Decreased effectivity associated with the revised formulation of the salbutamol aerosol from Sandoz®

Introduction

The efficacy of inhalation aerosols depends on several factors which are patient, drug or device related. Patient related factors include inhalation technique and compliance [1]. Device related factors like particle size, aerosol outflow and propellant formulation affects the lung deposition of salbutamol [2].

Salbutamol is a short acting beta agonist (SABA) used for the relief of bronchospasms in children and adults with asthma and chronic obstructive pulmonary disease (COPD) [3,4]. In the Netherlands several inhalation devices for salbutamol are available, including multi dose and single dose devices, dry powder and aerosol inhalers, produced by multiple pharmaceutical companies including Sandoz. Sandoz salbutamol aerosol has been on the market since 2001 (RVG: 27018 = 26833) [5]. In October 2014 Sandoz revised the aerosol (RVG: 34424) [6]. Both exterior changes and changes in the formulation of the propellant have been applied [6]. The mouthpiece had an oval shape first and now it is circular and the color from the cap now is the same as the aerosol. Also oleic acid was added to the propellant [6].

Reports

From April 2015 until July 2015 the Netherlands Pharmacovigilance Centre Lareb received 9 reports concerning possible decreased efficacy associated with the salbutamol aerosol of Sandoz® [7]. The cases were reported by five reporters: 2 specialist doctors and 3 consumer.

Case A-E (196661, 196662, 196663, 196664, 196665): The first reporter, a specialist doctor, reported 5 cases of children (1-11 years of age) that were hospitalized with an asthma exacerbation after using the revised salbutamol aerosol from Sandoz®. The children had been using the aerosol from Sandoz® for a longer time, but experienced decreased effectivity after they started to use the revised aerosol from Sandoz®. The asthma in these children had been moderately controlled, and the children were treated with inhalation corticosteroids chronically and salbutamol inhalation on demand. The reporter mentioned the latency is unknown and salbutamol aerosol from another brand was effective.

Case F (199973): The second reporter, a specialist doctor from another hospital, reported a case concerning a old boy aged 11-20 years that used salbutamol aerosol on demand. He was hospitalized after he developed an asthmatic exacerbation and was treated with intravenous salbutamol. Salbutamol aerosol Sandoz® had not been effective even though the patient inhaled it 10 times that day. Previously, the salbutamol aerosol from another brand had been effective.

Case G, H,I (201436, 203145, 203812): The last three cases are reported by consumers. Case G concerns a girl aged 11-20 years that experienced less effectiveness from the Sandoz® salbutamol aerosol during an asthmatic attack. The reporter mentioned that the salbutamol was less effective than before and was effective for a shorter duration. Case H concerns a old boy aged 2-4 years who had been using salbutamol aerosol from Sandoz since 2012, his asthma was controlled moderately. Since he started to use the revised salbutamol aerosol, the salbutamol inhalations seem less effective. The patient experienced more mucus in his lungs and was treated with unspecified antibiotic therapy, the dose for a beclomethasone inhalation was increased and the salbutamol aerosol was substituted to another brand. The patient is recovering. Case I concerns a boy aged 8-10 years that uses salbutamol aerosol (brand unknown) for a longer period. Since he uses salbutamol from the brand Sandoz® he experiences more dyspnoea, it is less effective than the salbutamol aerosol he used before. On this last case follow up about the products he used before and about the use of the revised aerosol of Sandoz in combination with the spacer are requested.

All patients used the salbutamol aerosol in combination with a spacer. Both professional reporters mention they have received similar signals from colleagues regarding the efficacy of the Sandoz® salbutamol aerosol.

Discussion

The reports the Netherlands Pharmacovigilance Centre Lareb received seem to indicate that salbutamol aerosol from Sandoz® became less effective after the revision of the device. All reporters mentioned that their patients had used salbutamol aerosol for a longer time, but the salbutamol aerosol from Sandoz® became less effective recently. Not all reporters clearly state it concerns the revised version from the salbutamol aerosol Sandoz® [7]. Regarding the fact that salbutamol Sandoz® is available since 2001 and Lareb received these reports in the last months, after the revision, is remarkable.

Three known changes have been introduced during revision from the Sandoz® salbutamol aerosol. The external look changed: the mouthpiece had an oval shape first and now it is circular [6]. This shape could be more difficult to put the aerosol into the spacer. The colour from the cap changed and could be less noticeable since it now has the same colour as the inhaler itself [6]. Besides the external changes, the formulation of the propellant changed as well [3,5].

Several confounding factors may have played a role in the resulting symptoms, like seasonal factors and the asthmatic status from the patients. Also the preference status of the aerosol from Sandoz® for some Dutch Health Insurance Companies [8,9,10,11] results in a great number of people use the Sandoz® aerosol.

In conclusion, the reports the Netherlands Pharmacovigilance Centre Lareb received suggest the salbutamol aerosol from Sandoz is less effective since the revision. The pharmaceutical company Sandoz should investigate whether this concerns a quality issue or another problem like a difficulty in the use in combination with the spacer.

- It should be investigate whether this decreased efficacy concerns a quality issue or another problem like a difficulty in the use in combination with the spacer.

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This signal has been raised on September 2015. It is possible that in the meantime other information became available. For the latest information, including the official SmPC's, please refer to website of the MEB www.cbg-meb.nl