

Antabuse (disulfiram) — a useful tool in General Practice

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Curriculum vitae

Dr Sylvain de Miranda was born in Holland and came to South Africa during the Second World War. He graduated at the University of the Witwatersrand in 1949 (MB BCH) and has been involved with alcohol programmes since 1951. He is presently Director and Head of Clinical Services of the SA National Council on Alcoholism and Drug Dependence, Johannesburg Society and part-time lecturer at both the University of the Witwatersrand and RAU. He is the author of many articles on alcohol and drug dependence and has received several awards for his dedicated humanitarian services in this field. He is married with two adult children.

It is conservatively estimated that 10% of patients seen in busy general practice are suffering from alcohol related problems, either due to irresponsible excessive drinking or to alcohol dependence per se.¹

Some general practitioners prefer not to manage alcohol related problems and shy away from getting involved. Frequently we tend to gloss over the problem stating "you should cut down a bit

Summary

It is conservatively estimated that 10% of patients seen in a busy general practice, are suffering from alcohol related problems. Much can however be done in family practice, as this article emphasises. It reviews the practical application of Antabuse-therapy in the effective management of this problem.

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on your booze" or else recommend referral to a psychiatric consultant or an alcohol specialist agency.

The reasons for this are usually attributed to insufficient time to devote to these people or the difficulty in monitoring them adequately, or to the high rate of non-compliance which makes the whole operation seem to be a waste of time.

Much can however, be done in family practice. In order to assist the family practitioner in the effective management of his alcohol-related problem patients, this article will review the practical application of "Antabuse" therapy.

Rationale

The properly supervised administration of Antabuse, is one of the very few methods available to the practitioner to ensure the discontinuation of the patient's drinking pattern and thereby ensure a prolonged period of alcohol-free

stabilisation, during which the necessary supportive counselling, psycho-therapy and family therapy can be successfully applied.

Method of administration

1. Antabuse exerts its action over a minimum period of 36-48 hours (usually longer). Therefore the *administration of 1 tablet on alternate days* is advocated.²

2. To ensure compliance, initially arrange for the patient to report to your rooms on alternate days, where your nursing sister will:

- administer the Antabuse in solution, under direct supervision;
- maintain an attendance register;
- monitor the patient for any adverse effect (ie alcohol-Antabuse reaction).

3. After 6-8 weeks, the patient's frequency of attendance is lessened — depending on general progress. The patient continues taking 1 Antabuse tablet on alternate days, which is supplied by ordinary prescription.

Precautions

1. Patient must be alcohol free for \pm 36 hours before commencing Antabuse therapy.

2. The full implications of the consequences of drinking alcohol whilst on Antabuse therapy must be fully explained to the patient.

NB Never allow Antabuse to be used without the patient's full knowledge (the method of surreptitiously administering Antabuse in the unsuspecting patient's food or beverage is often resorted to by desperate spouses!)

3. Advise the wearing of a "medic-alert".

Mode of Action

Antabuse blocks the oxidation of alcohol at the acetaldehyde level, by inactivating the enzyme acetaldehyde dehydrogenase. The resulting high level of blood acetaldehyde accounts for the signs and symptoms of the alcohol-Antabuse reaction.³

Signs and symptoms of the alcohol-Antabuse reaction

- flushing of the skin
- throbbing in head and neck
- throbbing headaches
- difficulty in breathing, with "tightness in the chest"
- nausea and vomiting
- sweating
- palpitations; rapid heart rate; drop in blood-pressure and fainting attacks

- in severe reactions there may be respiratory depression and cardio-vascular collapse.

The duration of this reaction can vary from 30 minutes to several hours.

Treatment of the alcohol-Antabuse reaction

- Treat for shock and restore blood-pressure
- Oxygen administration; glucose drinks and keeping foot of bed raised
- Intravenous injections of Vitamin C (500 milligrams) and anti-histamines (eg 2 ml Anthisan, 25 milligrams) can be most effective.

Contra-indications to the use of Antabuse

As in all medical applications of drugs, the physician must be guided by the following considerations:

1. absolute contra-indications;
2. relative contra-indications;
3. clinical evaluation (the so-called "calculated risk").

In my opinion, the only absolute contra-indication to the use of Antabuse is proven sensitivity or allergy to the substance.

Many GPs prefer not to get involved with a patient who has an alcohol problem

Relative contra-indications, which are self-evident from some of the above discussions, are:

- cardio-vascular disease (especially coronary artery disease and cardiac failure)
- severe hypertension
- chronic, severe respiratory disease
- pregnancy
- severe hepatitis or cirrhosis of the liver.

It is incumbent on the physician to be fully aware of, and to establish and assess, the existence of these conditions prior to treatment.

Whilst always urging a different approach when these relative contra-indications exist, it is my contention that if alternative treatment methods prove unsuccessful, the continued, severe abuse of alcohol will have far more disastrous effects on those conditions than the *controlled*, successful exhibition of Antabuse.

Although the teratogenic effect of Antabuse is not known, I have successfully administered Antabuse to a number of pregnant women, where their uncontrolled drinking gave real rise to fears of

foetal alcohol damage. Low grade alcohol consumption by these pregnant mothers treated with Antabuse, raises the spectre of abnormally high blood acetaldehyde levels. Acetaldehyde is known to be severely toxic to the foetus. However, no Antabuse related foetal damage has been observed in these babies after birth — again highlighting the need for strict monitoring in Antabuse therapy.

Suffice it to state, that all these cases provide a real test of clinical acumen and above all, a thorough, sound knowledge of all aspects of the pathology of alcohol dependence is required.

Other adverse reactions

1. Drug Interaction

Disulfiram can interfere with the metabolism of other drugs, thereby prolonging or altering their effect, or producing side effects. Common examples are:

all medication, foods or any substance containing alcohol or alcohol-like chemicals, eg

- many anti-cough preparations
- substances containing vinegar
- fermented foodstuffs (NB: the use of sour porridge in Black South African communities)
- certain cosmetic alcohol containing lotions (eg aftershave lotions, astringents).

Of special interest are those workers (on Antabuse therapy) at alcohol, chemical, industrial and fuel-energy plants, where the inhalation of fumes can cause severe alcohol-Antabuse reactions.

Properly supervised administration of Antabuse is one method available to the GP to ensure discontinuation of drinking.

Special Drugs

- Phenytoin (anti-convulsant) — administration of Antabuse can cause severe phenytoin toxicity due to the interference with phenytoin metabolism.
- Metronidazole (Flagyl) — has similar effects on alcohol metabolism as Antabuse. Their combined use may give rise to overdose "encephalopathy".
- Isoniazid (INH and Rifamate) — used extensively in the treatment of tuberculosis,

should not be administered concurrently with Antabuse.

- Anti-coagulants — dosage may need adjustment as Antabuse enhances the anti-coagulant effect.

2. Toxic Reactions Per Se (In absence of any of the above factors)

Antabuse has been blamed for a multitude of side-effects ranging from headaches and conjunctivitis, to loss of libido and impotence, to psychotic states. Having used and studied Antabuse in the treatment of alcohol dependence in some 35 000 cases since 1952, it may be pertinent here to express my views and findings on some of the commonest allegations:

Never allow a desperate spouse to put Antabuse in the food of an unsuspecting partner

- *General Somatic Symptoms* — such as headaches, fatigue, palpitations, etc, are invariably psychological manifestations of the patient's projection, directing his anger at Antabuse as the direct cause for his inability to drink. (Similar projections against spouse, nursing sister, doctor and therapist are often observed and must be recognised and dealt with as part of the prevailing psycho-dynamics of alcohol dependence). Low grade consumption of alcohol or alcohol-like substances should always be remembered, however, when such vague symptoms occur.

- *Loss of Libido and Impotence* — It has been my experience that this frequent complaint is strongly psycho-dynamically rooted rather than Antabuse related. Not many studies, using double blind trails, have been conducted. Those studies that have been reported, tend to prove that there seems to be no difference in side effects reported to disulfiram (Antabuse), calcium carbimide (Dipsan) or placebo. In fact, there appeared more sexual problems reported to placebo than to Antabuse and Dipsan⁴.

- *Allergy or Sensitivity* — There is a definite percentage incidence of Antabuse sensitivity. All degrees of dermatitis, from urticaria to exfoliative dermatitis have been observed. Intense pruritis and angioneurotic oedema often occur in these cases. All observed cases responded totally to antihistamine therapy and discontinuation of Antabuse.

NB: — History of contact dermatitis to leather should alert the clinician to possible antabuse sensitivity (see historical, original use of disulfiram to prevent oxidation in leather).

— A number of our nursing personnel, handling large volumes of Antabuse tablets, have exhibited varying degrees of allergic dermatitis. In these cases, the use of rubber gloves and face masks when handling Antabuse tablets, is indicated.

● *Effects on Central and Peripheral Nervous System* — Although the literature describes reported cases of psychotic states, confusional states; peripheral neuritis and optic neuritis, it has been our observation, clinically, that in most of these cases there was a history of repetitive low alcohol or alcohol-like consumption, surreptitiously or inadvertently. However, severe central nervous system encephalopathy-like syndromes have been reported as a result of severe over-dosage in both adults and children, in the absence of alcohol intake.^{5,6}

Patients may project their anger with Antabuse against their spouses or doctors – but it should be dealt with as part of the psycho-dynamics of alcohol dependence

3. The Implant

Disulfiram has been manufactured in the form of slow-release pellets to be implanted under the skin as a once-only operation lasting 6-12 months ("Esperal"). Unfortunately, its use has become the subject of much misguided media pronouncements, almost equating the use of the implant with the absolute cure for alcohol dependence (this certainly is not the claim of the manufacturers).

Except for some very few, highly selected cases, I am not in favour of routine use of disulfiram implants for the following reasons:

1. In spite of many years of existence, it has not obtained approval of the South African Medicine's Control Council (it can only be used for experimental purposes).
2. Bio-availability of implants is erratic.

3. Frequently, adequate supervision and control is abandoned because daily administration is unnecessary. This often leads to uncontrolled alcohol-disulfiram reactions.

NB: The administration of these substances does not cure alcohol dependence but only assists in the successful treatment thereof.

4. Being a "foreign body", often leads to "sepsis" as a result of "rejection reaction".

4. Additional Use of Antabuse

Recently, our Johannesburg Clinics have successfully applied the use of Antabuse in the treatment of the common cough-mixture addictions. This has been developed because of the presence of alcohol in many of these cough mixtures.

Conclusion

Despite the many detractors, the moral and philosophical opponents and a host of well-meaning ignorami, I strongly advocate the supervised administration of Antabuse as an indispensable concomitant of successful treatment for the alcohol dependent. In fact, today, at our Johannesburg Clinics, the acceptance of Antabuse has become part of the patient/clinic treatment contract.

Antabuse is *not* used in terms of applying aversive therapy, but simply and solely as an additional, mechanical safeguard to break the vicious cycle of alcohol addiction. In other words, it will not prevent the "craving for alcohol" so that on-going supportive therapy is an essential component of the successful treatment programme.

The above approach is strongly recommended to family practitioners; especially those practising in areas where no proper specialised alcohol treatment facilities exist.

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