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**Search details**

The effect of Ru-accutane (Isotretinoin) causing serious mental illness in children and young people.

**Resources searched**

NHS Evidence; TRIP Database; Cochrane Library; MEDLINE; PsychINFO; Google Scholar

**Database search terms:**

Side effects(drugs); treatment; drug therapy; suicidal ideation; major depression;

**Evidence search string(s):**

**Google search string(s):**

**Summary**


**Guidelines**


**Evidence-based reviews**

1. **Title:** Adverse effects of isotretinoin: A retrospective review of 1743 patients started on isotretinoin.
   **Citation:** Australasian Journal of Dermatology, 11 2010, vol./is. 51/4(248-53), 0004-
BACKGROUND/OBJECTIVES: Isotretinoin has revolutionized the management of acne vulgaris. However, concerns continue regarding the adverse effect profile of isotretinoin. This study aims to review the adverse effects experienced by patients started on isotretinoin by a single dermatologist.

METHODS: Retrospective chart review of 1743 patients started on isotretinoin for various dermatological conditions over a 6-year period. Details of the dose of isotretinoin used, concomitant medications, adverse effects and outcome were recorded.

RESULTS: One-fifth (18.5%) of patients reported no adverse effects during the study period. Cheilitis was the most commonly reported adverse effect, affecting 78% of users, followed by eczema and tiredness, seen in 12% each. However, these were clearly dose-dependent, as the group treated with doses of isotretinoin under 0.25 mg/kg/day only reported cheilitis in 47%, eczema in 7% and tiredness in 5%, compared with 96%, 16% and 18%, respectively, in those treated with more than 0.75 mg/gm/day. Twenty-four patients (1.4%) stopped isotretinoin because of adverse effects; a further three patients complained of severe adverse effects on at least one occasion, but continued taking the medication. The adverse effect(s) that led to patients stopping isotretinoin were cheilitis (22 patients), mood change (13), tiredness (12), eczema (6) and pregnancy (2). There were no reported instances of suicidal ideation or attempted suicide.

CONCLUSIONS: Other than the two oral contraceptive failures, there were no serious adverse events recorded during this review period. Isotretinoin is a very effective medication with a low adverse-effect profile when used at lower doses.

2. Title: Isotretinoin, depression and suicide: a review of the evidence.
Citation: British Journal of General Practice, 02 2005, vol./is. 55/511(134-8), 0960-1643;0960-1643 (2005 Feb)

Author(s): Magin P, Pond D, Smith W

Abstract: There is currently considerable controversy regarding a proposed causal relationship between the use of isotretinoin and depression and suicide. A search was made of the MEDLINE, EMBASE and PsycINFO databases using the search terms 'isotretinoin', 'depression' and 'suicide'. Despite numerous case reports linking isotretinoin to depression, suicidal ideation and suicide, there is, as yet, no clear proof of an association. While isotretinoin, used to treat acne vulgaris, has not been demonstrated to be associated with depression or suicide, the possibility of a relatively rare idiosyncratic adverse effect remains. GPs have a role in the clinical application of these findings.

3. Title: Genetic vulnerability and isotretinoin-induced psychiatric adverse events.
Citation: The World Journal of Biological Psychiatry, 2010, vol./is. 11/1-2(158-159), 1562-2975;1814-1412 (2010)

Author(s): Kontaxakis, Vassilis P, Ferentinos, Panagiotis P, Havaki-Kontaxaki, Beata J, Papadimitriou, George N

Abstract: Discusses isotretinoin, a synthetic retinoid that is used against severe, recalcitrant nodulocystic acne. It has been associated in several case-series and some retrospective and uncontrolled studies with various psychiatric side-effects (depression, violent behaviour, suicidality and psychotic symptoms). They present four patients consecutively hospitalized in their department whose psychiatric symptoms (depression, suicidality, psychotic symptoms) were possibly induced by isotretinoin administration. All patients had a positive family history for psychiatric disorders. The authors suggest that isotretinoin-induced psychiatric symptoms might be generated through a gene-environment interaction, with isotretinoin as an undifferentiated environmental stressor and its effects being modulated by the various types of genetic vulnerability of the exposed individuals. Therefore, increased caution with isotretinoin use in genetically
vulnerable individuals seems to be justified.

Citation: Journal of Affective Disorders, 05 2010, vol./is. 122/3(306-308), 0165-0327 (May 2010) Author(s): Schaffer, Linda C, Schaffer, Charles B, Hunter, Susan, Miller, Amber

Abstract: Background: Isotretinoin (Accutane) has been available for the treatment of severe cystic acne for about twenty-five years. There have been several reports of adverse psychiatric reactions to isotretinoin, including depressive symptoms and suicide. However, there have been only three case reports of patients with bipolar disorder (BD) who experienced an untoward psychiatric side effect while receiving isotretinoin treatment. In this study, the psychiatric side effects from isotretinoin were assessed in a larger group of BD patients than has previously been reported. Methods: A retrospective chart review of 300 BD outpatients identified ten patients treated with isotretinoin. Results: Nine of these ten patients experienced a significant worsening of mood symptoms, and three developed suicidal ideation. Eight experienced a reversal of the relapsed mood symptoms when the isotretinoin was discontinued, whether prematurely or after a full course. Limitations: The limitations of this study include small sample size, retrospective data collection, absence of double-blind controlled design, and inability to control for spontaneous mood episodes in patients with BD. Conclusions: These results indicate that BD patients treated with isotretinoin for acne are at risk for clinically significant exacerbation of mood symptoms, including suicidal ideation, even with concurrent use of psychiatric medicines for BD. The clinical implications of this study are especially relevant to the treatment of patients with BD because acne usually occurs during adolescence, which is often the age of onset of BD and because a common side effect of lithium (a standard treatment for BD) is acne.

5. Title: Isotretinoin, depression and suicide ideation in an adolescent boy.
Citation: Pharmacopsychiatry, 05 2007, vol./is. 40/3(128), 0176-3679;1439-0795 (May 2007)

Author(s): Bachmann, C, Grabarkiewicz, J, Theisen, F. M, Remschmidt, H

Abstract: Isotretinoin is a common, effective pharmacological substance in the treatment of severe acne. There has been a long history of controversial discussion as to whether or not treatment with isotretinoin may induce depressive symptoms, suicide ideation or even suicide. We here report the case of a 16-year-old boy who experienced two depressive episodes which were strongly associated with isotretinoin treatment. To our knowledge, this is the first case report using an objective causality assessment to support the link between isotretinoin treatment and depression. From a pharmacological point of view, it seems reasonable that the clinical symptomatology of isotretinoin treatment may not only be a result from the specific pharmacological properties of the drug, but also from pharmacogenetic influences. The current case report strongly indicates that isotretinoin may induce depression in idiosyncratic patients. Hence, prescribers of isotretinoin should be aware of this ADR and, if necessary, refer patients to psychiatric institutions.

6. Title: Lumps, Bumps, and Things That Go Itch in Your Office!
Citation: The Journal of School Nursing, 08 2004, vol./is. 20/4(245-246), 1059-8405 (Aug 2004)

Author(s): McLeod, Renee P

Abstract: Presents a short case study and differential diagnosis. It is followed by a discussion of the disease or condition and how the school nurse should handle it. C.B., a 16 year old male, was suffering from rashes on his chin and back. When his rashes did not improve after the use of over the counter products, he stopped using these. It got worse with time. On presentation his vital signs were normal. The rashes consisted of multiple papules, pustules, nodules, and a few scattered cysts on his back. This child has acne. Acne is so common that it usually does not bring a child to the school health office. Left untreated, this disease can cause severe scarring, disfigurement, and depression. Acne in teenagers begins as an overproduction of sebum. Successful treatment of acne is dependent on good patient compliance and a plan of care that considers the teenager's skin type. New treatment guidelines recommend starting with a topical retinoid. Topical
and systemic antibiotics are commonly used to treat acne. Isotretinoin is a systemic vitamin A derivative used to treat severe nodulocystic or inflammatory acne, but there are several severe side effects with this product. Key points for school nurses are included.

7. Title: Hypersomnia Associated with Isotretinoin in a Patient with Recurrent Major Depressive Disorder and Acne Vulgaris.
Citation: Sleep: Journal of Sleep and Sleep Disorders Research, 06 2004, vol./is. 27/4(821), 0161-8105;1550-9109 (Jun 2004)
Author(s): Shehi, G. Michael, Bryson, W. Jeff

Abstract: A case is presented in which an acute shift in sleep-disturbance extremes was reported by a patient shortly after the initiation of isotretinoin therapy. Mr. A, a 17-year-old Caucasian male with a history of recurrent major depressive disorder and acne vulgaris, was admitted to an in-patient acute care psychiatric hospital 3 months after isotretinoin therapy was initiated by a dermatologist. Mr. A reported that after 3 days of isotretinoin therapy his mood sharply declined and all of the previously reported depressive symptoms exacerbated with 1 notable exception. Unexpectedly, Mr. A reported that instead of experiencing severe sleep initiation and maintenance insomnia as he had before, he was now sleeping 14 to 15 hours per day. Upon Mr. A's admission to the in-patient psychiatric unit, the isotretinoin was discontinued, and the patient was placed under observation for safety due to his reports of suicidal ideation. After 3 days, the patient's depressive symptoms had drastically improved, and suicidal ideations had remitted. In addition, there was no longer evidence of hypersomnia, and the patient was able to function in scheduled activities. The purpose of this report is 2-fold. The first purpose of this report is to bring forth further awareness of the potential risk of using isotretinoin in patients with a positive history of clinically significant depression. Second, this report is intended to call attention to the possible effects of isotretinoin on sleep. At this time, knowledge of the effects of isotretinoin on sleep is quite limited.

8. Title: Depression and suicide in patients treated with isotretinoin.
Citation: The New England Journal of Medicine, 02 2001, vol./is. 344/6(460), 0028-4793;1533-4406 (Feb 2001)
Author(s): Wysowski, Diane K, Pitts, Marilyn, Beitz, Julie

Abstract: Briefly discusses reports received by the Food and Drug Administration of 431 cases of depression, suicidal ideation, suicide attempts, or suicide in US patients treated with isotretinoin, which is indicated for the treatment of severe nodular acne. Physicians should request that patients and their parents report promptly any changes in behavior that might be symptomatic of depression so that patients may be evaluated for appropriate treatment.

9. Title: An update on the presence of psychiatric comorbidities in acne patients, Part 2: Depression, anxiety, and suicide.
Citation: Cutis, 08 2011, vol./is. 88/2(92-7), 0011-4162;0011-4162 (2011 Aug)
Author(s): Saitta P, Keehan P, Yousif J, Way BV, Grekin S, Brancaccio R

Abstract: Acne vulgaris (AV) is a chronic inflammatory skin disease that affects millions of people. Psychologic disorders such as depression, anxiety, and body dysmorphic disorder are common in patients with AV and the reported prevalence of suicidal ideation and suicide completion in acne patients also is remarkable. Part 1 of this series provided an overview of the prevalence of psychologic disorders in patients with AV Part 2 reviews depression, anxiety, body dysmorphic disorder, and suicidal ideation and completion seen in AV patients. Treatments available for acne patients with coexisting psychiatric illness also are discussed, along with the relationship between oral isotretinoin and depression and suicide.

10. Title: A pilot study evaluating anxiety and depressive scores in acne patients treated
with isotretinoin.

**Citation:** Journal of Dermatological Treatment, 06 2004, vol./is. 15/3(153-7), 0954-6634;0954-6634 (2004 Jun)

**Author(s):** Ferahbas A,Turan MT,Esel E,Utas S,Kutlugun C,Kilic CG

**Abstract:** BACKGROUND: Isotretinoin therapy and its alleged adverse psychiatric effects have received considerable media attention during the past years. The aim of this pilot study was to investigate whether there was any association between isotretinoin therapy and anxiety, depression or suicidal ideation.

**METHODS:** Forty-five patients with severe recalcitrant acne were enrolled in this study. Isotretinoin was administered at a dose of 0.5-1 mg/kg per day in two divided doses with food for 16 weeks. All patients received a complete dermatological examination and the severity levels of their acne were scored according to the Leeds Revised Acne Grading system at baseline (before isotretinoin treatment) and follow-up assessments at weeks 4, 8 and 16 of the treatment.

Severity of anxiety and depressive symptoms were assessed with the Clinical Anxiety Scale and Montgomery-Asberg Depression Rating Scale before and upon completion of the 16-week isotretinoin treatment.

**RESULTS:** Twenty-three patients completed the final assessment. There was a statistically significant decrease in anxiety scores. Depression scores also decreased but were not statistically significant. No patient committed or attempted suicide.

**CONCLUSIONS:** This pilot study was unable to detect an association between the use of isotretinoin and an increased risk for anxiety, depression, or suicidal thoughts.

11. **Title:** Overview of existing research and information linking isotretinoin (accutane), depression, psychosis, and suicide.

**Citation:** American Journal of Therapeutics, 03-04 2003, vol./is. 10/2(148-59), 1075-2765;1075-2765 (2003 Mar-Apr)

**Author(s):** O'Donnell J

**Abstract:** Isotretinoin (Accutane; Hoffmann-La Roche, Nutley, NJ) is a drug closely related to the chemical structure of vitamin A. The pharmacology and toxicology of these two retinoids are similar enough to warrant comparison. Accutane is a powerful drug that its manufacturer, Roche, indicates is limited for severe recalcitrant nodular acne. This potency is also reflected in Accutane’s well-known ability to produce severe birth defects if taken during pregnancy. Less well known is the risk of this lipid-soluble chemical to affect the central nervous system. Reports of intracranial hypertension, depression, and suicidal ideation with Accutane use have prompted an examination of its serious and life-threatening potential. Although Roche has added a warning to its product label for signs of depression, and suicidal ideation, this product is overprescribed for all forms of acne, including mild and moderate cases that have not been treated with alternative medications with less risk of depression and suicide. There is no contesting that this drug is effective at clearing up the most severe forms of acne, but the public must be informed of the proper limited indication for its use, because depression and suicide can follow in patients with no prior history of psychiatric symptoms or suicide attempts.

12. **Title:** An analysis of reports of depression and suicide in patients treated with isotretinoin.

**Citation:** Journal of the American Academy of Dermatology, 10 2001, vol./is. 45/4(515-9), 0190-9622;0190-9622 (2001 Oct)

**Author(s):** Wysowski DK,Pitts M,Beitz

**Abstract:** BACKGROUND: The Food and Drug Administration (FDA) has received reports of depression and suicide in patients treated with isotretinoin.

**OBJECTIVE:** Our purpose was to provide the number and describe the cases of depression and suicide reported to the FDA in US patients treated with isotretinoin and to consider the nature of a
possible association between isotretinoin and depression.

METHODS: An analysis was made of reports of depression, suicidal ideation, suicide attempt, and suicide in US isotretinoin users voluntarily submitted to the manufacturer and the FDA from 1982 to May 2000 and entered in the FDA's Adverse Event Reporting System database.

RESULTS: From marketing of isotretinoin in 1982 to May 2000, the FDA received reports of 37 US patients treated with isotretinoin who committed suicide; 110 who were hospitalized for depression, suicidal ideation, or suicide attempt; and 284 with nonhospitalized depression, for a total of 431 patients. Factors suggesting a possible association between isotretinoin and depression include a temporal association between use of the drug and depression, positive dechallenges (often with psychiatric treatment), positive rechallenges, and possible biologic plausibility. Compared with all drugs in the FDA's Adverse Event Reporting System database to June 2000, isotretinoin ranked within the top 10 for number of reports of depression and suicide attempt.

CONCLUSION: The FDA has received reports of depression, suicidal ideation, suicide attempt, and suicide in patients treated with isotretinoin. Additional studies are needed to determine whether isotretinoin causes depression and to identify susceptible persons. In the meantime, physicians are advised to inform patients prescribed isotretinoin (and parents, if appropriate) of the possibility of development or worsening of depression. They should advise patients (and parents) to immediately report mood swings and symptoms suggestive of depression such as sadness, crying, loss of appetite, unusual fatigue, withdrawal, and inability to concentrate so that patients can be promptly evaluated for appropriate treatment, including consideration of drug discontinuation and referral for psychiatric care.

13. Title: The role of isotretinoin in acne therapy: why not as first-line therapy? facts and controversies.

Citation: Clinics in Dermatology, 01-02 2010, vol./is. 28/1(24-30), 0738-081X;1879-1131 (2010 Jan-Feb)

Author(s): Rigopoulos D,Larios G,Katsambas AD

Abstract: Acne is one of the most prevalent diseases in dermatology: Millions of people worldwide experience this distressing condition. To determine the appropriate therapeutic strategy, there is a strong need for a standardized classification system of acne. The exact molecular mechanism of action of isotretinoin is not completely understood; however, oral isotretinoin targets simultaneously at all major mechanisms of acne pathogenesis. Various mass media reports about the risk of teratogenicity and depression from isotretinoin usage as well as the creation of intense prevention programs have created an obstacle to the use of the most active available drug against acne, presenting isotretinoin as a very dangerous regimen. According to recommendations of several international experts, which we share, oral isotretinoin may be prescribed not only to patients with severe disease but indications should be broadened to also include patients with less severe forms of acne, especially in cases with scarring, significant psychologic stress, or failure to respond to conventional therapy.

14. Title: Monitoring people treated with isotretinoin for depression.

Citation: Psychological Reports, 06 2007, vol./is. 100/3 Pt 2(1312-4), 0033-2941;0033-2941 (2007 Jun)

Author(s): Brasic JR

Abstract: Depression has been reported in some patients treated with isotretinoin, an effective medication for nodulocystic acne, a serious disorder resulting in permanent scarring. Since major depression, a common disorder associated with multiple health risks including suicide attempts and treatment noncompliance, may occur during the course of treatment with isotretinoin, persons treated with isotretinoin must be screened for depression before starting treatment and monitored for depression regularly during the course of treatment with isotretinoin. Those with evidence of depression must then be referred for prompt treatment to abort serious adverse outcomes, including suicide.
Psychologists constitute key members of the treatment team of patients taking isotretinoin.

15. Title: Suicide, depression, and isotretinoin: is there a causal link?.

Citation: Journal of the American Academy of Dermatology, 11 2001, vol./is. 45/5(S168-75), 0190-9622;0190-9622 (2001 Nov)

Author(s): Jacobs DG, Deutsch NL, Brewer M

Abstract: This paper examines the existing literature and MedWatch reports concerning a proposed relationship between isotretinoin and depression and suicide. The authors provide a brief overview of the biology of isotretinoin and depressive disorder and find no basis for a putative molecular mechanism linking the two. They also address the complexities of Substance-Induced Mood Disorder (SIMD) as a psychiatric diagnosis and its relevance to isotretinoin. Based on this review, the authors conclude that there is no evidence to support a causal connection between isotretinoin and major depression or suicide, because reported cases do not meet the established criteria for causality. The authors also conclude, however, that it is important for dermatologists to be aware of the risk factors for suicide and to monitor patients who exhibit depressive symptoms.

There are a number of references to Isotretinoin on the TRIP database at www.trip.database.com

I have included this one – as it deals with pediatric dermatology. There are other documents which don’t look as though they deal specifically with the mental health implications of using this drug, though they may be worth looking at. I didn’t want to refer you to all of them at this stage. They are all full-text so you can have a look at the database easily. I just used the search terms ‘Isotretinoin’ and ‘Mental illness’.


Effective monitoring of isotretinoin safety in a pediatric dermatology population: a novel "patient symptom survey" approach.

Hodgkiss-Harlow CJ, Eichenfield LF, Dohil MA..

Abstract BACKGROUND: Assessment of adverse effects in pediatric patients on oral isotretinoin has not been standardized and the exact incidence is unknown.

OBJECTIVE: Our goal was to determine the usefulness of an isotretinoin symptom survey as a screening tool for assessment and quantification of adverse effects, including psychiatric symptoms, during isotretinoin treatment in a pediatric population of different age groups.

METHODS: We performed a retrospective chart review on a random sample of patients treated with isotretinoin at a tertiary pediatric dermatology clinic where patients completed an isotretinoin symptom survey at each visit. Responses were stratified by age group and psychiatric history.

RESULTS: The charts of 102 patients, representing 123 courses of isotretinoin and 760 treatment-months, were reviewed. A total of 722
(95.0%) symptom surveys were complete and 38 (5.0%) were incomplete/missing. Recorded side effects were similar to published adult data; dry lips/dry skin were reported in 94.25% and 72.13% of treatment-months of isotretinoin, respectively. Psychiatric symptoms were reported in 1.65%, with no statistical difference between patients with or without a mental health history. Patients aged 11 to 15 years had similar side-effect profiles to those aged 16 to 21 years. Impaired night vision, nosebleeds, and dry/bloodshot eyes were more common in the older age group.

**LIMITATIONS:** This was a retrospective chart review, with known limitations. The study was performed at a tertiary referral center for pediatric dermatology, possibly allowing patient selection bias.

**CONCLUSIONS:** The isotretinoin symptom survey appears to be an effective screening tool to standardize monitoring of isotretinoin side effects in the pediatric population.