants is that the patients have become dependent on them, experiencing potentially severe withdrawal symptoms upon dose reduction. The extent and severity of withdrawal symptoms can be minimized by a slow and gradual taper, but the optimal speed and need for support during the process seems currently unknown. As emotional issues may occur, psychotherapy, which involves emotion regulation, is hypothesized to be relevant during withdrawal.

OBJECTIVES: To assess the effects of different interventions aimed at helping patients come off antidepressant drugs safely. We seek to describe the efficacy of any intervention aiming at stopping treatment with an antidepressant drug.

METHODS: Systematic literature search according to the Cochrane guidelines for studies that in any way can inform us how patients can withdraw safely from antidepressant drugs, with a focus on randomized trials and cohort studies.

RESULTS: Research on antidepressant drug withdrawal is alarmingly scarce, considering the current psychiatric drug epidemic. Very few randomized trials compared different methods specifically aimed at complete withdrawal; most of them of poor quality and with profound limitations. Most studies investigated the effects of coming off vs. continued use, thus measuring the possibility of withdrawing as a secondary outcome, but without comparing the method with another method. In such studies, Mindfulness-based Cognitive Therapy (MBCT) was the most studied psychological intervention.

DISCUSSION AND CONCLUSION: Regarding duration of drug intake, long-term patients are heavily underrepresented, thus limiting our current evidence to fairly short-term patients not representing many of the real-world patients who struggle with, and would most likely benefit from, becoming drug-free. Due to scarce research, methodological deficiencies and limitations, non-representable populations and lack of acknowledgement of the nature and implications of withdrawal symptoms, no clear evidence-based guidelines on how to best and safest withdraw from antidepressant drugs can be derived. However, the evidence does show that withdrawing completely is possible, but we do not know by what means necessary or how many more patients could come off had they used a slower tapering scheme or received more elaborate support during the process.

Experiences of tapering antidepressants in the context of Mindfulness-Based Cognitive Therapy: Findings from the PREVENT trial.

Alice Tickell, Willem Kuyken, Catherine Crane, Mark Williams, et al.

Department of Psychiatry, University of Oxford, Prince of Wales International Centre, Warneford Hospital, Oxford, United Kingdom

Background: Individuals with a history of recurrent depression have a high risk of depressive relapse/recurrence. Maintenance anti-depressant medication (m-ADM), prescribed for at least 2 years, is the current recommended treatment to help people stay well in the long-term. However, many individuals are interested in psychological alternatives to medication. Furthermore, individuals on a course of m-ADM may decide to taper and/or discontinue their medication. A recent individual patient data meta-analysis suggests that mindfulness-based cognitive therapy (MBCT) may provide an alternative to m-ADM for people wishing to taper and/or discontinue (Kuyken et al., 2016).

Methods: The PREVENT trial (n=424), included in the above meta-analysis, randomised participants to mindfulness-based cognitive therapy combined with support to taper or discontinue anti-depressant medication (MBCT-TS) or m-ADM, and examined depressive relapse/recurrence over 24 months (Kuyken et al., 2010; Kuyken et al., 2015). It additionally included an embedded process evaluation to explore participants' experiences of MBCT-TS using qualitative data gathered from in-depth semi-structured interviews and written responses collected immediately after MBCT-TS, and again 12 and 24 months later.

Results: Emerging findings of a qualitative analysis of this process data, focussed on people's experiences over time as they tried to taper/discontinue medication and use skills learnt in MBCT-TS, will be presented.

Discussion: We will discuss the primary themes emerging from the data and explore how they relate to what we know about people's experiences of m-ADM tapering and discontinuation.

An Exploration of the Facilitators and Barriers of Discontinuation of Antidepressant Medication after Mindfulness-Based Cognitive Therapy in Patients with Recurrent Depression.

Carolien Wentink, et al.

Department of Psychiatry, Radboud University Nijmegen Medical Centre, Radboud University Nijmegen, Nijmegen, Netherlands

Background: For patients with major depressive disorder (MDD) the continuation of antidepressant medication (ADM) is widely used to prevent depressive relapse/recurrence. Mindfulness-Based Cognitive Therapy is offered as a viable alternative. Studies show contrasting results regarding relapse/recurrence rates during guided tapering. Little is known about facilitators and barriers with regard to the discontinuation of ADM. This study explored facilitators and barriers in the process of discontinuation of ADM in patients with recurrent depression after Mindfulness-Based Cognitive Therapy.

Methods: A mixed-methods study. Data were quantitative drawn from a randomized controlled trial (Huijbers et al, 2016) and qualitative from a supplementary study. In total 249 patients with recurrent depression (ADM > 6 months) were randomly assigned to MBCT with discontinuation of ADM (n=128) or MBCT plus maintenance ADM (n=121). Partial, full and no discontinuation of ADM and relapse in depression were used as outcome measures. From a purposive sample of patients (n=15) and their healthcare professionals (n=7) interviews were taken to examine facilitators and barriers of discontinuation.

Results: Of the patients allocated to MBCT with discontinuation 53% (N=68) managed to fully discontinue their ADM within 6 months after baseline, 48 had a relapse in depression and 39 restarted ADM within 15 months. Emerging themes regarding facilitators and barriers of discontinuation of antidepressant medication will be presented.

Discussion: We will discuss why discontinuation of antidepressant medication can be difficult and provide some suggestions for strategies to manage this process in clinical practice.

Preventive cognitive therapy compared to medication for relapse prevention in depression (DRD study): a three-arm randomised controlled trial.

Claudi Bockting, et al.

AMC, department of Psychiatry, University of Amsterdam, Amsterdam, Netherlands

Aims: Keeping individuals on antidepressants (AD) after remission or recovery is a leading strategy to prevent relapse/recurrence. Preventive Cognitive Therapy (PCT) has been proposed as alternative, but it remains unclear whether its addition will either allow AD to be tapered or enhance its efficacy. This presentation reports on the results of a study (Bockting et al., under review) with two primary objectives 1) to compare AD to PCT while tapering AD (PCT/-AD), and 2) assess the added value of PCT to AD (PCT+AD) in terms of relapse/recurrence.

Method: In this multicenter three-arm RCT, 289 participants with at least two previous depressive episodes who remitted/recovered on AD were assigned to PCT+AD, AD, and PCT/-AD. The primary outcome was time-related proportion of depressive relapse/recurrence (intention-to-treat) assessed four times over 24 months.

Results: Eligibility was assessed in 2560 participants of whom 289 were randomised. The overall log-rank test was statistically significant ($\chi2$ 8.60; p = 0.014). AD did not reduce the risk of relapse/recurrence more than PCT/-AD (HR 0.86, 95%CI:0.56-1.32, p = 0.502). Adding PCT to AD resulted in a statistically significant 41% relative risk reduction compared to AD (HR 0.59, 95%CI: 0.38-0.94, p = 0.026).

Discussion: Maintenance AD treatment is not superior to PCT after recovery. Adding PCT to AD after recovery yielded substantial protective effects over AD. Clinical implications will be discussed.