Carbamazepine Augmentation for Schizophrenia: How Good Is the Evidence?

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Background: Augmentation strategies in schizophrenia treatment remain an important issue because despite the introduction of several new antipsychotics, many patients remain treatment resistant. The aim of this study was to undertake a systematic review and meta-analysis of the safety and efficacy of one frequently used adjunctive compound: carbamazepine.

Data sources and study selection: Randomized controlled trials comparing carbamazepine (as a sole or as an adjunctive compound) with placebo or no intervention in participants with schizophrenia or schizoaffective disorder were searched for by accessing 7 electronic databases, cross-referencing publications cited in pertinent studies, and contacting drug companies that manufacture carbamazepine.

Method: The identified studies were independently inspected and their quality assessed by 2 reviewers. Because the study results were generally incompletely reported, original patient data were requested from the authors; data were received for 8 of the 10 randomized controlled trials included in the present analysis, allowing for a reanalysis of the primary data. Dichotomous variables were analyzed using the Mantel-Haenszel odds ratio and continuous data were analyzed using standardized mean differences, both specified with 95% confidence intervals.

Results: Ten studies (total N = 283 subjects) were included. Carbamazepine was not effective in preventing relapse in the only randomized controlled trial that compared carbamazepine monotherapy with placebo. Carbamazepine tended to be less effective than perphenazine in the only trial comparing carbamazepine with an antipsychotic. Although there was a trend indicating a benefit from carbamazepine as an adjunct to antipsychotics, this trend did not reach statistical significance.

Conclusion: At present, this augmentation strategy cannot be recommended for routine use. The most promising targets for future trials are patients with excitement, aggression, and schizoaffective disorder bipolar type.

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A substantial proportion of patients with schizophrenia do not fully respond to treatment with antipsychotics.[1] Despite the advantages of the "atypical" antipsychotics compared with conventional drugs, a convincing superiority in treatment-resistant patients has to date been proven only for clozapine.[2,3] Many attempts have therefore been made to augment the effect of antipsychotics by adding other psychoactive agents. One of the most popular augmentation strategies is carbamazepine, an anticonvulsant that is also used as a mood stabilizer in bipolar affective disorders.

Narrative reviews in the early 1990s generally supported the effectiveness of carbamazepine augmentation of antipsychotics.[4–6] This may be the reason why recent influential treatment guidelines such as the American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia,[7] the Schizophrenia Patient Outcomes Research Team treatment recommendations,[8] and the Texas Medication Algorithm Project schizophrenia algorithms[9] recommend the use of adjunctive carbamazepine in cases of refractory schizophrenia, albeit the level of evidence is typically described as "not robust" or "very little." However, according to a recent publication,[10] 54% of the inpatients with schizophrenia at New York State psychiatric hospitals received a mood stabilizer in 1998.

The conclusions of traditional reviews may be affected by publication biases,[11] language biases,[12] and the personal opinion of the reviewers. Systematic reviews address these problems by a comprehensive, unbiased search process and by use of explicit methods to limit bias. Such methodology provides more reliable results upon which to draw

conclusions and make decisions.[13] With respect to the use of medications to augment antipsychotics, the individual trials are often too small to allow the detection of small-to-moderate quantitative differences.[14] Meta-analysis enables the results of individual trials to be combined, which increases the statistical power to confidently detect significant effects. Finally, further randomized controlled studies using carbamazepine for schizophrenia have been conducted since the influential reviews published almost a decade ago.[4,15]

The aim of this review was to provide clinicians with an up-to-date, systematic review and meta-analysis of the use of carbamazepine as a sole agent and as an adjunct to antipsychotics for schizophrenia. In addition, we sought individual patient-level data in order to undertake a reanalysis of the primary data. This article is the first of a series of meta-analyses examining augmentation strategies for schizophrenia that are currently under investigation by our group. Other meta-analyses reviewing augmentation with lithium and benzodiazepines are to follow.

METHOD

Search

All published and unpublished randomized controlled trials that assessed the effectiveness of carbamazepine in the treatment of schizophrenia and schizophrenia-like psychoses (schizoaffective and schizophreniform disorders) were searched for using the following databases: Biological Abstracts, The Cochrane Library Central Register, Cochrane Schizophrenia Group's Register, EMBASE, LILACS, MEDLINE, and PsycLIT. The exact search strings have been reported elsewhere.[16] In addition, the reference sections of included articles and key reviews were screened, and the first authors of the included studies and pharmaceutical companies producing carbamazepine were asked whether they were aware of further trials. All citations identified by the searches were independently inspected by at least 2 reviewers before inclusion. Since most trials were incompletely reported and did not provide the information necessary to allow meta-analytic calculations, all relevant authors were contacted for inclusion assessment and, most importantly, for requesting the individual patient data.

Quality Assessment

Given that empirical research has shown that lack of adequate allocation concealment in randomized trials is associated with bias,[17] the reviewers independently evaluated the quality of the included trials. Concealment of the allocation prevents the possibility of conscious or subconscious manipulation of individual assignments. Inadequate concealment undermines the principle of randomization, because participants may then be allocated to a treatment according to prognostic variables rather than by pure chance. A rating was given for each trial based on the 3 quality categories described in the *Cochrane Collaboration Handbook*.[18] The inclusion criterion for this review was low or moderate risk of bias (category A or B, respectively). A further description of the quality of the trials was assessed using the Jadad Scale,[19] which measures a wider range of factors that have an impact on the quality of a trial: (1) adequacy of randomization, (2) double-blinding, and (3) adequate description of dropouts. The Jadad scores range from 1 (poor) to 5 (good).

Outcome Parameters

Since data on mental health outcomes are often not normally distributed, the main focus was placed on dichotomous outcomes, or an attempt was made to dichotomize the original patient data by defining cutoff points. The principal outcomes of interest were (1) acceptability of treatment as measured by the number of participants leaving the study early and (2) the number of participants with 3 degrees of improvement according to the Brief Psychiatric Rating Scale (BPRS)[20]: a relatively high degree of improvement (50% reduction in BPRS score), an intermediate degree of improvement (35% reduction), and a rather low degree of improvement (20% reduction). Other outcomes were relapse rates (maintenance studies) and side effects. We also examined specific aspects of the mental state such as positive symptoms, negative symptoms, aggressiveness, and depression by analyzing the study endpoint data of the respective scales. To estimate whether these data were normally distributed, the individual patient data were inspected. If individual patient data were not available, the data were excluded if the mean value of continuous endpoint data less the minimum score of the scale were less than twice the standard deviation, because this indicates a nonnormal distribution.[21] The results of the individual studies for which data were not normally distributed are presented in the Results section of the text. Two reviewers extracted data from each publication independent of each other; any disagreements were discussed, and the final decisions were documented.

Dropouts and Crossover Studies

In the case of dichotomous data, we assumed that participants who dropped out prior to completion had no change in their condition unless otherwise stated. Continuous data were reported as presented in the original studies without any assumptions about those lost to follow-up. However, continuous data were excluded if more than 50% of the participants were lost. Furthermore, in order to exclude the potential additive effect in the second or a later stage of crossover trials, only data from the first stage were analyzed.

Meta-Analytic Calculations

The outcome data found were combined into a meta-analysis. For dichotomous data, the odds ratio (OR), that

is, the ratio of the odds of an unfavorable outcome among treatment-allocated participants to the corresponding odds of an unfavorable outcome among those in the control group, was estimated. The odds ratios and 95% confidence intervals (CIs) were calculated with the Peto-modified Mantel-Haenszel fixed-effect model in the case of homogeneous outcomes and with the DerSimonian-Laird random-effects model in the case of heterogeneous outcomes. The standardized mean difference (SMD), which allows combination of the results of different scales used to assess the same outcome, and its 95% confidence interval were calculated for continuous data when measures of variance were available. Study heterogeneity was sought for by visual inspection of the graphs and with the chi-square test. The chi-square test was also used for calculating 2-tailed statistical significances of outcomes. In the case of significant results, the number of participants needed to treat (NNT) or the number of participants needed to harm were calculated.

Studies with negative results are less likely to be published than studies with significant results. The possibility of such publication bias was examined with a "funnel-plot" method described by Mulrow and Oxman.[18]

RESULTS

Search

Our broad search strategy identified several hundred citations, but just over 70 studies investigated the value of carbamazepine for schizophrenia and schizophrenia-like psychoses. Ten studies fulfilled our inclusion criteria (Table 1). The main reasons for exclusion were lack of (adequate) randomization (42 studies), lack of any original data (mainly reviews, 19 studies), lack of a placebo or no-intervention group (5 studies), or lack of any data presented in a suitable way for meta-analysis (3 studies). Full details of the excluded trials are available from the authors. Funnel plots did not suggest the existence of unpublished trials.

Study Characteristics

The studies could be classified according to 3 different comparisons: (1) carbamazepine as a sole treatment versus placebo, (2) carbamazepine as a sole treatment versus antipsychotics, and (3) carbamazepine as an adjunct to antipsychotics versus placebo (or no treatment) added to antipsychotics. The analysis of categories 1 and 2 was important, because if carbamazepine was effective as a sole treatment, its effectiveness as an augmenting agent would be more likely.

Most studies used a parallel-group design, but the studies by Svestka et al.,[23] Carpenter et al.,[22] Llorca et al.[28] and Neppe[24] were crossover studies. Participation rates in individual trials were low, with numbers ranging between 13 and 42. In total, the studies included 283 participants. Most suffered from schizophrenia, although there were some participants with schizoaffective disorder (schizomanic episode N = 4, schizodepressive episode N = 8) or other diagnoses (N = 3) and 23 participants for whom the diagnosis was not clearly indicated. Most studies used some form of standardized diagnostic criteria; however, since the studies from a large time period were reviewed, the criteria varied considerably. Four studies included only people with subtypes of schizophrenia: treatment-resistant participants,[28,30] participants suffering predominantly from negative symptoms,[29] and "psychotic patients with EEG [electroencephalogram] abnormalities."[24] The carbamazepine dose was commonly adjusted to yield levels that are considered to be therapeutic in anticonvulsant therapy. In the augmentation studies, haloperidol was typically used as the standard antipsychotic treatment (doses ranging from 6 to 65 mg/day).

Data Reporting and Study Quality

The efficacy data from individual studies were considerably improved by direct correspondence with authors; 8 of 10 sent their original patient data. However, side effects remained incompletely reported in most studies. Consequently, the quality of the studies according to the Jadad scale varied, with total scores ranging between 2 and 4.

Comparison 1: Carbamazepine as Sole Agent Versus Placebo

There was no randomized controlled trial that examined carbamazepine as the sole agent for managing patients with acute schizophrenia. However, 1 randomized controlled trial[22] compared carbamazepine as a sole agent versus placebo in maintenance treatment. This study showed that carbamazepine was no more effective than placebo in preventing relapse (Figure 1), and since the majority of participants in both groups did relapse, the study was halted at 3 months. Two participants in each group left the study early (OR = 1.07, 95% CI = 0.14 to 8.49, p = .9; Figure 2). Three people treated with carbamazepine developed a rash (OR = 9.1, 95% CI = 0.9 to 95.0, p = .3) and 1, leukopenia (OR = 7.9, 95% CI = 0.16 to 400, p = .06). Transient sedation and nausea were reported in the carbamazepine group, but no figures are available.

Comparison 2: Carbamazepine as Sole Agent Versus Antipsychotics

The study by Svestka et al.[23] is the only trial that compared carbamazepine as a sole agent versus an antipsychotic—perphenazine—in participants with schizophrenia or schizoaffective disorder. There was no significant difference concerning the number of dropouts (OR = 7.05, 95% CI = 0.42 to 117.54, p = .17; see Figure 2) or the number of participants with either 50%, 35%, or 20% BPRS score reduction (OR = 0.53, 95% CI = 0.14 to 2.07, p = .4; OR = 0.36, 95% CI = 0.10 to 1.27, p = .11; and

Table 1. Randomized Controlled Trials Evaluating Carbamazepine as a Treatment for Schizophrenia[a]

Study	Participants (diagnosis, N, mean age or range)	Design (blinding, parallel or crossover, duration, setting)	Interventions (mean dose or range)[b]	Jadad Quality Score
Carbamazepine vs placebo as sole treatment Carpenter et al,[22] 1991	Stabilized schizophrenia (DSM-III; maintenance study), N = 34, 33 y	Double-blind, crossover, 28 wk, outpatients	1. CBZ (800–1200 mg/d) 2. PBO	4
Carbamazepine vs antipsychotics as sole treatment Svestka et al,[23] 1989	Acute schizophrenia and schizoaffective disorder (ICD-9), N = 38, 38 y	Single-blind, crossover, 6 wk, inpatients	1. CBZ (1374 mg/d) 2. Perphenazine (53 mg/d)[c]	2
Carbamazepine vs placebo (or no additional treatment) as an adjunct to antipsychotics				
Neppe,[24] 1983	Chronic schizophrenia with "poor response" and EEG abnormalities,[d] (clinical data and DSM-III), N = 13, 34 y	Double-blind, crossover, 15 wk, inpatients	1. Antipsychotics (762 mg/d CPZe)[e] + CBZ 2. Antipsychotics (1000 mg/d CPZe)[e] + PBO	3
Dose et al,[25] 1987	Acute schizophrenia (ICD-9 and DSM-III), N = 41	Double-blind, parallel, 5 wk, inpatients	1. HPL (8.1 mg/d)[c] + CBZ 2. HPL (10.9 mg/d)[c] + PBO	3
Martin-Munoz et al,[26] 1989	Paranoid schizophrenia (RDC), N = 20, 29 y	Open, parallel, 2.5 wk, inpatients	1. HPL 30 mg/d[e] + CBZ 2. HPL 30 mg/d[e] without additional treatment	3
Mair et al,[27] 1990	Schizophrenia(-like) psychoses (ICD-9), N = 23, 31–44 y	Open, parallel, 5 wk, inpatients	1. HPL or clozapine[c] + CBZ 2. HPL or clozapine[c] without additional treatment	2
Llorca et al,[28] 1993	Treatment-resistant schizophrenia (DSM-III-R), N = 24, 44 y	Double-blind, crossover, 4 × 5 wk, inpatients	HPL (15–65 mg/d)[e] + CBZ or PBO or bromocriptine or cyproheptadine	3
Nachshoni et al,[29] 1994	Residual schizophrenia with negative symptoms (DSM-III-R), N = 30, 46 y	Double-blind, parallel, 5 wk, inpatients	1. Antipsychotics[c] + CBZ 2. Antipsychotics[e] + PBO (300–800 mg/d CPZe in both groups)	3
Simhandl et al,[30] 1996	Treatment-resistant schizophrenia (DSM-III-R), N = 42, 35 y	Double-blind, parallel, 8 wk, inpatients	1. Antipsychotics[e] + CBZ 2. Antipsychotics[e] + PBO 3. Antipsychotics[e] + lithium	4
Hesslinger et al,[31] 1998	Acute schizophrenia or schizoaffective disorder (ICD-10), N = 27, 32 y	Single-blind, parallel, 4 wk, inpatients	1. HPL (18.3 mg/d)[e] + CBZ 2. HPL (13.1 mg/d)[e] without additional treatment 3. HPL (15.0 mg/d)[e] + valproate	3

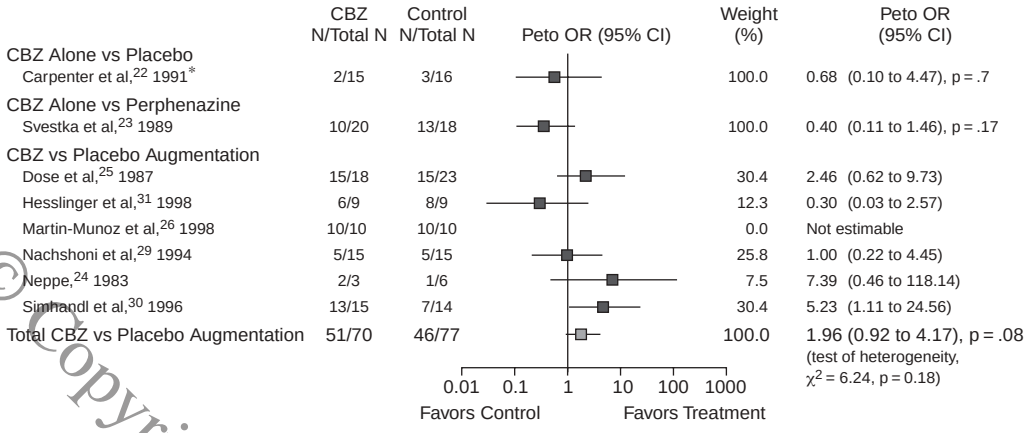
[a]Abbreviations: CBZ = carbamazepine, CPZe = chlorpromazine equivalents, EEG = electroencephalogram, HPL = haloperidol, PBO = placebo, RDC = Research Diagnostic Criteria.
[b]Most studies adjusted the CBZ dose to reach blood concentrations used for seizure treatment. Therefore only the mean antipsychotic doses (or ranges) are shown.
[c]Flexible dose.
[d]There were also other diagnoses, but these patients were not included in the meta-analysis.
[e]Fixed dose.

OR = 0.40, 95% CI = 0.11 to 1.46, p = .17, respectively; the results of 20% BPRS score reduction are displayed in Figure 1). When participants with schizoaffective disorder were excluded, significantly more participants treated with perphenazine than with carbamazepine reached 20% and 35% BPRS score reduction, but not 50% BPRS score reduction (OR = 0.12, 95% CI = 0.02 to 0.66, p = .01; OR = 0.16, 95% CI = 0.04 to 0.73, p = .02; and OR = 0.18, 95% CI = 0.02 to 1.80, p = .15, respectively). Extrapyramidal side effects in terms of parkinsonism (OR = 0.03, 95% CI = 0.01 to 0.10, p < .001) and number of participants who used antiparkinson medication (OR = 0.07, 95% CI = 0.02 to 0.24, p < .001) were significantly more frequent in the perphenazine group. For all other side effects reported, no significant differences were found.

Comparison 3: Carbamazepine Versus Placebo as an Adjunct to Antipsychotics

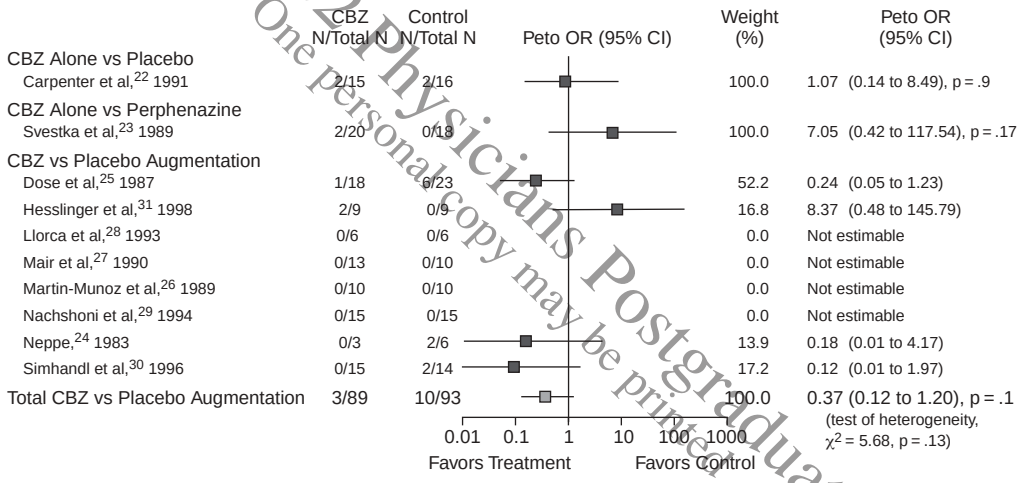
All 8 studies provided data on "number of participants leaving the study early"; there was no significant difference between carbamazepine and placebo augmentation in number of patients leaving studies early (OR = 0.37, 95% CI = 0.12 to 1.20, p = .1; see Figure 2). On combining the results of 6 studies, a trend in favor of carbamazepine in terms of 20% (OR = 1.96, 95% CI = 0.92 to 4.17, p = .08; see Figure 1) and 35% BPRS score reduction (OR = 1.91, 95% CI = 0.89 to 4.07, p = .09) was found that did not reach statistical significance. The results for 50% BPRS score reduction were heterogeneous. Close inspection of 2 studies[25,31] with opposite results did not reveal an obvious reason for this heterogeneity so that both were in-

Figure 1. Number of Patients With a ≥ 20% Reduction in Brief Psychiatric Rating Scale (BPRS) Score[a]



[a]Abbreviations: CBZ = carbamazepine, CI = confidence interval, OR = odds ratio.
*Since this is a maintenance study, the main outcome parameter "number of patients not relapsed"—not 20% BPRS reduction—is displayed here.

Figure 2. Number of Patients Leaving the Studies Early[a]



[a]Abbreviations: CBZ = carbamazepine, CI = confidence interval, OR = odds ratio.

cluded in the calculation of a pooled effect size using the random-effects model (OR = 1.01, 95% CI = 0.17 to 6.02, p = 1). Furthermore, although only a few of the included studies monitored specific aspects of the mental state, no significant differences were found between carbamazepine and placebo at endpoint in presence of positive symptoms (2 studies,[29,31] SMD = 0.31, 95% CI = –1.07 to 1.70, p = .7), negative symptoms (2 studies,[29,30] SMD = –0.31, 95% CI = –0.86 to 0.23, p = .3), and depression (1 study,[29] SMD = –0.14, CI = –0.91 to 0.63, p = .7).

Side effects were poorly reported in the studies. The mean scores of extrapyramidal symptoms as measured with the Simpson-Angus Scale (SAS) were too skewed to allow meta-analysis. Dose et al.[25] found lower mean ± SD SAS scores with carbamazepine versus placebo (1.03 ± 0.86 vs. 2.84 ± 2.18, p < .01), whereas Nachshoni et al.[29] (0.9 ± 0.9 vs. 0.4 ± 0.5, p > .05) and Simhandl et al.[30] (0.27 ± 0.19 vs. 0.31 ± 0.35, p = .9) did not. The same was true for the mean dose of antiparkinson medication (biperiden) used. In the Dose et al.[25] study, the carbamazepine group had received a lower mean biperiden dose than the placebo group (1.3 ± 1.6 vs. 3.8 ± 2.3 mg/day, p < .01), whereas in the Hesslinger et al.[31] and the Simhandl et al.[30] studies, there was no significant difference (3.9 ± 0.8 vs. 2.9 ± 1.0 mg/day, p > .05, and 2.67 ± 2.89 vs. 2.67 ± 4.62 mg/day, p > .05, respectively). In the Martin-Munoz et al.[26] study, fewer participants suffered from extrapyramidal side effects with carbamazepine augmentation than with placebo (OR = 0.15, 95% CI = 0.03 to 0.82, p = .03, NNT = 2.0). All other side effects were adequately

reported by no more than 1 study each, and no significant difference between carbamazepine and placebo was found on any occasion.

DISCUSSION

One of the main advantages of a meta-analysis is that it can increase statistical power by combining several studies with sample sizes too small to detect significant differences. A weakness is that it cannot necessarily do justice to the design features of individual studies. Indeed, the studies included varied in respect of study design and the clinical characteristics of the subjects. However, none of the individual trials showed a consistent superiority of carbamazepine. The variability of the individual studies was furthermore reduced by requesting the original patient data from the authors. Doing so provides the opportunity to assess all studies in a standardized, uniform, and objective way. This approach is superior to meta-analyses in which effect sizes are derived from the variably defined outcomes. Several researchers shared their data with us.[22–26,29–31] This cooperation is especially noteworthy because without their contributions, this meta-analysis would not have been possible. We would like to encourage similar cooperations in the future, because they substantially improve meta-analytic studies.

It has been argued that language bias is an important problem in conventional reviews, because trials that are published in languages other than English are often not considered.[12] Indeed, data from French,[28] Czech,[23] Austrian,[27] and Spanish[26] trials were incorporated into our meta-analysis that had not been included in the frequently quoted conventional reviews by Christison[4] and Siris.[6] In addition, 3 randomized controlled trials[29–31] using carbamazepine for schizophrenia were published after these earlier reviews.

It was important to assess carbamazepine as a sole agent first, because an effectiveness as a monotherapy would make add-on effects more likely. In the only trial comparing carbamazepine as a sole agent versus placebo,[22] carbamazepine was not more effective in preventing relapse than the latter. Again, only 1 trial compared carbamazepine as a sole agent with an antipsychotic. When participants with schizoaffective disorder were excluded, a statistical superiority of perphenazine versus carbamazepine in terms of 20% and 35% BPRS score reduction was found. Despite the small sample size in this study, carbamazepine cannot be considered as a reasonable alternative to antipsychotics, at least for the treatment of patients with nonaffective psychoses.

Most studies examined carbamazepine as an adjunct to antipsychotics for schizophrenia. The meta-analysis did not show a significant superiority of carbamazepine augmentation, neither in terms of various levels of improvement of global schizophrenic symptomatology nor in specific aspects of mental state such as positive symptoms, negative symptoms, or depression. However, there was a trend in favor of carbamazepine, and although 6 trials could be combined, the total number of about 150 participants was still small. It has been shown that subsequent randomized controlled trials using large sample numbers may change the results of a meta-analysis. Therefore, our results should be regarded as inconclusive rather than negative.[32] Three further randomized controlled trials could not be used, since it was impossible to extract data suitable for inclusion in this meta-analysis. In the small studies by Kidron and Averbuch[33] and Möller et al.,[34] augmentation with carbamazepine did not significantly reduce symptoms. Klein et al.[35] found a superiority of carbamazepine augmentation compared with placebo on most BPRS items in participants with schizophrenia or schizoaffective disorder with "excited states." The same holds true for another large study[36] examining carbamazepine as an adjunct to antipsychotics in "excited psychoses" that was excluded because group allocation was not randomized (alternate allocation). A post hoc analysis of individual mental state scale items of the latter study suggested that the superiority of carbamazepine was related to an effect on disturbances of affective or emotional functions, whereas other items such as hallucinatory behavior worsened with adjunctive carbamazepine. However, given the promising results of further uncontrolled trials,[37–39] patients with "excitement" or "aggression" despite full treatment with antipsychotics might be promising as participants in future randomized trials.

Carbamazepine augmentation was not associated with significantly more participants leaving the studies early; thus, it seems to be quite acceptable to people with schizophrenia, at least within the confines of a trial. The reporting of side effects was, however, less consistent than that of efficacy, which makes conclusions on safety difficult. Most noteworthy are extrapyramidal side effects, because these were less frequent with carbamazepine augmentation compared with placebo in some of the studies. A possible explanation is a reduction of plasma haloperidol levels by carbamazepine, which has been reported in several of the included studies.[25,27,31,33] The reason for this reduction seems to be an induction of liver enzymes responsible for the metabolism of haloperidol, mainly cytochrome P450 3A4.[40] This interaction is problematic because although side effects and mood might be sometimes improved, the interaction can also lead to clinical deterioration, as was shown in one of the included trials[31] and in other reports.[36,41,42] This issue must be considered whenever clinicians coprescribe carbamazepine and haloperidol.

We conclude that there is currently insufficient evidence from randomized controlled trials to recommend the use of carbamazepine for schizophrenia. Treatment guidelines should take this into account, but since the database is not very robust and since there is a trend in favor

of carbamazepine, further trials are necessary. These trials should be undertaken using participants with treatment-resistant schizophrenia—the situation in which effective adjunctive compounds are most needed. Other important research areas are schizophrenic patients with excitement and/or aggression as discussed above. Furthermore, the effectiveness of carbamazepine for schizoaffective disorder has been surprisingly poorly studied by randomized controlled trials, although it is frequently used for this condition in the daily routine. Only 12 patients in the included studies had schizoaffective disorder. Given the relatively well-established antimanic properties of carbamazepine,[43] future studies focusing on the bipolar type of schizoaffective disorder may be warranted.

Drug names: biperiden (Akineton), carbamazepine (Tegretol and others), chlorpromazine (Thorazine and others), clozapine (Clozaril and others), cyproheptadine (Periactin), haloperidol (Haldol and others), perphenazine (Trilafon and others).

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