

Dependency upon Salbutamol Inhalers

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SUMMARY A case of dependency on salbutamol inhalers has been described. This has been discussed in relation to abuse of other drugs by alveolar absorption and other effects of salbutamol. It is not known whether the dependency is due to the salbutamol itself or to the fluorinated hydrocarbons used as propellants.

Drug abuse involving alveolar absorption dates back to the smoking of opium and cannabis. Since then there have been descriptions of the abuse by this route of anaesthetic agents, such as nitrous oxide and ether, gasoline, household and model cements (for use with polystyrene plastics) and glues, lighter fluids, paint and lacquer thinners, cleaning solutions and finger nail polish removers (Press and Done, 1967). More recently propellant gases in aerosol containers have been misused. These include spray deodorants, furniture polish, spot removers, non-stick frying pan sprays and pressurized refrigerants, for example cocktail glass chillers. They contain drugs that have actions on the CNS, such as toluene, trichlorethylene, acetone, petroleum naphtha and a range of other aliphatic, aromatic and halogenated hydrocarbons, ketones, esters, alcohols and glycols (Hofman and Hofman, 1975). Most reported cases of abuse by inhalation are in boys between the age of 10 and 15; thereafter this type of behaviour decreases.

Despite this pattern of drug abuse, addiction to inhalants is not a significant hazard of treatment, although the risk must clearly exist with a vulnerable subject and the chance introduction to an inhalant with psychoactive properties. Gluckman (1974) reported a case of toxic psychosis in a woman who used excessive amounts of salbutamol (Ventolin) orally and by inhalation. She found that the drug relieved her distress brought about by bereavement and her fear of cerebrovascular disease and made her feel bright and alert. She experienced attacks which she believed to be asthmatic but these

were episodes of hyperventilation caused by anxiety.

Other doctors have suspected that their patients might have been abusing their salbutamol inhalers. For example one general practitioner thought that two of his patients, a boy aged 14 years, and a girl of 18, 'had been using [salbutamol inhalers] in excess not necessarily for bronchospasm but as a "boost" in or before a situation of stress. Both showed signs of addiction and withdrawal symptoms' (Committee on Safety of Medicines, 1978). However, we can find no other documented evidence of dependency. The following case is presented as it demonstrates that abuse of, and dependency on, salbutamol inhalers can occur.

Case Report

The patient, a 24-year-old caretaker, was an anxiety-prone man with a low tolerance for stress. In the past he had drunk alcohol in excess and behaved in an impulsive way with suicidal gestures when faced with problems in his turbulent relationship with his common-law wife. He developed asthma at the age of three years. This had previously been treated with aminophylline, beclomethasone dipropionate and sodium cromoglycate. Even though he responded to these drugs he did not take them regularly as prescribed. For the last five years he had received salbutamol inhalers. Although advised to take 8–10 100 µg inhalations a day, he was using up to three inhalers a week (approximately 60–90 inhalations a day), which was in contrast to his previous irregular utilization of prescribed drugs. He became dependent upon the inhalers and tolerant of their effects and behaved in a way more reminiscent of a drug abuser than that of a man distressed by asthma. He frequently presented himself to his general practitioner saying that he had lost his prescription and requesting a repeat, while showing only minimal signs of bronchospasm. He had also come into conflict with the law for using false names at doctors'

surgeries and forging prescriptions. He denied receiving any pleasurable effects from the inhalers but claimed that, without them he became short of breath. He denied abusing other drugs although he had, in the past, forged prescriptions for phenobarbitone which he took for epilepsy.

Investigations

The patient was admitted to hospital and the response of his airways to bronchodilator drugs was tested after discontinuing medication for twelve hours. The FEV₁ and FVC were then measured before and after challenge doses of salbutamol by inhalation and infusion and isoprenaline by inhalation. Each challenge was carried out on separate days. The results are outlined in the Table together with the response to salbutamol by inhalation six weeks after treatment with all beta-agonists had been discontinued. The response to all the adrenergic drugs was poor but respiratory function improved after treatment was discontinued. While the resistance to bronchodilators may indicate fixed airways obstruction, in the presence of mild asthma an alternative explanation might be beta-adrenergic resistance caused by aerosol abuse (Keighley, 1966; Van Metre, 1969). The patient's improved response six weeks after discontinuation of beta-agonists supports this.

Discussion

Salbutamol, a butyl derivative of isoprenaline, is a synthetic non-catechol beta-adrenergic agonist, which has proved valuable in the treatment of asthma because of its beta-2 specificity for relaxing bronchial smooth muscle (Hartley *et al*, 1968). Its known unwanted effects include palpitations, tachycardia and changes in blood pressure due to beta-1 stimulation, and tremor, tension and restlessness due to beta-2 stimulation. The effects are dose-related. They are minimized by using metered-dose aerosols (Larsson and Svedmyr, 1977), although even with these headache, sleep disturbance, loss of appetite and nausea may occur (Nakayama, 1971).

The case described suggests that salbutamol has, in addition to these actions, effects on higher cerebral functions capable of causing dependency. The evidence for this lies in the patient's abuse of salbutamol inhalers in the absence of severe bronchospasm, his devious attempts to obtain excessive supplies and the tolerance acquired.

Like other pressurized aerosols used in the treatment of asthma, salbutamol inhalers contain a mixture of fluorinated analogues of methane and ethane as propellants. These are absorbed into the blood stream after inhalation

TABLE
Spirometry data before and after treatment

Treatment	Before treatment*		After treatment	
	FEV ₁ (l)	FVC (l)	FEV ₁ (l) % response	FVC (l)
Salbutamol 200 µg by inhalation	1.93	4.20	2.14 (+10.9%)	4.50
Salbutamol 10 µg/min over 3 hrs by infusion	1.80	4.20	2.00 (+11.2%)	4.80
Isoprenaline 160 µg by inhalation	1.30	4.20	1.40 (+7.7%)	4.50
Salbutamol 200 µg by inhalation 6 weeks after beta-agonists stopped	2.07	4.82	2.57 (+24.2%)	5.36

* Predicted volumes for height and weight: FEV₁ 4.00 l, FVC 4.70 l.

(Dollery *et al*, 1970). As they have central stimulant properties it is possible that they were responsible for the dependency. However, the alternative possibility that the salbutamol itself was responsible should be kept in mind, especially as a recent open study suggests that it has antidepressant properties (Widlocher *et al*, 1977). If this is confirmed by controlled studies and salbutamol becomes more widely used as an antidepressant it will be necessary to remain vigilant to the possibility of dependency.

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