

Bölüm 14

İNHALER TEDAVİ

Hasan ÖLMEZ¹, Mustafa TOSUN² Edhem ÜNVER³

Giriş

Astım ve Kronik obstrüktif akciğer Hastalığı(KOAH) kronik inflamatuvar hastalıklardır. 2016 yılı itibarı ile dünya genelinde 339 milyon kişinin bu hastalıklardan etkilendiği düşünülmektedir. Her iki hastalıkta da hava akımı kısıtlanması mevcuttur ve tedavinin temelini inhaler tedavi oluşturur (Naghavi ark., 2017). Inhaler teknolojisindeki son gelişmeler ile cihaz sayısında bir patlama olmuştur (Brand, 2005). Ancak hiç bir cihaz «mükemmel cihaz» değildir ve birçok çalışmada astım ve KOAH hastalarının inhaler cihaz kullanım hatalarının yüksek olduğu gösterilmiştir (Lavorini & Usmani, 2013). Inhaler cihazların hatalı kullanımı astım ve KOAH hastalarında tedavi uyumsuzluğuna (Astım ve KOAH hastalarında tedaviye uyum sadece % 50 civarındadır) semptom skorların artışına, daha fazla akut atak ve acil başvurusuna, daha fazla hastaneye yatışa, hastalığın kötüleşmesine, iş gücü kaybına ve artan maliyetlere sebep olur. Inhaler cihaz seçimi ve inhaler cihaz eğitimi bu sebeple dolayı hayati önem taşımaktadır (Darbà ark., 2016; Lavorini ark., 2008; Levy, Hardwell, McKnight, & Holmes, 2013; Molimard ark., 2017; van Boven ark., 2014). Bu derlemede en sık yapılan inhaler kullanım hataları, bu hataların nedenleri, doğru inhaler cihaz seçimi ilgili yapılan çalışmaların gözden geçirilmesi amaçlanmıştır.

Inhaler tedavi uzun ve kısa $\beta 2$ agonistler, inhaler kortikosteroidler ve kısa ve uzun etkili antimuskarinik ilaçları içerir. Nebülizatör, ölçülü doz inhaler, kuru toz inhaler ve yavaş akım inhaler cihazlarla etken maddenin hızlı ve direk olarak patolojik bölgeye gönderimi sağlanır. Bu kadar değişik cihaz olmasına rağmen inhaler cihaz kullanım başarısı ve tedavi uyumu düşüktür (Dudvarski Ilic ark., 2016; GINA.,2015; GOLD., 2017)Günlük solunum uygulamalarında aerosol haline getirilmiş ilacı uygulamak için kullanılan en yaygın cihazlar ölçülü doz inhaler (ÖDİ) ve kuru toz inhaler (KTİ) cihazlardır. ÖDİ cihazlar en sık reçete edilen inhaler cihazlardır (Pritchard, 2015). Solunum hastalıklarını doğru tedavi etmek için inhaler cihazların doğru kullanımıyla ilacın akciğerlere etkili bir şekilde ulaştırılmasını sağlamak gerekir. İlacın

¹ Dr. Öğr. Üyesi, Erzincan Binali Yıldırım Üniversitesi, Tıp Fakültesi. Göğüs Hastalıkları Anabilim Dalı / Erzincan Binali Yıldırım University Faculty of Medicine, Department of Chest Diseases E-posta / E-mail:drhasan2024@gmail.com

² Dr. Öğr. Üyesi, Erzincan Binali Yıldırım Üniversitesi, Tıp Fakültesi. Göğüs Hastalıkları Anabilim Dalı / Erzincan Binali Yıldırım University Faculty of Medicine, Department of Chest Diseases E-posta / E-mail:drmustafatosun@hotmail.com

³ Dr. Öğr. Üyesi, Erzincan Binali Yıldırım Üniversitesi, Tıp Fakültesi. Göğüs Hastalıkları Anabilim Dalı / Erzincan Binali Yıldırım University Faculty of Medicine, Department of Chest Diseases E-posta / E-mail:ethemunver@hotmail.com

Sonuç

İnhaler ilaçların astım ve KOAH gibi kronik solunum yolu hastalıklarının tedavisinde hayati önemi olduğu, gelişen teknoloji ile birlikte inhaler cihaz sayısında patlama olduğu, ancak yine de inhaler cihaz kullanım başarısının ve inhaler cihaz hasta uyumunun çok düşük olduğu görülmüştür. Bunun nedeni inhaler cihaz seçiminde inhaler cihazın teknik özelliklerini dikkate almamak olabilir. İnhaler cihaz seçerken hastaların yaşının, eğitim durumunun, kognitif fonksiyonlarının, hastalığın ağırlığının, inspiratuar kapasitesinin dikkate alınmaması da etken olabilir. Hastaya inhaler cihaz eğitimi için yeteri kadar zaman ayırmak gerekir. İnhaler cihaz eğitim yeri veya metodu doğru olmalıdır. İnhaler cihaz eğitimi veren sağlık çalışanı inhaler cihaz kullanımını doğru anlatmalıdır. Hastalara çok fazla sayıda ve değişik tasarım yapısına sahip inhaler cihazları öğretmeye çalışılmamalıdır. Hastanın inhaler cihazı sevmesi, benimsemesi ve etkili olacağına inanması gerekir. Hastaların inhaler cihazın bağımlılık yaptığına, çok sayıda yan etki görüleceğine dair endişeleri ortadan kaldırılmalıdır. Özellikle adölesan dönemdeki hastalar ilaç almaktan utanıyor ve kasıtlı ilacını kullanmıyor olabilir. Bu hastalara doğru inhaler cihaz kullanımı ve tedavi uyumunun önemini anlatmak için daha fazla çaba harcanmalıdır. Hastalara ilacı ne zaman kullanması gerektiği tam olarak anlatılmalıdır. Özellikle yaşlı ve çocuk hastalar doğru inhaler cihaz kullanımını unutmış olabilir. Bu hastalara fırsat bulunca inhaler cihaz eğitimi tekrarlanmalıdır. Çünkü hatalı inhaler cihaz kullanımı etken maddenin akciğerlere ulaşmasına engel olur, hastanın şikayetleri inhaler cihaz kullanmasına rağmen geçmez. Bu nedenle hasta ilacın faydalı olmadığını düşünerek ilacını keser. Hastaların acil başvurusu, hastane yatışı artar, hastalığın kötüleşmesine ve artan maliyetlere sebep olur. Tüm bu nedenlerden dolayı hastalara inhaler cihaz reçete ederken inhaler cihazların özelliklerini, avantaj ve dezavantajlarını bilmemiz, hastaya ait faktörleri göz önünde bulundurmamız, inhaler cihaz eğitimi önemsememiz ve zaman ayırmamız gerekir.

Kaynakça

- Al-Showair, R. A. M., Pearson, S. B., & Chrystyn, H. (2007). The potential of a 2Tone Trainer to help patients use their metered-dose inhalers. *Chest*, 131(6), 1776–1782. <https://doi.org/10.1378/chest.06-2765>
- Allen, S. C., Jain, M., Ragab, S., & Malik, N. (2003). Acquisition and short-term retention of inhaler techniques require intact executive function in elderly subjects. *Age and Ageing*, 32(3), 299–302. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/12720616>
- Armitage, J. M., & Williams, S. J. (1988). Inhaler technique in the elderly. *Age and Ageing*, 17(4), 275–278. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/3177088>
- Armour, C. L., Reddel, H. K., LeMay, K. S., Saini, B., Smith, L. D., Bosnic-Anticevich, S. Z., ... Krass, I. (2013). Feasibility and effectiveness of an evidence-based asthma service in Australian community pharmacies: a pragmatic cluster randomized trial. *The Journal of Asthma : Official Journal of the Association for the Care of Asthma*, 50(3), 302–309. <https://doi.org/10.3109/02770903.2012.754463>
- Basheti, I. A., Armour, C. L., Bosnic-Anticevich, S. Z., & Reddel, H. K. (2008). Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique. *Patient Education and Counseling*, 72(1), 26–33. <https://doi.org/10.1016/j.pec.2008.01.014>
- Basheti, I. A., Reddel, H. K., Armour, C. L., & Bosnic-Anticevich, S. Z. (2007). Improved asthma outcomes with a simple inhaler technique intervention by community pharmacists. *Journal of Allergy and Clinical Immunology*, 119(6), 1537–1538. <https://doi.org/10.1016/j.jaci.2007.02.037>

- Batterink, J., Dahri, K., Aulakh, A., & Rempel, C. (2012). Evaluation of the use of inhaled medications by hospital inpatients with chronic obstructive pulmonary disease. *The Canadian Journal of Hospital Pharmacy*, 65(2), 111–118. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22529403>
- Boise, E., & Rotella, M. (2015). ABCs of asthma inhaler and device training. *International Forum of Allergy & Rhinology*, 5 Suppl 1, S71–5. <https://doi.org/10.1002/alf.21605>
- Bonini, M., & Usmani, O. S. (2015). The importance of inhaler devices in the treatment of COPD. *COPD Research and Practice*, 1(1), 9. <https://doi.org/10.1186/s40749-015-0011-0>
- Bosnic-Anticevich, S. Z. (2018). Continued Innovation in Respiratory Care: The Importance of Inhaler Devices. *Tuberculosis and Respiratory Diseases*, 81(2), 91–98. <https://doi.org/10.4046/trd.2017.0119>
- Bosnic-Anticevich, S. Z., Sinha, H., So, S., & Reddel, H. K. (2010). Metered-dose inhaler technique: the effect of two educational interventions delivered in community pharmacy over time. *The Journal of Asthma : Official Journal of the Association for the Care of Asthma*, 47(3), 251–256. <https://doi.org/10.3109/02770900903580843>
- Brand, P. L. P. (2005). Key issues in inhalation therapy in children. *Current Medical Research and Opinion*, 21 Suppl 4(sup4), S27–32. <https://doi.org/10.1185/030079905X61767>
- Cain, W. T., Cable, G., & Oppenheimer, J. J. (2001). The ability of the community pharmacist to learn the proper actuation techniques of inhaler devices. *The Journal of Allergy and Clinical Immunology*, 108(6), 918–920. <https://doi.org/10.1067/mai.2001.119153>
- Camilleri, K., Balzan, M., Bardon, M., ... E. S.-E. R., & 2015, undefined. (n.d.). Predictors of good inhaler technique in asthma and COPD. *Researchgate.Net*. Retrieved from https://www.researchgate.net/profile/Martin_Balzan/publication/283740093_Predictors_of_good_inhaler_technique_in_asthma_and_COPD/links/5676fda308ae125516ec0531.pdf
- Capanoglu, M., Dibeke Misirlioglu, E., Toyran, M., Civelek, E., & Kocabas, C. N. (2015). Evaluation of inhaler technique, adherence to therapy and their effect on disease control among children with asthma using metered dose or dry powder inhalers. *The Journal of Asthma : Official Journal of the Association for the Care of Asthma*, 52(8), 838–845. <https://doi.org/10.3109/02770903.2015.1028075>
- Capstick, T. G. D., & Clifton, I. J. (2012). Inhaler technique and training in people with chronic obstructive pulmonary disease and asthma. *Expert Review of Respiratory Medicine*, 6(1), 91–101; quiz 102–3. <https://doi.org/10.1586/ers.11.89>
- Cheng, Y. S. (2014). Mechanisms of pharmaceutical aerosol deposition in the respiratory tract. *AAPS PharmSciTech*, 15(3), 630–640. <https://doi.org/10.1208/s12249-014-0092-0>
- Chrystyn, H., Small, M., Milligan, G., Higgins, V., Gil, E. G., & Estruch, J. (2014). Impact of patients' satisfaction with their inhalers on treatment compliance and health status in COPD. *Respiratory Medicine*, 108(2), 358–365. <https://doi.org/10.1016/j.rmed.2013.09.021>
- Chrystyn, H., van der Palen, J., Sharma, R., Barnes, N., Delafont, B., Mahajan, A., & Thomas, M. (2017). Device errors in asthma and COPD: systematic literature review and meta-analysis. *NPJ Primary Care Respiratory Medicine*, 27(1), 22. <https://doi.org/10.1038/s41533-017-0016-z>
- Ciciliani, A.-M., Langguth, P., & Wachtel, H. (2017). In vitro dose comparison of Respimat® inhaler with dry powder inhalers for COPD maintenance therapy. *International Journal of Chronic Obstructive Pulmonary Disease*, 12, 1565–1577. <https://doi.org/10.2147/COPD.S115886>
- Dalby, R. N., Eicher, J., & Zierenberg, B. (2011). Development of Respimat® Soft Mist™ Inhaler and its clinical utility in respiratory disorders. *Medical Devices (Auckland, N.Z.)*, 4, 145–155. <https://doi.org/10.2147/MDER.S7409>
- Dalcin, P. de T. R., Grutcki, D. M., Laporte, P. P., Lima, P. B. de, Menegotto, S. M., & Pereira, R. P. (n.d.). Factors related to the incorrect use of inhalers by asthma patients. *Jornal Brasileiro de Pneumologia : Publicacao Oficial Da Sociedade Brasileira de Pneumologia e Tisiologia*, 40(1), 13–20. <https://doi.org/10.1590/S1806-37132014000100003>
- Darbà, J., Ramírez, G., Sicras, A., García-Bujalance, L., Torvinen, S., & Sánchez-de la Rosa, R. (2016). Identification of factors involved in medication compliance: incorrect inhaler technique of asthma treatment leads to poor compliance. *Patient Preference and Adherence*, 10, 135–145. <https://doi.org/10.2147/PPA.S95303>
- De Blaquiére, P., Christensen, D. B., Carter, W. B., & Martin, T. R. (1989). Use and misuse of metered-dose inhalers by patients with chronic lung disease. A controlled, randomized trial of two instruction methods. *The American Review of Respiratory Disease*, 140(4), 910–916. <https://doi.org/10.1164/ajrccm/140.4.910>
- De Simoni, A., Horne, R., Fleming, L., Bush, A., & Griffiths, C. (2017). What do adolescents with asthma really think about adherence to inhalers? Insights from a qualitative analysis of a UK online forum. *BMJ Open*, 7(6), e015245. <https://doi.org/10.1136/bmjopen-2016-015245>

- Deerojanawong, J., Promsaka na Sakolnakorn, V., Prapphal, N., Hanrutakorn, C., & Sritippayawan, S. (n.d.). Evaluation of metered-dose inhaler administration technique among asthmatic children and their caregivers in Thailand. *Asian Pacific Journal of Allergy and Immunology*, 27(2-3), 87-93. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/19839493>
- Dekhuijzen, P. N. R., Lavorini, F., & Usmani, O. S. (2016). Patients' perspectives and preferences in the choice of inhalers: the case for Respimat® or HandiHaler®. *Patient Preference and Adherence*, 10, 1561-1572. <https://doi.org/10.2147/PPA.S82857>
- Dekhuijzen, P. N. R., Vincken, W., Virchow, J. C., Roche, N., Agusti, A., Lavorini, F., ... Price, D. (2013). Prescription of inhalers in asthma and COPD: towards a rational, rapid and effective approach. *Respiratory Medicine*, 107(12), 1817-1821. <https://doi.org/10.1016/j.rmed.2013.09.013>
- Dolovich, M. (1993). Lung Dose, Distribution, and Clinical Response to Therapeutic Aerosols. *Aerosol Science and Technology*, 18(3), 230-240. <https://doi.org/10.1080/02786829308959600>
- Dolovich, M., Ruffin, R. E., Roberts, R., & Newhouse, M. T. (1981). Optimal delivery of aerosols from metered dose inhalers. *Chest*, 80(6 Suppl), 911-915. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7307637>
- Donnell, D. (2001). Optimizing drug delivery to the lung: design of a CFC-free corticosteroid metered-dose aerosol system. *Drug Development and Industrial Pharmacy*, 27(2), 111-118. <https://doi.org/10.1081/DDC-100000477>
- Dudvarski Ilic, A., Zugic, V., Zvezdin, B., Kopitovic, I., Cekerevac, I., Cupurdija, V., ... Barac, A. (2016). Influence of inhaler technique on asthma and COPD control: a multicenter experience. *International Journal of Chronic Obstructive Pulmonary Disease*, 11, 2509-2517. <https://doi.org/10.2147/COPD.S114576>
- European Respiratory Society, M., Mitsui, K., Ido, M., Koyama, M., Matsumoto, M., Inoue, D., ... Fukui, M. (2011). *European respiratory journal*. *European Respiratory Journal* (Vol. 38). ERS Journals. Retrieved from http://erj.ersjournals.com/content/38/Suppl_55/p2845.short
- Fink, J. B., & Rubin, B. K. (2005). Problems with inhaler use: a call for improved clinician and patient education. *Respiratory Care*, 50(10), 1360-74; discussion 1374-5. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16185371>
- GBD 2016 Causes of Death Collaborators, M., Abajobir, A. A., Abbafati, C., Abbas, K. M., Abd-Allah, F., Abera, S. F., ... Murray, C. J. L. (2017). Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet (London, England)*, 390(10100), 1151-1210. [https://doi.org/10.1016/S0140-6736\(17\)32152-9](https://doi.org/10.1016/S0140-6736(17)32152-9)
- Giraud, V., Allaert, F.-A., & Roche, N. (2011). Inhaler technique and asthma: Feasibility and acceptability of training by pharmacists. *Respiratory Medicine*, 105(12), 1815-1822. <https://doi.org/10.1016/j.rmed.2011.07.004>
- Giraud, V., & Roche, N. (2002). Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *The European Respiratory Journal*, 19(2), 246-251. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11866004>
- Global Initiative for Asthma [GINA]. Global strategy for asthma management and prevention [Update2015]. Available from: http://www.ginasthma.org/local/uploads/files/GINA_Report_2015.pdf. (n.d.).
- Global Initiative for Chronic Obstructive Lung Disease, Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, Vol. 2017, Global Initiative for Chronic Obstructive Lung Disease, New York, NY, USA, 2017. (n.d.).
- Göriş, S., Taşci, S., & Elmali, F. (2013). The Effects of Training on Inhaler Technique and Quality Of Life in Patients with COPD. *Journal of Aerosol Medicine and Pulmonary Drug Delivery*, 26(6), 336-344. <https://doi.org/10.1089/jamp.2012.1017>
- Gray, S. L., Williams, D. M., Pulliam, C. C., Sirgo, M. A., Bishop, A. L., & Donohue, J. F. (1996). Characteristics predicting incorrect metered-dose inhaler technique in older subjects. *Archives of Internal Medicine*, 156(9), 984-988. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8624178>
- Hanania, N. A., Wittman, R., Kesten, S., & Chapman, K. R. (1994). Medical personnel's knowledge of and ability to use inhaling devices. Metered-dose inhalers, spacing chambers, and breath-actuated dry powder inhalers. *Chest*, 105(1), 111-116. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8275720>
- Hesselink, A. E., Penninx, B. W. J. H., van der Windt, D. A. W. M., van Duin, B. J., de Vries, P., Twisk, J. W. R., ... van Eijk, J. T. M. (2004). Effectiveness of an education programme by a general practice assistant for asthma and COPD patients: results from a randomised controlled trial. *Patient Education and Counseling*, 55(1), 121-128. <https://doi.org/10.1016/j.pec.2003.08.007>

- Hillyer, E. V, Price, D. B., Chrystyn, H., Martin, R. J., Israel, E., van Aalderen, W. M. C., ... Roche, N. (2018). Harmonizing the Nomenclature for Therapeutic Aerosol Particle Size: A Proposal. *Journal of Aerosol Medicine and Pulmonary Drug Delivery*, 31(2), 111–113. <https://doi.org/10.1089/jamp.2017.1396>
- Inhaler Error Steering Committee, Price, D., Bosnic-Anticevich, S., Briggs, A., Chrystyn, H., Rand, C., ... Bousquet, J. (2013). Inhaler competence in asthma: common errors, barriers to use and recommended solutions. *Respiratory Medicine*, 107(1), 37–46. <https://doi.org/10.1016/j.rmed.2012.09.017>
- Jackevicius, C. A., & Chapman, K. R. (1999). Inhaler education for hospital-based pharmacists: how much is required? *Canadian Respiratory Journal*, 6(3), 237–244. <https://doi.org/10.1155/1999/695365>
- Jarvis, S., Ind, P. W., & Shiner, R. J. (2007). Inhaled therapy in elderly COPD patients; time for re-evaluation? *Age and Ageing*, 36(2), 213–218. <https://doi.org/10.1093/ageing/af174>
- Jones, J. S., Holstege, C. P., Riekse, R., White, L., & Bergquist, T. (1995). Metered-dose inhalers: do emergency health care providers know what to teach? *Annals of Emergency Medicine*, 26(3), 308–311. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7661420>
- Kaplan, A., & Price, D. (2018). Matching Inhaler Devices with Patients: The Role of the Primary Care Physician. *Canadian Respiratory Journal*, 2018, 9473051. <https://doi.org/10.1155/2018/9473051>
- Kelling, J. S., Strohl, K. P., Smith, R. L., & Altose, M. D. (1983). Physician knowledge in the use of canister nebulizers. *Chest*, 83(4), 612–614. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/6831948>
- Khassawneh, B. Y., Al-Ali, M. K., Alzoubi, K. H., Batarseh, M. Z., Al-Safi, S. A., Sharara, A. M., & Alnasr, H. M. (2008). Handling of inhaler devices in actual pulmonary practice: metered-dose inhaler versus dry powder inhalers. *Respiratory Care*, 53(3), 324–328. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/18291048>
- Klijn, S. L., Hiligsmann, M., Evers, S. M. A. A., Román-Rodríguez, M., van der Molen, T., & van Boven, J. F. M. (2017). Effectiveness and success factors of educational inhaler technique interventions in asthma & COPD patients: a systematic review. *NPJ Primary Care Respiratory Medicine*, 27(1), 24. <https://doi.org/10.1038/s41533-017-0022-1>
- Labiris, N. R., & Dolovich, M. B. (2003a). Pulmonary drug delivery. Part I: physiological factors affecting therapeutic effectiveness of aerosolized medications. *British Journal of Clinical Pharmacology*, 56(6), 588–599. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/14616418>
- Labiris, N. R., & Dolovich, M. B. (2003b). Pulmonary drug delivery. Part II: the role of inhalant delivery devices and drug formulations in therapeutic effectiveness of aerosolized medications. *British Journal of Clinical Pharmacology*, 56(6), 600–612. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/14616419>
- Lavorini, F., & Fontana, G. A. (2009). Targeting drugs to the airways: The role of spacer devices. *Expert Opinion on Drug Delivery*, 6(1), 91–102. <https://doi.org/10.1517/17425240802637862>
- Lavorini, F., Magnan, A., Dubus, J. C., Voshhaar, T., Corbetta, L., Broeders, M., ... Crompton, G. K. (2008). Effect of incorrect use of dry powder inhalers on management of patients with asthma and COPD. *Respiratory Medicine*, 102(4), 593–604. <https://doi.org/10.1016/j.rmed.2007.11.003>
- Lavorini, F., & Usmani, O. S. (2013). Correct inhalation technique is critical in achieving good asthma control. *Primary Care Respiratory Journal : Journal of the General Practice Airways Group*, 22(4), 385–386. <https://doi.org/10.4104/pcrj.2013.00097>
- Lawford, P., & McKenzie, D. (1983). Pressurized aerosol inhaler technique: how important are inhalation from residual volume, inspiratory flow rate and the time interval between puffs? *British Journal of Diseases of the Chest*, 77(3), 276–281. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/6615704>
- Leach, C. L., Davidson, P. J., & Boudreau, R. J. (1998). Improved airway targeting with the CFC-free HFA-beclomethasone metered-dose inhaler compared with CFC-beclomethasone. *The European Respiratory Journal*, 12(6), 1346–1353. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/9877489>
- Levy, M. L., Dekhuijzen, P. N. R., Barnes, P. J., Broeders, M., Corrigan, C. J., Chawes, B. L., ... Pedersen, S. (2016). Inhaler technique: facts and fantasies. A view from the Aerosol Drug Management Improvement Team (ADMiT). *NPJ Primary Care Respiratory Medicine*, 26, 16017. <https://doi.org/10.1038/npjpcrm.2016.17>
- Levy, M. L., Hardwell, A., McKnight, E., & Holmes, J. (2013). Asthma patients' inability to use a pressurised metered-dose inhaler (pMDI) correctly correlates with poor asthma control as defined by the global initiative for asthma (GINA) strategy: a retrospective analysis. *Primary Care Respiratory Journal : Journal of the General Practice Airways Group*, 22(4), 406–411. <https://doi.org/10.4104/pcrj.2013.00084>
- Lewis, A., Blackney, M., Torvinen, S., Holmes, J., Osborne, M., Dale, J., ... Plich, A. (2014). The Budget Impact of Duoresp® Spiromax® (Budesonide + Formoterol Fumarate Dihydrate) Compared With Symbicort® Turbohaler® for the Management of Asthma and Chronic Obstructive Pulmonary Disease in the

United Kingdom: Impact on Health Care Costs and Inhalation Technique. *Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, 17(7), A591. <https://doi.org/10.1016/j.jval.2014.08.2027>

Lewis, A., Blackney, M., Torvinen, S., Lindqvist, F., Safioti, G., Grundström, J., ... Plich, A. (2014). The Potential Societal Cost Benefits of Improved Inhalation Technique With Duoresp® Spiromax® (Budesonide + Formoterol Fumarate Dihydrate) Compared With Symbicort® Turbuhaler® for the Management of Asthma and Chronic Obstructive Pulmonary Disease in Sweden. *Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, 17(7), A598-9. <https://doi.org/10.1016/j.jval.2014.08.2070>

Lewis, A., Torvinen, S., Dekhuijzen, P. N. R., Chrystyn, H., Watson, A. T., Blackney, M., & Plich, A. (2016). The economic burden of asthma and chronic obstructive pulmonary disease and the impact of poor inhalation technique with commonly prescribed dry powder inhalers in three European countries. *BMC Health Services Research*, 16(1), 251. <https://doi.org/10.1186/s12913-016-1482-7>

Melani, A. S., Bonavia, M., Cilenti, V., Cinti, C., Lodi, M., Martucci, P., ... Gruppo Educazionale Associazioni Italiana Pneumologi Ospedalieri. (2011). Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respiratory Medicine*, 105(6), 930-938. <https://doi.org/10.1016/j.rmed.2011.01.005>

Menckeberg, T. T., Bouvy, M. L., Bracke, M., Kaptein, A. A., Leufkens, H. G., Raaijmakers, J. A. M., & Horne, R. (2008). Beliefs about medicines predict refill adherence to inhaled corticosteroids. *Journal of Psychosomatic Research*, 64(1), 47-54. <https://doi.org/10.1016/j.jpsychores.2007.07.016>

Molimard, M., Raherison, C., Lignot, S., Balestra, A., Lamarque, S., Chartier, A., ... Girodet, P.-O. (2017). Chronic obstructive pulmonary disease exacerbation and inhaler device handling: real-life assessment of 2935 patients. *The European Respiratory Journal*, 49(2), 1601794. <https://doi.org/10.1183/13993003.01794-2016>

National Asthma Council Australia. *Information paper for health professionals. Inhaler technique in adults with asthma or COPD. 2008.* <http://www.nationalasthma.org.au/uploads/publication/inhaler-technique-in-adults-with-asthma-or-copd.pdf>. Accessed July 1. (n.d.).

Newman, S. P. (2000). Can lung deposition data act as a surrogate for the clinical response to inhaled asthma drugs? *British Journal of Clinical Pharmacology*, 49(6), 529-537. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10848716>

Newman, S. P., Pavia, D., & Clarke, S. W. (1981). How should a pressurized beta-adrenergic bronchodilator be inhaled? *European Journal of Respiratory Diseases*, 62(1), 3-21. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/6112156>

Newman, S. P., Wilding, I. R., & Hirst, P. H. (2000). Human lung deposition data: the bridge between in vitro and clinical evaluations for inhaled drug products? *International Journal of Pharmaceutics*, 208(1-2), 49-60. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11064211>

Pothirat, C., Chaiwong, W., Phetsuk, N., Pisalathanapuna, S., Chetsadaphan, N., & Choomuang, W. (2015). Evaluating inhaler use technique in COPD patients. *International Journal of Chronic Obstructive Pulmonary Disease*, 10, 1291. <https://doi.org/10.2147/COPD.S85681>

Press, V. G., Arora, V. M., Shah, L. M., Lewis, S. L., Charbeneau, J., Naureckas, E. T., & Krishnan, J. A. (2012). Teaching the Use of Respiratory Inhalers to Hospitalized Patients with Asthma or COPD: a Randomized Trial. *Journal of General Internal Medicine*, 27(10), 1317-1325. <https://doi.org/10.1007/s11606-012-2090-9>

Price, D. B., Román-Rodríguez, M., McQueen, R. B., Bosnic-Anticevich, S., Carter, V., Gruffydd-Jones, K., ... Chrystyn, H. (2017). Inhaler Errors in the CRITIKAL Study: Type, Frequency, and Association with Asthma Outcomes. *The Journal of Allergy and Clinical Immunology. In Practice*, 5(4), 1071-1081.e9. <https://doi.org/10.1016/j.jaip.2017.01.004>

Price, D., Chrystyn, H., Kaplan, A., Haughney, J., Román-Rodríguez, M., Burden, A., ... van der Molen, T. (2012). Effectiveness of same versus mixed asthma inhaler devices: a retrospective observational study in primary care. *Allergy, Asthma & Immunology Research*, 4(4), 184-191. <https://doi.org/10.4168/aaair.2012.4.4.184>

Price, D., David-Wang, A., Cho, S.-H., Ho, J. C.-M., Jeong, J.-W., Liam, C.-K., ... Neira, G. (2015). Time for a new language for asthma control: results from REALISE Asia. *Journal of Asthma and Allergy*, 8, 93-103. <https://doi.org/10.2147/JAA.S82633>

Pritchard, J. N. (2015). Industry guidance for the selection of a delivery system for the development of novel respiratory products. *Expert Opinion on Drug Delivery*, 12(11), 1755-1765. <https://doi.org/10.1517/17425247.2015.1056148>

- Rootmensen, G. N., van Keimpema, A. R. J., Jansen, H. M., & de Haan, R. J. (2010). Predictors of incorrect inhalation technique in patients with asthma or COPD: a study using a validated videotaped scoring method. *Journal of Aerosol Medicine and Pulmonary Drug Delivery*, 23(5), 323–328. <https://doi.org/10.1089/jamp.2009.0785>
- Sadowski, C., Banh, H., ... K. C.-J. of the A., & 2013, undefined. (n.d.). inhaler Device Technique in Community-dwelling Older Adults.: b26. *Insights.Ovid.Com*. Retrieved from <https://insights.ovid.com/americian-geriatrics-society/jamger/2013/04/001/comprehensive-geriatric-assessment-cga-community/236/00004495>
- Sanchis, J., Gich, I., Pedersen, S., & Aerosol Drug Management Improvement Team (ADMIT). (2016). Systematic Review of Errors in Inhaler Use: Has Patient Technique Improved Over Time? *Chest*, 150(2), 394–406. <https://doi.org/10.1016/j.chest.2016.03.041>
- Sulaiman I, Seheult J, Sadasivuni N, Cushen B, Mokoka M, Costello R. ark. Inhaler technique errors have an impact on drug delivery. *Am J Respir Crit Care Med*. 2016;193:A-1715. (n.d.).
- Tashkin, D. P. (2016). A review of nebulized drug delivery in COPD. *International Journal of Chronic Obstructive Pulmonary Disease*, 11, 2585–2596. <https://doi.org/10.2147/COPD.S114034>
- Usmani, O. S. (2015). Small-airway disease in asthma: pharmacological considerations. *Current Opinion in Pulmonary Medicine*, 21(1), 55–67. <https://doi.org/10.1097/MCP.0000000000000115>
- Usmani, O. S., Lavorini, F., Marshall, J., Dunlop, W. C. N., Heron, L., Farrington, E., & Dekhuijzen, R. (2018). Critical inhaler errors in asthma and COPD: a systematic review of impact on health outcomes. *Respiratory Research*, 19(1), 10. <https://doi.org/10.1186/s12931-017-0710-y>
- van Aalderen, W. M., Garcia-Marcos, L., Gappa, M., Lenney, W., Pedersen, S., Dekhuijzen, R., & Price, D. (2015). How to match the optimal currently available inhaler device to an individual child with asthma or recurrent wheeze. *Npj Primary Care Respiratory Medicine*, 25(1), 14088. <https://doi.org/10.1038/npjpcrm.2014.88>
- van Boven, J. F. M., Chavannes, N. H., van der Molen, T., Rutten-van Mölken, M. P. M. H., Postma, M. J., & Vegter, S. (2014). Clinical and economic impact of non-adherence in COPD: A systematic review. *Respiratory Medicine*, 108(1), 103–113. <https://doi.org/10.1016/j.rmed.2013.08.044>
- van der Palen, J. (2003). Peak inspiratory flow through diskus and turbuhaler, measured by means of a peak inspiratory flow meter (In-Check DIAL). *Respiratory Medicine*, 97(3), 285–289. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/12645837>
- van der Palen, J., Klein, J. J., Kerkhoff, A. H., van Herwaarden, C. L., Zielhuis, G. A., & Seydel, E. R. (1999). Inhalation technique of 166 adult asthmatics prior to and following a self-management program. *The Journal of Asthma : Official Journal of the Association for the Care of Asthma*, 36(5), 441–447. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10461933>
- Westerik, J. A. M., Carter, V., Chrystyn, H., Burden, A., Thompson, S. L., Ryan, D., ... Price, D. B. (2016). Characteristics of patients making serious inhaler errors with a dry powder inhaler and association with asthma-related events in a primary care setting. *The Journal of Asthma : Official Journal of the Association for the Care of Asthma*, 53(3), 321–329. <https://doi.org/10.3109/02770903.2015.1099160>
- Yu, A. P., Guérin, A., Ponce de Leon, D., Ramakrishnan, K., Wu, E. Q., Mocarski, M., ... Setyawan, J. (2011). Therapy persistence and adherence in patients with chronic obstructive pulmonary disease: multiple versus single long-acting maintenance inhalers. *Journal of Medical Economics*, 14(4), 486–496. <https://doi.org/10.3111/13696998.2011.594123>