

Salbutamol inhalation and dental caries

Introduction

Salbutamol (Ventolin[®]) is a β_2 -sympathomimetic drug, which was granted a marketing authorization in 1973. It is indicated for *the treatment of reversible airway obstruction in bronchial asthma, chronic bronchitis and emphysema* [1]. Both child and adult asthmatics use this inhalation medication, the difference lies in the dosage and vehicle of delivery. Dental caries as an ADR of salbutamol use is well-described in literature and seen regularly by health professionals but is not listed in the SPC.

Reports

Up to September 5, 2007 the Netherlands Pharmacovigilance Centre Lareb received five reports of dental caries in association with salbutamol. In some reports the application form was mentioned, which is shown in table 1. Ventolin Rotadisk[®] contains lactose. Ventolin[®] aerosol does not. Lareb received no reports of dental caries on other selective β_2 -sympathomimetic drugs.

Table 1. Reports of dental caries associated with the use of salbutamol

Patient, Sex, age	Drug Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, outcome
A M, 9	salbutamol 1 DF as necessary not reported	beclomethasone cromoglicin	dental caries	2 years not reported
B M, 5	salbutamol inhaler 100 μ g QID as necessary not reported fluticasone 125 μ g BID not reported	not reported	dental caries	years not reported
C M, 5	salbutamol aerosole 100 μ g TID aerochamber fluticasone 125 μ g BID aerochamber	sodium cromoglicate nasal spray	dental caries (8 dmfs*) growth retardation	not reported not reported
D M, 7	salbutamol inhaler 200 μ g as necessary not reported	not reported	dental caries	since start with inhalation powder striking number of holes in teeth not reported
E F, 6	salbutamol aerosole 100 μ g as necessary asthma	none	dental caries	2 months not recovered

* dmfs means decayed, missing or filled surface

Other sources of information

Literature

Dental caries is the result of a disturbed balance between saliva, oral bacteria, tooth structure, the existence of plaque, and dietary substrates [2]. The amount of saliva and of plaque, the saliva pH (SpH) and the plaque pH (PpH) play important

roles. The lower secretion rate of whole saliva consequently means that the availability of biologically active components, like amylase, calcium, secretory IgA, and peroxidase is decreased. The decreased output of antibacterial components favours both bacterial colonization and plaque growth. Furthermore the lowered secretion per minute of calcium and protein implies an unfavourable effect in critical pH [3]. This 'critical pH', at which the enamel begins to dissolve in the plaque environment, is not known, although its existence is widely assumed. It is generally accepted that a drop of plaque pH below 6.0 should be considered potentially harmful [4].

In the study by Ryberg *et al.* asthmatic patients chronically using the β -adrenoceptor terbutaline or salbutamol have a significantly lower secretion rate for whole saliva and higher titres of lactobacilli than healthy non-users [3].

Furthermore, they showed a positive relationship between decreasing saliva secretion rate and an increased dosage of β -agonists [3].

A relative difference between caries prevalence in primary and mixed dentitions has been demonstrated in several studies. Reddy *et al.* found an increasing prevalence of caries when examining children with primary (70%), mixed (78%), and permanent dentitions (83%), respectively [5]. The higher risk of caries in the more developed mixed or permanent dentition is also shown by Wogelius *et al.* and by Milano *et al.* [6,7]. A case-control study with 1-year follow-up showed that salbutamol inhaler increased caries rate compared to control, salbutamol tablets and beclomethasone inhaler [8].

There is also a difference in potential of lowering PpH between pressurized metered dose inhalers (MDIs) and dry powder inhalers (DPIs). The latter contains lactose, which has been shown to depress PpH and SpH more than DPIs.

In the study by Kargul *et al.* the results suggest that asthmatic children on long-term inhaler use have inherently lower oral pH than the normal population and that inhalers, even in the MDI form, whether corticosteroid or β_2 -agonist, are potentially acidogenic [2].

Databases

On September 4, 2007 the Lareb database contained 46 reports of dental caries and 227 reports on salbutamol. The reporting odds ratios are shown in table 2.

Table 2. reports of tooth caries associated with the use of salbutamol in the Lareb database and the WHO database in the 2nd quarter of 2007

	reports of tooth caries on salbutamol (n)	ROR (95%CI)
Lareb	5	34.2 (13.4-87.3)
WHO	19	8.2 (5.2-13.0)

Discussion

Dental caries affect many patients in Europe [9], and a significant proportion of children in the Netherlands has caries [10]. Dental caries is a well-described adverse drug reaction of salbutamol and other β -agonists, and well-known by dentists and paediatric health-professionals [3-9]. This might explain the low

number of reports in the Lareb database: when an ADR is well-known, it will be less often reported.

Three of the five patients used corticosteroids next to salbutamol. Corticosteroids are weak organic acids and generally are not metabolised by oral bacteria. They therefore should not pose a pH threat, except when lactose-based inhalers are used [4]. Concomitant medication was not reported in the fourth patient. The fifth patient used only salbutamol. So the role of corticosteroids is absent in this patient.

Conclusion

Five case reports of dental caries in the Lareb database are associated with the use of salbutamol. Literature supports the relation and probable mechanisms are proposed.

References

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