CORRESPONDENCE

Nitroprusside and Isoproterenol Use after Major Price Increases

TO THE EDITOR: A number of important pharmaceuticals have undergone dramatic price increases recently. For example, nitroprusside prices have increased by a factor of 30 (wholesale acquisition cost [WAC, the manufacturer's published catalogue or list price to wholesalers, which may not represent the actual transactional price] per 50 mg, $27.46 in 2012 and $880.88 in 2015), and isoproterenol prices have increased by a factor of almost 70 (WAC per milligram, $26.20 in 2012 and $1,790.11 in 2015).[1,2] It has been claimed in public testimony that these dramatic price increases would not decrease utilization of or patients' access to these two drugs.[3] There is no intrinsic demand from patients or direct-to-consumer advertising for nitroprusside or isoproterenol, so we can examine the effect of these huge price increases on physician prescribing behavior for the drugs, which are used for the treatment of life-threatening cardiovascular conditions.

We identified 47 hospitals in the Vizient (formerly University HealthSystem Consortium) database that had complete data for 2012 through 2015 on the utilization of nitroprusside and isoproterenol, as well as data on two intravenous cardiovascular drugs for which pricing was stable during that period: nitroglycerin (WAC per 50 mg, $5.92 in 2012 and $17.57 in 2015) and dobutamine (WAC per gram, $17.78 in 2012 and $16.50 in 2015).[2,4] Nitroglycerin and dobutamine served as comparators for nitroprusside and isoproterenol, respectively. Repeated-measures analysis of variance of the natural logarithmic transformation of the rate of utilization was used for statistical testing.

From 2012 to 2015, the absolute number of patients treated with nitroprusside decreased by 53%, and the number treated with isoproterenol decreased by 35% (Table 1). The number of patients treated with nitroprusside per 1000 inpatients per hospital decreased by 46%; the corresponding decrease for isoproterenol was 40% ($P<0.001$ for both decreases). In contrast, during the same period, the absolute number of patients treated with nitroglycerin increased by 118%, and the number treated with dobutamine increased by 7%. The number of patients treated with nitroglycerin per 1000 inpatients per hospital increased by 89% ($P<0.001$), and the corresponding increase for dobutamine was 4% ($P=0.74$). The difference in the rate of utilization per 1000 inpatients per hospital between nitroprusside and nitroglycerin and between isoproterenol and dobutamine increased with time ($P<0.001$ for both comparisons).

In our study, we identified large decreases in the utilization of nitroprusside and isoproterenol in response to very large price increases, changes that were not seen in the use of similar intravenous cardiovascular drugs with stable prices. Clearly, physicians have decreased their rate of prescribing the drugs even though in the hospital setting both they and patients are typically insulated from the cost increases. Understanding exactly how pharmacists, physicians, and hospitals have decreased utilization of the drugs is an area for future investigation. These findings re-

THIS WEEK'S LETTERS

594 Nitroprusside and Isoproterenol Use after Major Price Increases

595 Novel Treatments for Airway Disease

598 Exercise Type in Dieting Obese Older Adults

600 A Man with Pain and Swelling of the Left Calf and a Purpuric Rash

Table 1. Changes in the Utilization of Nitroprusside and Isoproterenol, as Compared with Nitroglycerin and Dobutamine, in 47 U.S. Hospitals from 2012 to 2015.*

Variable	2012	2013	2014	2015	P Value
No. of inpatients					
Total	1,435,440	1,452,723	1,437,824	1,470,007	—
Per hospital	30,541±12,542	30,909±12,702	30,592±12,685	31,277±12,797	0.06
No. of patients receiving nitroprusside					
Total	17,242	16,761	13,304	8,159	—
Per 1000 inpatients per hospital	9.30±13.41	9.11±12.19	7.71±9.49	4.99±5.13	<0.001
No. of patients receiving nitroglycerin					
Total	21,778	26,465	40,140	47,377	—
Per 1000 inpatients per hospital	16.17±16.53	18.99±14.29	27.70±15.87	30.55±25.76	<0.001
No. of patients receiving isoproterenol					
Total	4,079	4,058	3,335	2,650	—
Per 1000 inpatients per hospital	2.76±2.31	2.66±2.48	2.17±1.90	1.65±1.29	<0.001
No. of patients receiving dobutamine					
Total	11,762	11,848	12,180	12,552	—
Per 1000 inpatients per hospital	8.02±5.14	7.96±5.36	8.24±5.77	8.31±5.65	0.74

* Plus–minus values are means ±SD.

fute the claim that price increases do not reduce patients' access to these medications. Decreasing demand also indicates a correcting market response to increased prices that may be a valuable restraining force to pharmaceutical price increases.

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Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

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Novel Treatments for Airway Disease

TO THE EDITOR: The study by Cahill et al. (May 18 issue)[1] shows reductions in airway hyperresponsiveness, mast-cell counts, and tryptase release after treatment with imatinib, a KIT inhibitor, in 62 patients with severe refractory asthma. Targeting mast cells with KIT inhibitors is indeed an appealing, innovative approach for severe asthma. We have previously investigated another KIT inhibitor, masitinib, in 44 patients with severe glucocorticoid-dependent asthma.[2] At 16 weeks of treatment, a similar reduction in oral glucocorticoids was observed with masitinib and placebo. However, the Asthma Control Questionnaire score showed significantly better control in the masitinib group than in the placebo group. Furthermore, a bronchial epithelial KIT-positive subpopulation exists and is increased in asthma.[3] We thus propose that KIT inhibitors may target