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Asthma rescue treatments, time to reboot

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Short-acting β_2-agonists (SABAs) are inseparable from asthma. The word "Ventolin" has not only entered common language, but it profoundly symbolises relief from breathing distress, quite similar to how "nitroglycerin" supposedly rescues the heart. After the Second World War, synthetic corticosteroids revolutionised asthma management and gained nobility once an inhaled formulation was available [1]. Intriguingly, despite the fact that chronic airway inflammation is inherent to the definition of asthma, as needed SABA was kept in guidelines as the preferred option for the mildest patients, and this until the very recent latest update from the Global Initiative for Asthma (GINA) [2]. Erroneous conclusions were driven from pharmaco-epidemiological studies when it was reported that more than half of asthma patients fell into this "first-step". In hindsight, the latter classification seems overly facile and in denial of any notion of chronicity, not to mention the possibility of addressing a more difficult inflammation management strategy requiring treatment adherence or patient education. Simultaneously, the medical community was faced with a diagnostic paradox given that spirometry improvement (forced expiratory volume in 1 s) during a SABA challenge should indicate the appropriateness of an ICS. The resulting "pro-irresponsible-SABA" environment may help explain why SABA continues to beat all records as the top anti-asthma drug consumed worldwide.

"Blue inhalers" are so generalised [note: in most countries, inhalers are color-coded: inhalers containing SABA are blue and those containing inhaled corticosteroids (ICS) are pink; it is unfortunately not the case worldwide] and available that evidence characterising their use can be overlooked [3]. The death epidemic in New Zealand that was associated with SABA overuse [4, 5] cautioned us and led to issued warnings against regular monotherapy, but did not prevent their overuse by the patients. Drazen *et al.* [6] demonstrated early on that regular SABA use was a deleterious strategy, and now the medical/scientific community concurs that SABA use is a key item for the assessment of asthma control [7] and relatively recent data from about 400 asthma deaths in the UK show that these deaths could be associated with SABA over-prescription [8]. In this issue of the *European Respiratory Journal*, the Swedish part of the SABINA study provides SABA use data that are as reliable as they are worrisome [9]. Using national health registries covering more than 350 000 patients, the authors show that SABA overuse was reported in an astounding one third, and this is not a surprise, and may not be the worst rate on earth. Nevertheless, this overuse was associated with an increased risk of death. These data come at a time where SABA alone has become available over the counter in Switzerland! The GINA committee perspicaciously anticipated

these data and down-ranked SABA whenever it was possible [2]. Although not all payers have approved an as-needed ICS–LABA strategy, the latter is likely just a question of time. Giving appropriate consideration to the weight of such a measure, given the history and place of "blue inhalers," is crucial to the domain. Considering the benefits associated with ICS, as well as their low cost of production, the addition of ICS to any anti-asthma inhaler (*i.e.* combined with a SABA or LABA) is feasible and affordable. A worldwide agreement among asthma stakeholders to defend this new axis would quite likely find success.

Coming back to this new opus, eloquently presented by Nwaru *et al.* [9], in the quest of getting rid of SABA, we can hear echoes of the challenges that oral corticosteroid (OCS) stewardship initially faced [10]. The latter required generating evidence to recall and prove the existence of detrimental OCS side-effects that were already notorious and soundly proven. A strangely similar situation seems to be emerging for SABINA. We can now say that SABAs should be viewed as a very special rescue medication that has its own set of consequences. It is highly likely that restricting their use to emergency room/intensive care unit/ward situations would be achievable quickly, without leaving any figurative orphans along the roadside. However, the immediate consequence of the Swedish SABINA study should be the largest involvement of patients, pharmacists and primary care providers for better awareness and patient education on safe treatment options and the identification of patients that should be referred.

Finally, the biologic era brings the opportunity to fully reboot how we manage asthma. Our aim should be to somehow reverse the unfortunate ranking of anti-asthma drug consumption, currently and historically dominated by two rescuers, SABAs and OCS. 40 years of communication about the necessity of quantifying and monitoring levels of asthma control, as opposed to relying heavily on rescue treatments, has rather pitifully reached a plateau. In a world where complexity must fit on a tweet, the latter message just isn't limpid enough. It stands that OCS–SABA use are excellent surrogate markers of poor asthma control since they are clearly associated with poor outcomes, including death. Their prescription can easily be monitored and can generate automatic warnings for education and eventually referral when reaching upper thresholds. Smart inhaler devices might also be particularly useful in this context. However, markers of poor asthma control are elements that we should hope *to minimise*.

At a glance, SABA, and OCS, rescuers are still the most-used anti-asthma drugs, whereas it is now clearly established that they shouldn't be. The Swedish SABINA study, as a key proof of SABA misuse, raises a new warning for safety and reinforces the need for change in real-life rescue asthma management. Evidence generated from OCS use should emphasise the real need for change in the organisation of SABA phase-outs. There is a clear need for a global paradigm change beyond the realm of traditional asthma stakeholders and towards true SABA stewardship.

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