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EAD PLUS

Educação em Saúde

APLICAÇÕES CLÍNICAS NO TRANSTORNO DO ESPECTRO AUTISTA E PROMOÇÃO DA SAÚDE

MARCELO MOREN NETTO

Médico pela Universidade do Grande Rio, Pós graduado em Pediatra pela Facis/SP e Geriatra pela IBCMED/SP, Prescritor de Cannabis Medicinal certificado pela Unifesp/SP, Faculdade Unyleya/DF, com certificação internacional pela We Cann Academy, sócio fundador e diretor técnico da SOUL Clínica Canábica, Membro da Associação Médica Brasileira de Endocanabinologia/AMBCANN.

1908 – Eugene Bleuler

1943 – Leo Kammer

1944 – Hans Asperg

1952 – DSM (Manual Diagnóstico)

1978 – Michael Rutter

1980 – Na 3ª Edição incorpora-se o autismo, na 4ª Edição aparece Sd. Asperger, Autismo, Sd. Rett, Transtorno invasivo do desenvolvimento.

2013 – Na 5ª Edição aparece o TEA (Transtorno do Espectro Autista)

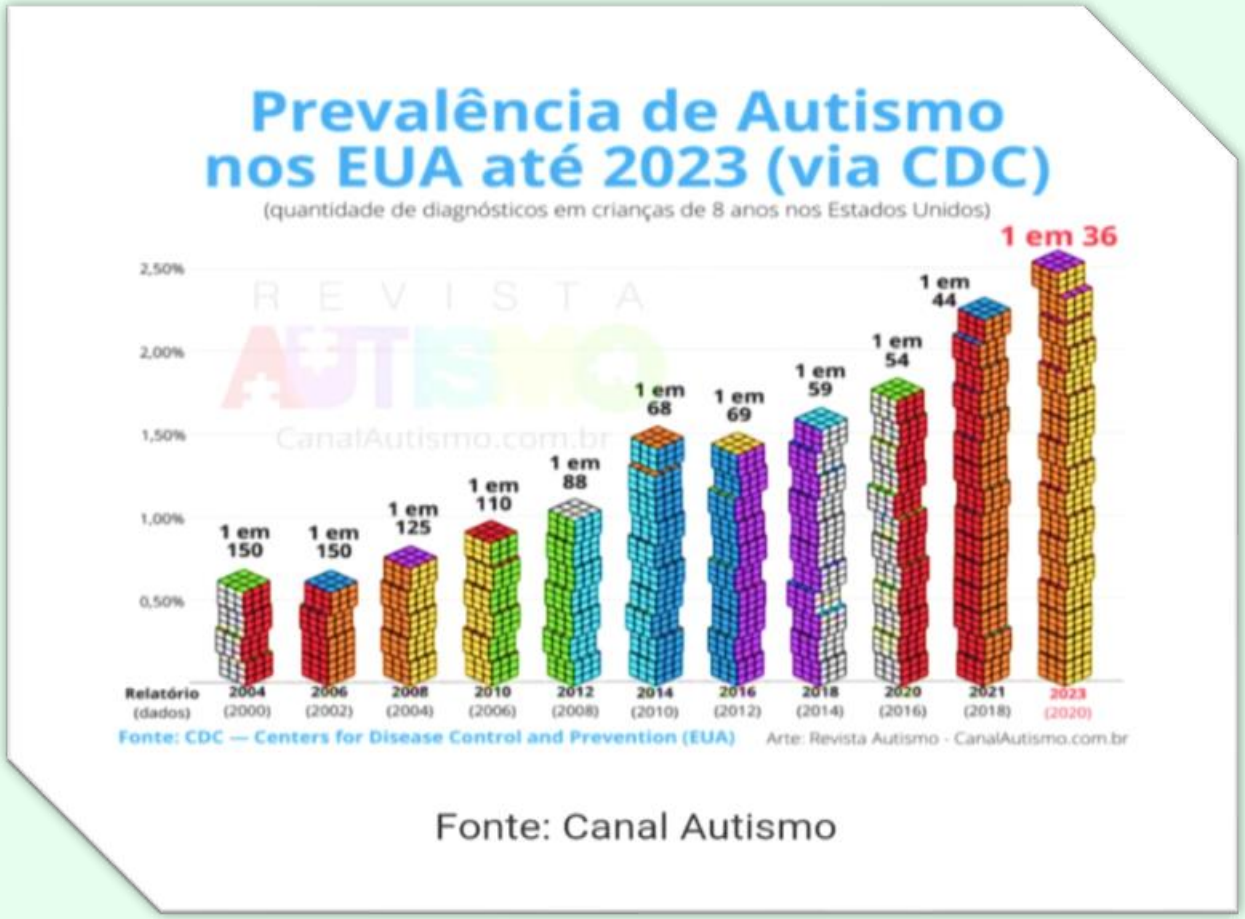
O QUE É O TEA?

DOIS DOMÍNIOS DEFICITÁRIOS

Dificuldade na comunicação e interação social

Interesse restrito e repetitivo de comportamento, interesses e atividades

PORQUE O AUTISMO AUMENTOU TANTO NOS ÚLTIMOS ANOS



Fonte: Canal Autismo

1% da população mundial = 70 milhões de indivíduos dentro no TEA no mundo

O arsenal terapêutico habitual no manejo (TEA)

- Antipsicóticos (Risperidona ou Aripiprazol) 67% inicia;
- Ansiolíticos (Fluoxetina, Escitalopram, Sertralina...);
- Estabilizadores de humor (Valproato; Oxicarbazepina; Carbamazepina);
- Psicoestimulantes (Ritalina, Conserta, Venvanse);
- Anti-hipertensivo (Clonidina).

* Limitações claras em termos de eficácia e frequentemente associados a efeitos colaterais importantes.

Ministério da Saúde
Secretaria de Atenção Especializada à Saúde

PORTARIA CONJUNTA Nº 7, DE 12 DE ABRIL DE 2022

Aprova o Protocolo Clínico e Diretrizes Terapêuticas do Comportamento Agressivo no Transtorno do Espectro do Autismo.

A SECRETÁRIA DE ATENÇÃO ESPECIALIZADA À SAÚDE e a SECRETÁRIA DE CIÊNCIA, TECNOLOGIA, INOVAÇÃO E INSUMOS ESTRATÉGICOS EM SAÚDE, no uso de suas atribuições,

Considerando a necessidade de se atualizarem os parâmetros sobre o Comportamento Agressivo no Transtorno do Espectro do Autismo no Brasil e diretrizes nacionais para diagnóstico, tratamento e acompanhamento dos indivíduos com esta condição;

Considerando que os protocolos clínicos e diretrizes terapêuticas são resultado de consenso técnico-científico e são formulados dentro de rigorosos parâmetros de qualidade e precisão de indicação;

Considerando o Registro de Deliberação n o 712/2022 e o Relatório de Recomendação n o 716 - Fevereiro de 2022 da Comissão Nacional de Incorporação de Tecnologias no SUS (CONITEC), a atualização da busca e avaliação da literatura; e

Considerando a avaliação técnica do Departamento de Gestão e Incorporação de Tecnologias e Inovação em Saúde (DGITIS/SCTIE/MS), do Departamento de Assistência Farmacêutica e Insumos Estratégicos (DAF/SCTIE/MS) e do Departamento de Atenção Especializada e Temática (DAET/SAES/MS), resolvem:

Art. 1º Fica aprovado o Protocolo Clínico e Diretrizes Terapêuticas - Comportamento Agressivo no Transtorno do Espectro do Autismo.

Parágrafo único. O Protocolo objeto deste artigo, que contém o conceito geral do comportamento agressivo no transtorno do espectro do autismo, critérios de diagnóstico, critérios de inclusão e de exclusão, tratamento e mecanismos de regulação, controle e avaliação, disponível no sítio https://www.gov.br/saude/pt-br/assuntos/protocolos-clinicos-e-diretrizes-terapeuticas-pcdt, é de caráter nacional e deve ser utilizado pelas Secretarias de Saúde dos Estados, do Distrito Federal e dos Municípios na regulação do acesso assistencial, autorização, registro e ressarcimento dos procedimentos correspondentes.

Art. 2º É obrigatória a cientificação do paciente, ou de seu responsável legal, dos potenciais riscos e efeitos colaterais (efeitos ou eventos adversos) relacionados ao uso de procedimento ou medicamento preconizados para o tratamento do Comportamento Agressivo no Transtorno do Espectro do Autismo.

Art. 3º Os gestores estaduais, distrital e municipais do SUS, conforme a suas competências e pactuações, deverão estruturar a rede assistencial, definir os serviços referenciais e estabelecer os fluxos para o atendimento dos indivíduos com essa condição em todas as etapas descritas no anexo a esta Portaria, disponível no sítio citado no parágrafo único do art. 1º.

Art. 4º Fica revogada a Portaria SAS/MS n o 324, de 31 de março de 2016, publicada no Diário Oficial da União nº 62, de 01 de abril de 2016, Seção 1, página 105.

Art. 5º Esta Portaria entra em vigor na data de sua publicação.

MAÍRA BATISTA BOTELHO

Secretária de Atenção Especializada à Saúde

SANDRA DE CASTRO BARROS

Secretária de Ciência, Tecnologia, Inovação e Insumos Estratégicos em Saúde

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SCIENTIFIC REPORTS

OPEN

Real life Experience of Medical Cannabis Treatment in Autism: Analysis of Safety and Efficacy

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Lihi Bar-Lev Schleider[1,2], Raphael Mechoulam[3], Naama Saban[2], Gal Meiri[4,5] & Victor Novack[1]

There has been a dramatic increase in the number of children diagnosed with autism spectrum disorders (ASD) worldwide. Recently anecdotal evidence of possible therapeutic effects of cannabis products has emerged. The aim of this study is to characterize the epidemiology of ASD patients receiving medical cannabis treatment and to describe its safety and efficacy. We analysed the data prospectively collected as part of the treatment program of 188 ASD patients treated with medical cannabis between 2015 and 2017. The treatment in majority of the patients was based on cannabis oil containing 30% CBD and 1.5% THC. Symptoms inventory, patient global assessment and side effects at 6 months were primary outcomes of interest and were assessed by structured questionnaires. After six months of treatment 82.4% of patients (155) were in active treatment and 60.0% (93) have been assessed; 28 patients (30.1%) reported a significant improvement, 50 (53.7%) moderate, 6 (6.4%) slight and 8 (8.6%) had no change in their condition. Twenty-three patients (25.2%) experienced at least one side effect; the most common was restlessness (6.6%). Cannabis in ASD patients appears to be well tolerated, safe and effective option to relieve symptoms associated with ASD.

There has been a 3-fold increase during the last 3 decades in the number of children diagnosed with autism spectrum disorders worldwide[1–5]. No specific treatments are currently available and interventions are focussing on lessening of the disruptive behaviors, training and teaching self-help skills for a greater independence[6].

Recently, CBD enriched cannabis has been shown to be beneficial for children with autism[7]. In this retrospective study on 60 children, behavioural outbreaks were improved in 61% of patients, communication problems in 47%, anxiety in 39%, stress in 33% and disruptive behaviour in 33% of the patients. The rationale for this treatment is based on the previous observations and theory that cannabidiol effects might include alleviation of psychosis, anxiety, facilitation of REM sleep and suppressing seizure activity[8]. A prospective single-case-study of Dronabinol (a THC-based drug) showed significant improvements in hyperactivity, lethargy, irritability, stereotypy and inappropriate speech at 6 month follow-up[9]. Furthermore, Dronabinol treatment of 10 adolescent patients with intellectual disability resulted in 8 patients showing improvement in the management of treatment-resistant self-injurious behaviour[10].

In 2007, The Israel Ministry of Health began providing approvals for medical cannabis, mainly for symptoms palliation. In 2014, The Ministry of Health began providing licenses for the treatment of children with epilepsy. After seeing the results of cannabis treatment on symptoms like anxiety, aggression, panic, tantrums and self-injurious behaviour, in children with epilepsy, parents of severely autistic children turned to medical cannabis for relief.

Although many with autism are being treated today with medical cannabis, there is a significant lack of knowledge regarding the safety profile and the specific symptoms that are most likely to improve under cannabis treatment. Therefore, the aim of this study was to characterize the patient population receiving medical cannabis treatment for autism and to evaluate the safety and efficacy of this therapy.

Estudo retrospectivo, observacional, em uso de CBD (CBD – THC = 20:1)

- Melhora comportamental em 61%;
  - Melhora de linguagem (verbal e não verbal 47%;
  - Melhora na ansiedade em 39%;
  - Melhora no comportamento disruptivo em 33%
  - Qualidade de vida = 33% melhorou com 1mês e 66% em 6meses;
  - Uso de outras medicações = reduziu em 34% dos pacientes.

Aran *et al. Molecular Autism* (2021) 12:6
https://doi.org/10.1186/s13229-021-00420-2

Molecular Autism

RESEARCH Open Access

Cannabinoid treatment for autism: a proof-of-concept randomized trial

Adi Aran[1*], Moria Harel[1], Hanoch Cassuto[1], Lola Polyansky[1], Aviad Schnapp[1], Nadia Wattad[1], Dorit Shmueli[2], Daphna Golan[3] and F. Xavier Castellanos[4]

Abstract

Background: Endocannabinoid dysfunction in animal models of autism spectrum disorder (ASD) and accumulating, albeit anecdotal, evidence for efficacy in humans motivated this placebo-controlled double-blind comparison of two oral cannabinoid solutions in 150 participants (age 5–21 years) with ASD.

Methods: We tested (1) BOL-DP-O-01-W, a whole-plant cannabis extract containing cannabidiol and Δ9-tetrahydrocannabinol at a 20:1 ratio and (2) BOL-DP-O-01, purified cannabidiol and Δ9-tetrahydrocannabinol at the same ratio. Participants ($N = 150$) received either placebo or cannabinoids for 12-weeks (testing efficacy) followed by a 4-week washout and predetermined cross-over for another 12 weeks to further assess tolerability.

Registered primary efficacy outcome measures were improvement in behavioral problems (differences between whole-plant extract and placebo) on the Home Situation Questionnaire-ASD (HSQ-ASD) and the Clinical Global Impression-Improvement scale with disruptive behavior anchor points (CGI-I). Secondary measures were Social Responsiveness Scale (SRS-2) and Autism Parenting Stress Index (APSI).

Results: Changes in Total Scores of HSQ-ASD (primary-outcome) and APSI (secondary-outcome) did not differ among groups. Disruptive behavior on the CGI-I (co-primary outcome) was either much or very much improved in 49% on whole-plant extract ($n = 45$) versus 21% on placebo ($n = 47$; $p = 0.005$). Median SRS Total Score (secondary-outcome) improved by 14.9 on whole-plant extract ($n = 34$) versus 3.6 points after placebo ($n = 36$); $p = 0.009$). There were no treatment-related serious adverse events. Common adverse events included somnolence and decreased appetite, reported for 28% and 25% on whole-plant extract, respectively ($n = 95$); 23% and 21% on pure-cannabinoids ($n = 93$), and 8% and 15% on placebo ($n = 94$).

Limitations

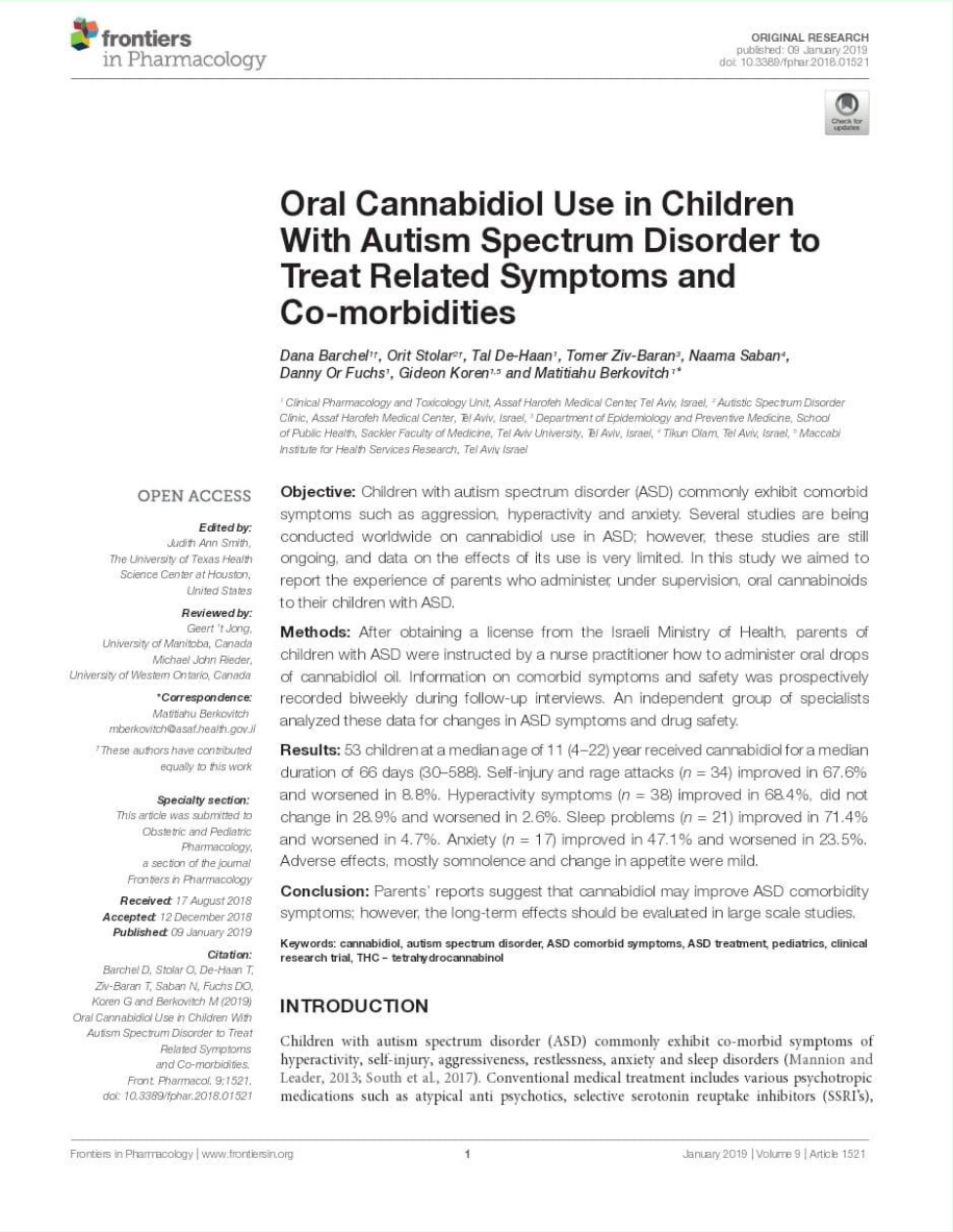
Lack of pharmacokinetic data and a wide range of ages and functional levels among participants warrant caution when interpreting the results.

Conclusions: This interventional study provides evidence that BOL-DP-O-01-W and BOL-DP-O-01, administrated for 3 months, are well tolerated. Evidence for efficacy of these interventions are mixed and insufficient. Further testing of cannabinoids in ASD is recommended.

Trial registration ClinicalTrials.gov: NCT02956226. Registered 06 November 2016, https://clinicaltrials.gov/ct2/show/NCT02956226

Estudo comparativo, duplo-cego comparando a eficácia do placebo, canabidiol isolado e canabidiol *full spectrum* em indivíduos com TEA.

- Melhora comportamental muito significativa com full 49%, isolado 38% e placebo 21%;
- Principais EA: sonolência, diminuição do apetite;
- Melhora na escala SRS-2 mostrando evidências preliminares na melhora dos sintomas centrais do autismo.



frontiers in Pharmacology

ORIGINAL RESEARCH
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Oral Cannabidiol Use in Children With Autism Spectrum Disorder to Treat Related Symptoms and Co-morbidities

Dana Barchel[†], Orit Stolar[2†], Tal De-Haan[1], Tomer Ziv-Baran[3], Naama Saban[4], Danny Or Fuchs[1], Gideon Koren[1,5] and Matitiahu Berkovitch[1]*

[1] Clinical Pharmacology and Toxicology Unit, Assaf Harofeh Medical Center, Tel Aviv, Israel, [2] Autistic Spectrum Disorder Clinic, Assaf Harofeh Medical Center, Tel Aviv, Israel, [3] Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, [4] Tikun Olam, Tel Aviv, Israel, [5] Maccabi Institute for Health Services Research, Tel Aviv, Israel

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Edited by:
Judith Ann Smith,
The University of Texas Health Science Center at Houston, United States

Reviewed by:
Geert 't Jong,
University of Manitoba, Canada
Michael John Rieder,
University of Western Ontario, Canada

****Correspondence:***
Matitiahu Berkovitch
mberkovitch@asaf.health.gov.il

[†]These authors have contributed equally to this work

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Objective: Children with autism spectrum disorder (ASD) commonly exhibit comorbid symptoms such as aggression, hyperactivity and anxiety. Several studies are being conducted worldwide on cannabidiol use in ASD; however, these studies are still ongoing, and data on the effects of its use is very limited. In this study we aimed to report the experience of parents who administer, under supervision, oral cannabinoids to their children with ASD.

Methods: After obtaining a license from the Israeli Ministry of Health, parents of children with ASD were instructed by a nurse practitioner how to administer oral drops of cannabidiol oil. Information on comorbid symptoms and safety was prospectively recorded biweekly during follow-up interviews. An independent group of specialists analyzed these data for changes in ASD symptoms and drug safety.

Results: 53 children at a median age of 11 (4–22) year received cannabidiol for a median duration of 66 days (30–588). Self-injury and rage attacks (n = 34) improved in 67.6% and worsened in 8.8%. Hyperactivity symptoms (n = 38) improved in 68.4%, did not change in 28.9% and worsened in 2.6%. Sleep problems (n = 21) improved in 71.4% and worsened in 4.7%. Anxiety (n = 17) improved in 47.1% and worsened in 23.5%. Adverse effects, mostly somnolence and change in appetite were mild.

Conclusion: Parents' reports suggest that cannabidiol may improve ASD comorbidity symptoms; however, the long-term effects should be evaluated in large scale studies.

Keywords: cannabidiol, autism spectrum disorder, ASD comorbid symptoms, ASD treatment, pediatrics, clinical research trial, THC – tetrahydrocannabinol

INTRODUCTION

Children with autism spectrum disorder (ASD) commonly exhibit co-morbid symptoms of hyperactivity, self-injury, aggressiveness, restlessness, anxiety and sleep disorders (Mannion and Leader, 2013; South et al., 2017). Conventional medical treatment includes various psychotropic medications such as atypical anti psychotics, selective serotonin reuptake inhibitors (SSRI's),

Estudo retrospectivo CBD:THC 20:1(TL)

53 crianças TEA tratadas com CBD por 66 dias.

- Melhora em 67,6% na agressividade e auto agressividade, piora em 8,8%;
- Agitação com melhora em 71,4% e piora em 4,7%;
- Ansiedade: melhora em 47,1% piora em 23,5%;
- EA comuns = sonolência e discreta supressão do apetite;
- Overall = melhora segundo os pais de 74,5%, sem mudança em 21,6% e piora em 3,9%.

QUANDO PRESCREVER?

Comorbidades e sintomas atrapalhando a qualidade de vida do indivíduo.
Transtornos comportamentais
Agressividade
Autoagressividade
Distúrbios do sono
Hiperatividade
Epilepsia
Efeitos Colaterais de outros fármacos

Recomendação da OMS – boa tolerabilidade e segurança principalmente a partir de 02 anos de idade

Interações medicamentosas

Donepezila Não metabolizada	Clozapina 1 A2, 3 A4 *(Agranulocitose)*	Bupropiona 2 B6
Galantamina 2 D6, 3 A4	Risperidona 2 D6 *(↑ Prolactina)*	Fluoxetina 2 D6, 2 C19
Rivastigmina Não metabolizada	Quetiapina 3 A4 (↑peso, dislipidemia)	Fluvoxamina 2 D6
Memantina (não metabolizado)	Olanzapina 1 A2	Sertralina 2B6, 2D6, 2C9, 2C19,3A4.
Zolpidem 1 A2, 3 A4	Agomelatina 1 A2, 2 C19 *(Hepatotoxicidade)*	Clobazam

- ❑ Não existem restrições absolutas.
- ❑ Interações clinicamente relevantes são infrequentes.
- ❑ Canabinoides metabolizados pelo citocromo P450.
- ❑ CBD e o THC inibem as atividades das enzimas CYP, podendo estimular ou inibir os efeitos das drogas.
- ❑ Clobazam aumento da sedação.

- ❑ Risperidona: Monitorar aumento de prolactina

POSOLOGIA

" Start Slow and Stay Slow “

Semanas	1	2	3	4
Dosagem/dia	2,5mg/kg	5mg/kg	10mg/kg	15mg/kg

Dose máxima 25mg/kg/dia

Obs: em duas doses tomadas via oral.

OBRIGADO

Não há limites para o amor que sente um autista, limitada mesmo é a cabeça de quem ainda possui preconceitos!

@drmarcelomoren

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atendimento@eadplus.com.br
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