

· **Commentary** ·

Antipsychotics for previously untreated individuals with schizophrenia

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The recent article in the Archives by Yang and colleagues^[1] confirmed much of what we know about antipsychotic treatment with olanzapine, quetiapine, and risperidone for people with recent-onset schizophrenia. Response rates and the risk of weight gain are high. In addition, the drugs have similar efficacy but diverse side effect profiles^[2,3].

Study Summary

The authors conducted a prospective cohort study of 398 treatment-naïve individuals early in the course of schizophrenia who began treatment with olanzapine, quetiapine, or risperidone. Treatment assignment was based on clinician recommendation, patient preference, and ability to pay. Follow-up was for one year, with changes in symptoms and adverse effects as the main outcome measures. As acknowledged by the authors, open-label treatment and non-random treatment assignments are significant limitations. On the other hand, important strengths include real-world treatment conditions, a large number of patients who were treatment-naïve, and one-year completion rates that are much higher than have been typically reported in clinical trials^[3] or in evaluations using administrative data^[4].

Symptom reductions measured by the Positive and Negative Syndrome Scale (PANSS) scores were similar in all treatment groups. Treatment discontinuation and relapse rates were also similar among the groups. Sedation and weight gain were the most common side effects, with olanzapine associated with the most weight gain and olanzapine and quetiapine with the most sedation. Risperidone was most associated with extrapyramidal side effects (EPS) and this group of patients was most likely to use trihexylphenidyl. All of these findings are consistent with previous research from randomized trials.

A remarkable and unique finding in this study, which was conducted at the Shanghai Mental Health Center, is the high rate of completion of one

year of treatment on monotherapy with the first antipsychotic started. The 67% completion rate on initial treatment in Shanghai is more than double the 30% rate in the Comparison of Antipsychotics in First Episode (CAFÉ) study, a one-year randomized trial of first-episode patients in the U. S.^[4] The contrast with Finland is even greater, where only 46% of patients discharged from a first psychotic episode continued with any antipsychotic for more than 30 days, according to a recently reported retrospective cohort study^[5]. In the European First-Episode Schizophrenia Trial (EUFEST), discontinuations over one year for olanzapine were similar to those in Shanghai, but the rates of stopping quetiapine were higher in Europe^[6].

Implications

Overall, the results comparing the effects of the antipsychotics used in this study from China are similar to results of studies in the West. The major difference is that patients in China stayed on their first antipsychotic medication at a much higher rate. The conditions of an observational study, in which treatments are assigned clinically rather than randomly, may account for some of the differences between Western RCTs and the cohort study in Shanghai. However, the extremely high rate of treatment discontinuation in Finland could not be due to randomization so there may be other factors involved in the high continuation rate in Shanghai.

What can be learned from the remarkable follow-up rates in China? An investigation to discover the explanation for the reason for high treatment retention rates in Shanghai could be extremely helpful to caregivers in other settings. A study using qualitative methods to understand clinical, family, social, and treatment variables in Shanghai and an appropriate comparison site from the West would be one way to make this determination. If the causes of success in keeping patients engaged in treatment in Shanghai can be identified and replicated in other

settings, then this would represent a major opportunity for better outcomes in the many places where complete treatment disengagement is common.

References

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· 述评 ·

既往未治疗的精神分裂症患者的抗精神病药治疗

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上一期刊登的杨晓敏等^[1]的研究进一步证实了许多我们已知的采用奥氮平、喹硫平和利培酮治疗近期发病的精神分裂症患者。治疗的有效率高,存在高风险的体重增加。此外,药物的疗效相似,但不良反应各异^[2,3]。

研究小结

作者对 398 例处于疾病早期的、未经治疗的精神分裂症患者开展了前瞻性队列研究,给予奥氮平、喹硫平和利培酮治疗。根据医生建议、患者的偏爱及其支付能力分配治疗药物。随访 1 年,主要结局指标为症状改变和不良反应。正如作者所承认的,开放性的治疗和非随机治疗药物分组是该研究的明显不足之处。而另一方面,该研究重要的优点包括真实的治疗情形,大量的未用过药的患者,患者完成 1 年治疗的比例高,远高于其他临床试验^[3] 或对管理数据^[4] 进行分析所报道的。

采用阳性和阴性症状量表评分评定症状的减少,三组的减分率相似。三组的中断治疗率和复发率也相似。镇静和体重增加是最常见的不良反应,奥氮平治疗组体重增加者最多,奥氮平和喹硫平组镇静最多见。患者报告的锥体外系不良反应和使用苯海索与利培酮治疗关系最密切。所有这些发现均与既往随机研究的结果一致。

在上海市精神卫生中心进行的该研究值得注意的、独特的发现是,开始首次抗精神病药治疗后,患者完成 1 年单药治疗的比例高。在上海,首次治疗后有 67% 的患者完成治疗,而一项在美国开展的为期 1 年的随机试验比较了首发患者的抗精神病药使用情况 (CAFCAFE),发现有 30% 的患者

完成治疗^[4],前者的完成治疗率是后者的 2 倍还多。而根据最新报道的回顾性队列研究^[5],与芬兰的研究结果差异更大,只有 46% 的首发精神病性障碍患者出院后服用任一抗精神病药超过 30 天。在欧洲进行的首发精神分裂症试验中 (EUFEST),1 年里中断奥氮平治疗的比例与上海的研究结果相近,但欧洲患者停止喹硫平治疗的比例较高^[6]。

意义

大体来说,来自中国的此研究中用到的抗精神病药的疗效比较,其结果与西方研究的结果相似。主要的不同在于中国患者坚持服用首个抗精神病药治疗的比例高得多。在观察性研究中,治疗是根据临床情况而不是随机分配,可能部分解释了西方随机对照试验与上海此项队列研究结果的不同。然而,并非随机化设计导致了芬兰的治疗中断率极高,所以可能存在其他的因素,使上海患者的持续治疗比例高。我们能从中国这一值得注意的随访率中学到什么? 旨在揭示上海高的维持治疗率的研究将会对其他地方的照顾者非常有帮助。采用定性研究的方法去了解上海的临床、家庭、社会和治疗变量,并与西方研究进行适当的比较,将是一种确定高维持治疗率原因的方法。患者不能完全依从治疗的情况相当普遍,如果能够找出上海的研究中患者成功地维持持续治疗的原因,并能在其他机构得到重复,那么将有助于提高其他地区患者的治疗结局。

参考文献

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