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Research in Developmental Disabilities 27 (2006) 309–336
Research in Developmental Disabilities

Guidelines for the use of clozapine in individuals with developmental disabilities

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Received 7 February 2005; received in revised form 5 May 2005; accepted 9 May 2005

Abstract

Clozapine is the most effective antipsychotic medication currently in use, but there has been a paucity of well-controlled research on its efficacy with people with developmental disabilities. We present a set of guidelines to ensure proper utilization of clozapine in individuals with developmental disabilities, because it can offer them therapeutic advantages similar to those observed in people with schizophrenia. We provide recommendations regarding the use of clozapine that are based on three main sources: literature and published professional practice guidelines regarding the use of clozapine in individuals who do not have developmental disabilities, the limited literature on the use of clozapine in individuals who have developmental disabilities, and our own clinical experience. The first part of the guidelines contains an overview of necessary practical knowledge regarding side effects, dose and blood level considerations, and interactions with other medications, diet and tobacco smoking. In the second part, we offer procedures for selecting individuals for clozapine therapy based on proper indications and contraindications for treatment. We also include requirements regarding informed consent, dosage and special laboratory and clinical monitoring.

Keywords: Clozapine; Clozapine guidelines; Individuals with developmental disabilities; Antipsychotic medication

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0891-4222/$ – see front matter
doi:10.1016/j.ridd.2005.05.002

1. Introduction

Clozapine is an atypical or new generation antipsychotic (NGA) medication currently manufactured by Novartis Pharmaceutical Corporation and marketed under the trade name of Clozaril. It is indicated for use in individuals with schizophrenia who are either resistant or intolerant to other antipsychotic drugs (Baldessarini & Frankenburg, 1991; Kane, Honigfeld, Singer, & Meltzer, 1988). The efficacy of clozapine in people with schizophrenia has been proven to be superior to that of the conventional or first-generation antipsychotic (FGA) agents according to individual studies (Kane et al., 1988; Singer & Law, 1974) and a meta-analytic review (Wahlbeck, Cheine, Essalie, & Adams, 1999). Clozapine may also be superior to other NGA agents (Conley & Buchanan, 1997). Both positive and negative symptoms appear to improve when treated with clozapine (Tandon et al., 1993). Clozapine can help achieve a treatment response characterized by not only symptom reduction but also improvement in certain aspects of cognitive functioning, social functioning and quality of life, decreased need for hospitalization, and enhanced compliance with treatment (Grace et al., 1996; Meltzer, 1992; Meltzer, Burnett, Bastani, & Ramirez, 1990). Furthermore, treatment with clozapine significantly reduces suicidal behavior among schizophrenic individuals (Barclay, 2003; Meltzer et al., 2003).

Clozapine has been also shown to be effective in individuals with schizoaffective and psychotic mood disorders (McElroy, 1991; Zarate, Tohen, & Baldessarini, 1995), non-psychotic rapid cycling bipolar disorder (Suppes, Phillips, & Judd, 1994), and Parkinson's disease with drug-induced and other concomitant psychosis (Friedman & Lannon, 1989; TPSG, 1999). Furthermore, clozapine has been demonstrated to be effective in individuals with brain injury (Michals, Crismon, Roberts, & Childs, 1993), co-morbid schizophrenia and substance use disorder (Green, Zimmet, Strous, & Schildkraut, 1999), and severe borderline personality disorder with aggression and self-abusive behavior (Benedetti, Sforzini, Colombo, Maffei, & Smeraldi, 1998; Chengappa, Ebeling, Kang, Levine, & Parepally, 1999). Although studies are limited, clozapine appears to be the best treatment for polydipsia associated with severe mental illness (Canuso & Goldman, 1999; Verghese, de Leon, & Josiassen, 1996). While polydipsia is typically associated with schizophrenia, it is also reported in 5% of hospitalized individuals with mental retardation (Bremner & Regan, 1991; Deb, Bramble, Drybala, Boyle, & Bruce, 1994; Hayfron-Benjamin, Peters, & Woodhouse, 1996). In individuals with schizophrenia, the polydipsia response to clozapine appears to be independent from the antipsychotic response (Verghese et al., 1996).

The use of clozapine among individuals with developmental disabilities is becoming increasingly accepted due to efficacy and safety profiles similar to those reported among individuals without developmental disabilities. Since the early 1990s, several retrospective analyses (Antonacci & de Groot, 2000; Buzan, Dubovsky, Firestone, & Dal Pozzo, 1998), case reports/series (Cohen & Underwood, 1994; Gobbi, 2001; Pary, 1994; Sajatovic, Ramirez, Kenny, & Meltzer, 1994), and single blind studies (Hammock, Levine, & Schroeder, 2001) have shown that relatively low doses of clozapine are effective in improving psychotic symptoms, self-injurious behavior, aggression, property destruction and stereotyped behavior. A few double-blind placebo-controlled studies have confirmed the efficacy of clozapine in this population (Hammock, Schroeder, & Levine, 1995;