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Adolescents at high risk for psychosis ("Ultra High Risk"): an integrative review

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ABSTRACT

OBJECTIVE

Many psychotic disorders such as schizophrenia can start with attenuated psychotic symptoms and/or declining social and occupational functions. People who present with these "prodromal" characteristics are described as being at Ultra High Risk (UHR) for psychosis. Due to the impact that these disorders have on their quality of life, it is important to review the existing literature. The aim was to conduct an integrative review on UHR and its impact on the quality of life in children and adolescents.

METHODS

Searched for articles in the Pubmed database in the period 2010-2019 with the following descriptors: "Psychotic Disorders", "Risk Factors", "Schizophrenia", "Clinical Diagnosis".

RESULTS

The search selected 10 articles and an Australian guideline Orygen, of which seven were selected for the present review after analysis. According to the results found, several psychotic disorders may have prodromal characteristics that are the same as Ultra High Risk (UHR).

CONCLUSIONS

Patients with psychosis have worsened quality of life and more unfavorable prognosis, therefore, UHR present an opportunity for intervention to prevent the onset of the first psychotic episode. In clinical trials conducted with UHR patients, both the duration and periods of intervention have been relatively short. Thus, the question remains whether this intervention in the productive phase is effective over time. There should be more discussion about the cost benefit of treatments in UHR patients.

DESCRIPTORS

Psychotic Disorders, Risk Factors, Schizophrenia, Clinical Diagnosis.

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INTRODUCTION

Many psychotic disorders such as schizophrenia may begin with attenuated psychotic symptoms and/or decline in social and occupational functions. Individuals presenting with these "prodromal" features are described as being at Ultra High Risk (UHR) for psychosis[1].

To be considered UHR, individuals seeking medical service must be in the age range of highest risk for psychosis which would be late adolescence and early adulthood, in addition to meeting one or more of the following 3 criteria: Attenuated psychotic symptoms: sub-threshold positive psychotic symptoms during the past 12 months; Intermittent Brief and Limited Psychotic Symptoms: frank psychotic symptoms for less than a week that resolve spontaneously; Genetic vulnerability when they meet the criteria for Schizotypal Personality Disorder or have a first-degree relative with a psychotic disorder. These risk criteria must also be associated with deteriorating social functioning or chronically poor social functioning[1-4].

Most individuals who meet the UHR criteria will not develop a psychotic disorder but may have persistent attenuated psychotic symptoms with impaired quality of life. Thus, if psychosis is not adequately treated early on, the patient has a worse prognosis, more intense psychotic conditions, worsening response to antidepressants, and worsening quality of life.[2] UHR individuals, therefore, present the opportunity for prevention of onset of full psychotic disorder, or at least reduction in disability and delay in onset of the first episode of psychosis[1,2]. Therefore the aim of this study is to conduct an integrative systematic review for early diagnosis of UHR patients to prevent transition to psychosis[1,2].

METHODS

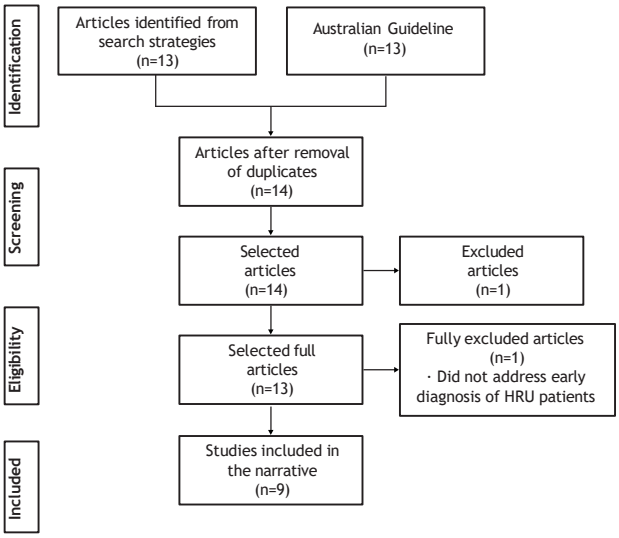
This research is a systematic review of integrative nature and aimed to review articles about the risks of early onset of psychosis - "ultra-high risk" in adolescents and their transition to psychosis. The authors performed an analysis of scientific journals from the PubMed (National Library of Medicine) and SciELO databases. The following descriptors were obtained from the Descriptors in Health Sciences (DECS) and used as keywords for the search: psychotic disorders, risk factors, schizophrenia, and clinical diagnosis.

The following inclusion criteria were considered: articles published between the years 2010 and 2019; English and Portuguese language; presentation of digital object identifier (DOI); presentation as main theme the early detection of HRU patients to prevent or delay the transition to psychosis. From the articles selected in the digital search, the bibliographic references were analyzed regarding the inclusion criteria. The exclusion criteria were articles that did not address the chosen theme. After the selection of the eligible articles, a critical reading of them was carried out, aiming at extracting the results that were in accordance with our objective, and then a narrative synthesis of the results obtained was carried out.

RESULTS

Through our digital keyword search strategy, 10 articles were found, dating from 2010 to 2019. Also 1 Australian Orygen guideline and 2 more articles were added by the similar search. All 12 articles and guideline had their abstracts evaluated, and 10 of these were selected to be read in full. After reading, we selected 9 articles that met our eligibility criteria, as they matched the objective of this work on early diagnosis of UHR patients to prevent their transition to psychotic disorders such as schizophrenia, as can be seen in Figure 1.

Figura 1. Flowchart: Study selection



One of the main challenges in preventing the transition to schizophrenia is to identify specific and sensitive signs and symptoms that may predict future psychosis. The prodrome is a clinical phenomenon identified retrospectively after the psychotic break. It is usually characterized by evolving attenuated positive symptoms, negative symptoms, cognitive deficits and functional impairment[5]. To help identify "Prodromic" young people "UHR" and "baseline symptoms" criteria were introduced (Cornblatt et al., 2003; Klosterkötter et al., 2001; Yung et al., 2003) which enabled several international research groups to study on the subject[6].

One such study was conducted between 2001-2011 by "Outreach and Support in South London", South London, in order to predict which symptoms, make UHR patients seek help. It was found that the main reason patients seek help from the service is affective symptoms, mainly depression and anxiety (47.1%). Subthreshold psychotic symptoms were reported by 39.8%. Despite not presenting a higher risk of developing psychosis, patients with complaints of affective symptoms were more likely to have a worse future functional outcome, therefore the assessment of subjective complaints in the HRU may help to identify predictors of future functional outcome as well as its treatment[7].

The Alberta group, Tomassi, Maina, Tosato (2018) also highlight the possibility that the transition from psychosis is possibly linked to non-psychotic symptoms. The same authors reinforce the issue that studies in this area have been gaining strength to have a better understanding regarding the identification of subjects at risk of developing the disease before the first psychotic break. Concomitant to this, the authors show that the prevalence rates of depressive and anxiety disorders have been observed in individuals in RHU. In this way a systematic review and meta-analysis showed a prevalence of 40.7% for depressive disorders and 15.3% for any anxiety disorders in individuals in RHU. Thus, from this issue the same authors highlight that hypothetically different psychopathologies may have a different impact on the risk of transition to frank psychosis in at-risk individuals[8].

According to Tsuang et al (2013), it is reported the importance of identifying the disease as soon as possible and that late diagnosis, is related to a poor prognosis due to socio-occupational decline and this is difficult to reverse. Therefore, the form of evaluation was changed for the definition of syndromes of risk of psychosis and this way, observing, the treat-

ments that can prevent the transition to psychosis in these ultra-high-risk groups. It is noted that individuals with attenuated psychotic symptoms, had one or more psychiatric comorbidities. In DSM-V, we have the inclusion of the attenuated symptoms syndrome which are negative symptoms (e.g., diminished emotional expression or avolism) expressed in an attenuated manner, such as odd beliefs and unusual perceptual experiences. It was included in the DSM-V as a condition in further study[9].

A study conducted in Child and Adolescent Psychiatry Department of the University Medical Center Utrecht recruited seventy-two adolescents aged 12 to 18 years who met UHR criteria or basic symptoms of cognitive disorders (COGDIS). Of these 57 patients completed a two-year follow-up. At the end of the follow-up period 15.6% of adolescents in UHR had experienced psychotic transition; 35.3% still met UHR criteria and 49.1% of individuals in UHR had remitted from the condition[6].

These patients who experience transition increase healthcare costs as clarified by Krann et al (2017). Even in patients without the transition, the adversities of childhood bring harm with decreased productivity in adulthood and increase health costs[10].

Other authors, such as Mokhtari and Rajarethinam (2013)[11] reinforce the importance of early detection and intervention for patients at risk of developing schizophrenia, especially in childhood. They further reiterated that high-risk individuals have subtle symptoms, and without adequate intervention, one third of these individuals develop psychosis within a year. Finally, they reveal two possible interventions: medication and psychotherapy[11].

Looking at interventions, a meta-analysis conducted according to the PRISMA guideline identified 10 studies reporting 12-month follow-up data on transition to psychosis, and 5 studies with follow-up ranging from 24 to 48 months. Overall, the risk reduction with early intervention at 12 months was 54% (RR = 0.463; 95%CI = 0.33-0.64) with a Number Needed to Treat (NNT) of 9 (95%CI = 6-15). At 24- to 48-month follow-ups they were associated with a 37% risk reduction (RR = 0.635; 95% CI = 0.44-0.92) and an NNT of 12 (95% CI = 7-59). Antipsychotic medication has shown efficacy, but more trials are needed. After all, data on antipsychotic medication is based on small trials and more evidence is needed to demonstrate efficacy and safety. Omega-3 was promising in preventing a first episode of psychosis, but this impression is based on a small trial and requires replication. The findings regarding Cognitive and Behavioural Therapy (CBT) seem robust, but the 95% confidence interval is still wide[12].

On CBT, there are several papers that talk about this subject. Morrison et al. reported that it significantly reduces the likelihood of transition to psychosis. Van der Gaag and colleagues also found that CBT reduced the transition to psychosis at the end of 18 months of follow-up. Another recent study by Bechdolf and colleagues described that this intervention for patients in an "early prodromal state" reduced transition to psychosis. Only 3.2% of participants who received CBT transitioned to a first episode of psychosis, compared to 16.9% who did not receive CBT[13].

As for antipsychotic medication particularly low dose, it may be effective in preventing or delaying transition to psychosis in the short term when combined with CBT. The PRIME study was a randomized double-blind study comparing efficacy of 5-15 mg olanzapine with placebo. Eight weeks follow-up suggested that olanzapine was associated with significant improvement in psychotic symptoms compared with the placebo group and there was less transition to psychosis in the olanzapine group at 1 year follow-up. However, there was no difference in the two groups if viewed at 2-year follow-up[13].

A meta-analysis by Pagsberg AK and co-workers that studied the use of antipsychotics, in young people with schizophrenia spectrum compared to placebo. It involved 8 antipsychotics (aripiprazole, asenapine, paliperidone, risperidone, quetiapine, olanzapine, molindone and ziprasidone). All antipsychotics were superior to placebo, except ziprasidone. Olanzapine, quetiapine, and risperidone showed higher frequency weight gain. Quetiapine had higher triglyceride increase than placebo. Treatment discontinuation, sedation, insomnia did not differ between antipsychotics[12].

DISCUSSION

The idea that psychiatric illnesses, such as schizophrenia, do not start suddenly and that there are prodromes that predict the illness is not new in the literature. In the 19th century, Kraepelin already mentioned that it was possible to notice a period around weeks to years in which mild symptoms were present before the first psychotic episode. In the prodromal phase the symptoms would be insufficient to make the diagnosis of a psychosis, but the individual's functioning is already clearly altered[14]. Currently patients in this phase, are considered HRU. The PACE (Personal Assessment and Crisis Evaluation) group, Australia pioneered the observation of individuals in UHR for an extended period and advanced the clinical characterization of UHR. The PACE clinic was founded in 1994 with the strategy of performing early interventions in patients in prodromal stages and its criteria were adopted in other services around the world[15].

The UHR criteria were introduced to identify young people with a high risk of onset of psychotic disorders, i.e., patients in the prodromal stages of the disease. The goal of clinical intervention in individuals in UHR is to alleviate their problems and symptoms that bother them. Individuals in UHR typically have symptoms that cause distress and disrupt their daily lives, so they seek medical help.

Individuals (UHR) who will convert to psychosis remain an unresolved problem. It remains to be fully understood whether the risk of transition to psychosis is increased by the presence of non-psychotic symptoms, such as mood disorders. There is a need for further studies on this issue. Non-psychotic symptoms are a prevalent concern in individuals in UHR and are the main cause of help-seeking, so it would be interesting to treat non-psychotic symptoms for relief of suffering in UHR patients.

Overall, the studies found indicate that CBT seems to reduce psychotic symptomatology preventing or delaying the transition to psychosis, in addition to improving social functioning in UHR patients[11,12]. Regarding drug treatment, antipsychotics seem to be effective in reducing UHR symptoms. There is some concern about the use of antipsychotics in these patients; these include the side effects that may be particularly distressing for young people (e.g. weight gain, sexual dysfunction, extrapyramidal side effects; self-stigmatization. There is a need for further studies on the long-term use of antipsychotics in these patients[11].

In the clinical trials conducted, both the duration and periods of intervention in HRU patients have been relatively short. Thus, doubt remains about the extent of treatment that should be given and whether over time, the intervention is effective, as antipsychotics have many side effects. There should be more discussion about cost-effectiveness in treatments in UHR patients.

Clinical monitoring of these UHR patients for early signs of psychosis is quite effective in reducing the duration of untreated psychosis and seems to decrease the severity of the first episode. Further follow-up studies of these UHR patients are still needed.

CONCLUSION

The UHR criteria were introduced to identify young people at a high risk for psychotic disorders, i.e., in the prodromal stages of the illness. By delaying the first psychotic episode, there is a decrease in the impairment of the patient's quality of life, as well as a decrease in healthcare costs. There is also the need to treat non-psychotic symptoms such as depression and anxiety that may be associated with these patients. Clinical trials with HRU patients are for short follow-up periods, there is a need for further studies on whether interventions are effective over time.

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