

The Effects of Washing on EpiPen Epinephrine Auto-Injector Device Integrity and Function

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Abstract

Background: Prescribing information for EpiPens state that the carrier tube is not waterproof. No studies have shown the effects of submerging EpiPens in water.

Objective: We aimed to determine the function and integrity of EpiPens after washing in a washing machine.

Methods: For 68 pairs of same-dose, same-lot, post-consumer expired EpiPens (Fifteen 0.3mg and fifty-three 0.15mg), one was washed in its carrier tube in top-loading washing machine, while its pair was kept at usual conditions. Both were then fired into meat. The increase in meat mass and decrease in device mass were measured to estimate the mass of solution fired. Paired t-tests measured if the average difference in mass between washed devices and control devices differed. Generalized estimating equations assessed the effects of device dose (0.3 mg vs. 0.15 mg) and expiration date on the difference in outcomes. An additional 14 washed but unfired devices were dissected to assess for moisture and damage.

Results: Washed devices fired a greater mass of epinephrine solution into meat during firing, versus controls (0.353 vs. 0.257, paired t-test p-values <0.0001). (0.353 vs. 0.257, paired t-test p-values <0.0001). Devices lost more mass during firing, (0.396 vs. 0.263, paired t-test p-values <0.0001). Ten washed devices failed to deploy the needle cover after firing. The effect of washing did not differ by dose or expiration date. Fifteen unfired dissected devices had moisture around the syringe but dry needles.

Conclusion: Washing EpiPens impaired their function. These devices should not be used if accidentally placed through a washing machine cycle.

Keywords: Anaphylaxis; Auto; Injector; Epinephrine; EpiPen; Temperature; Device function

INTRODUCTION

Anaphylaxis is a potentially life-threatening allergic reaction that must be treated promptly with epinephrine to reduce morbidity and prevent serious adverse outcomes [1]. People with life-threatening allergies should carry Epinephrine Auto-Injectors (EAI) routinely to be able to rapidly administer the medication and prevent serious injury and death [2]. EAI are commonly stored in the pockets of clothing and are sometimes left behind after that clothing is removed. They can then accidentally be placed in the washing machine and washed along with clothing. To date, no studies have been conducted on the effects of immersing EAI in water, or the functionality of the device afterwards. We aimed to determine the effects of a washing cycle on the function and integrity of EpiPen devices.

METHODS

We hypothesized that washed EpiPen devices would fire 5% less epinephrine on average than their paired controls. This was assessed by firing the washed devices and paired control devices into meat and comparing the difference in epinephrine solution ejected between the two groups, as measured by changes in meat mass and device mass.

Consumers (colleagues, patients and parents of children with allergies) were contacted via social media and asked to donate expired EpiPen devices for this study; 80 pairs of expired and 2 non-expired post-consumer epinephrine auto-injector devices (65 pairs of EpiPen Jrs and 17 pairs of EpiPens) were collected. Devices were paired by dose, lot number, expiration date, and consumer.

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Of these, 53 pairs of 0.15 mg devices and 15 pairs of the 0.5mg devices were washed. One of each pair, the ‘washed’ device, was added to a load of laundry run through a regular color wash cycle with medium heat. The other of the pair, the “control”, was stored in manufacturers’ recommended conditions. The washing machine selected for the study was a top-loading Maytag LAT9900AAW washing machine, after an informal survey on a large social media allergy group revealed that 63% of 224 respondents use a top-loading washing machine. The standard load of laundry for each test wash cycle consisted of seven pairs of underwear, seven pairs of socks, five short sleeve t-shirts, two long sleeve t-shirts, three pairs of jeans and a towel. The total mass of this load was 4.7 Kg and filled roughly half of the washing machine drum, based on laundry load size recommendations [2]. The recommended dosage for a medium load of Tide liquid laundry detergent was added to each load [2].

Washed and paired control devices were fired into a section of marbled beef, used in this study to simulate human muscle tissue. The beef was placed in a 30 mm diameter plastic tube during the triggering of the device. The beef and the device were weighed pre-injection and post-injection using a Mettler Toledo analytical balance scale with accuracy to 0.001 g. The difference between pre-injection and post-injection weights of both the device and the beef were used to estimate the amount of epinephrine solution fired. The beef was replaced after each time a device was fired into it.

The primary aim was assessed in two ways: by comparing the increase in meat mass between washed and control devices, and by comparing the decrease in device mass between washed and control devices. Both measures were used to estimate the amount of epinephrine solution fired. Since the epinephrine solution of junior devices is diluted, devices delivering 0.15 mg and 0.3 mg of epinephrine were both expected to eject 0.3 ml, equivalent to 0.3mg, of epinephrine solution.

For each analysis, the difference in mass of meat and the difference in mass of device before and after firing the device were obtained and these differences in mass were compared between the washed device and controls, taking into account the pairing of the washed and control devices. Unadjusted analyses were performed using a paired t-test. Adjusted analyses were performed using generalized linear equations which adjusted for device dose (0.15 mg vs. 0.3 mg) and expiration date (in months).

Our secondary aim was to evaluate for washing water contamination of the device needle and inner compartment. Whether the needle had been exposed to laundry water was tested by sawing open triggered washed and control devices. An additional 14 paired devices were examined for exposure to water around the syringe and needle. They were first inspected visually from the outside. The plastic housing was then carefully sawed open just below the level of the rear case. The rear case, compressed drive spring, syringe and needle were then removed as a single unit from the shroud and carrier. The syringe, area around the plunger, spaces between the plunger stopper rings and the rubber needle cover were visually inspected for moisture. The needle cover was removed, and the needle area was tested using chlorophenol red detection paper to determine if the needle was wet due to contact with washing water. The syringe plunger was also gently compressed to assess for fluid leakage, which could indicate a break in the seal between the syringe and the needle.

Based on data by Cooper et al., [3] we estimated that in a paired t-test, testing 22 pairs of devices would provide 90% power to detect a 5% difference in mean mass of an average control device between washed and control devices for both the meat and device outcomes. Based on these calculations and device availability, 68 pairs of devices (17 0.3 mg and 65 0.15 mg) were studied, providing sufficient power for the primary outcome, evaluating all devices (EpiPen and EpiPen Jr) together.

RESULTS

All 68 washed and 68 paired control devices triggered and fired epinephrine solution. In unadjusted comparisons meat gained more mass when devices activated, versus controls (0.353 versus 0.257, paired t-test p-value <0.0001) and washed devices lost less mass when activated, versus controls (0.396 versus 0.263, paired t-test p-value <0.0001), indicating that washed devices fired a greater mass of epinephrine solution compared with their paired controls. The amount of mass fired by washed devices exceeded manufacturers specifications of 0.3 mg (Figures 1 and 2). After adjusting for solution type and expiration date, the results remained significant.

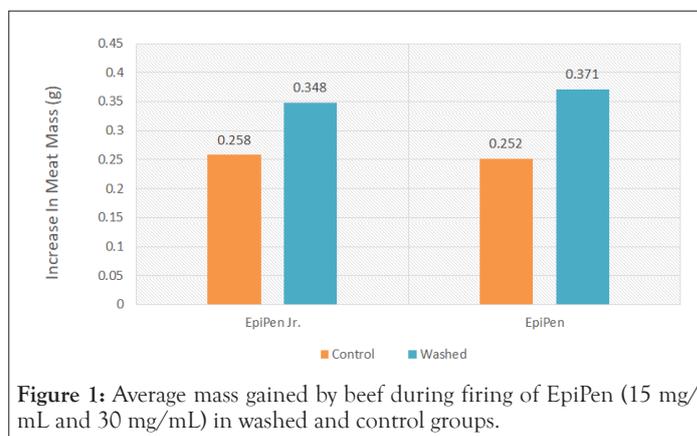


Figure 1: Average mass gained by beef during firing of EpiPen (15 mg/mL and 30 mg/mL) in washed and control groups.

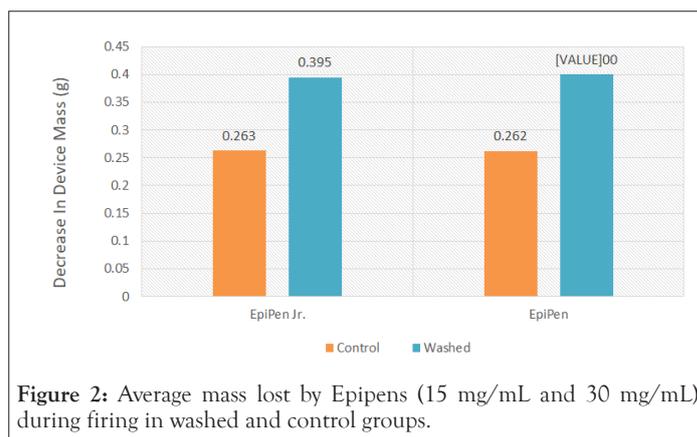


Figure 2: Average mass lost by EpiPens (15 mg/mL and 30 mg/mL) during firing in washed and control groups.

All washed devices were inspected externally, and all were visibly wet both outside and inside the housing, looking through the viewing window (Figure 3). Ten washed devices (nine (14%) EpiPen Jrs and one (6%) EpiPen) had needle shrouds that failed to deploy, leaving exposed needles (Figure 4); all control device needle shrouds deployed as expected, covering the needle. Over time, many washed devices developed an odor, concerning for bacterial or mildew contamination.



Figure 3: Washed EpiPen and EpiPen Jr. devices that didn't release the orange needle shroud after they were triggered, leaving exposed needles.



Figure 4: A washed EpiPen with visible drops of liquid beneath the clear plastic housing.

On dissection of an additional 15 washed untriggered devices (three 0.3 mg and twelve 0.15 mg) to assess for internal damage and exposure to liquid, there were visible drops of liquid surrounding all the syringes, plastic components and the outside of the rubber needle covers. There was no liquid in between the rings of the black plunger stoppers, and no visible liquid around the needles when the needle covers were removed, suggesting that washing fluid did not penetrate inside of the syringe. The chlorophenol red paper did not detect water on any of the needles. Gentle pressure did not reveal any break in the seal between any of the syringes and needles.

DISCUSSION

Official patient information for EAI's marketed in the United States all include guidance related to exposure to temperatures, [4-7] and EpiPen includes guidance related to being dropped, but the guidance related to water exposure is limited. The prescribing information for EpiPen and the Amneal/Impax generic for Adrenaclick both state that the carrying case is not waterproof, but neither states whether or not the device itself is waterproof. The Auvi-Q patient information indicates only that the trainer is not waterproof. None of the devices have patient information that recommends a course of action if the device is soaked in water or placed through a washing cycle.

The EpiPen website has a frequently asked questions page which addresses water submersion [8]. The questions "Is the EpiPen® and EpiPen Jr® Auto-Injector carrier tube waterproof? What about Mylan's authorized generic carrier tube?" are answered: No. The carrier tube has no rubber seal, and it is not waterproof. If your EpiPen® Auto-Injector or its authorized generic is ever submerged in water or another liquid, contact your healthcare professional immediately to obtain a new prescription.

Contrary to our hypothesis that washed devices would eject less medication than their unwashed counterparts, they ejected a statistically significantly larger mass than their unwashed pairs. One potential reason for the observed result is that the devices are firing more epinephrine after washing (Figure 5). A more likely cause is that the device is firing the usual epinephrine solution as well as washing machine water either trapped inside the inner carrier or soaked into the rubber needle cover, which gets compressed against the front of the carrier during activation. If this is the case, then the washed device could inject contaminated washing water along with epinephrine solution.



Figure 4: A washed EpiPen with visible drops of liquid beneath the clear plastic housing.

The cost of EpiPens is high, and the devices have a short shelf life [9]. Carrying a device daily increases the risk of losing it or exposing it to water. While it is disappointing to discover a device has been run through a washing machine, our study demonstrates the importance of replacing such a device. While this study only applies to EpiPens, other devices do not appear to be waterproof, and none are described as waterproof, in or out of their cases.

Manufacturers could do more to address this issue. At a minimum, patient information handouts should indicate that these devices are not waterproof and should be replaced if submerged in water. A more elegant solution would be to provide waterproof cases, which would also serve to better protect devices during use in adverse weather conditions. In addition, smart cases could alert the consumer that the device is in the washing room. This technology is not out of reach: Veta (Aterica Digital Health, Waterloo, Ontario) is a smart case for EpiPen that that already includes temperature monitoring, location tracking, and alerts when the case has been

opened or separated from the phone of the user [10].

The issue of washing EAI, and other challenges related to carrying and maintaining these devices, would be solved if epinephrine could be taken sublingually instead of by injection and work equally effectively. Improving the bioavailability of sublingual epinephrine using microcrystals or nanocrystals may one day provide an elegant new solution to this long-standing problem [11-12].

CONCLUSION

EpiPen devices run through a cycle of a washing eject a larger amount of solution than paired controls, possibly including laundry water trapped in the carrier or needle cover of the device. In addition, water penetrates as far as the outside of the syringe in all cases, and some shrouds do not move into place to cover the needle after the device is triggered. Consequently, a washed EpiPen should not be considered a safe or functional device.

CONFLICT OF INTREST

None.

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