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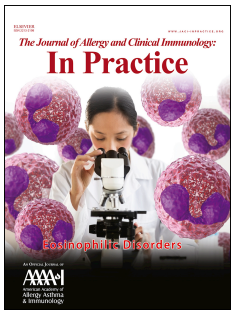

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Abstract

Polyethylene glycols (PEG) or macrogols are hydrophilic polymers found in everyday products such as foods, cosmetics and medications. We present five cases of confirmed PEG allergy, which to our knowledge is the largest case series to date. Four of the five cases developed anaphylaxis to medications containing PEG, with one near-fatal case resulting in cardiac arrest. Skin tests (ST) were undertaken to the index medications and to PEGs of different molecular weights . Three were confirmed with positive skin prick test (SPT) to PEG one confirmed with a positive intradermal test (IDT) and one confirmed following positive oral challenge. Two patients developed anaphylaxis following IDT to PEG and one a systemic allergic reaction (SAR) (without hypotension or respiratory distress) following PEG SPTs. Prior to diagnosis all 5 patients were mis-labelled as allergic to multiple medications and their clinical management had become increasingly challenging. An algorithm is proposed to safely investigate suspected PEG allergy, with guidance on PEG molecular weights and skin test dilutions to minimize the risk of SAR. Investigation carries considerable risk without knowledge and informed planning so should only be conducted in a specialist drug allergy centre.

Introduction

Polyethylene glycol (PEG)s or macrogols are hydrophilic polymers used widely in pharmaceuticals. They are also used in medical (e.g. wound dressings, hydrogels), household products (e.g. detergents and polishes) [1], food (e.g. preservatives to food supplements) [2] and cosmetic products (as emollients and emulsifiers) due to their water soluble properties.

PEGs have molecular weights (MW) between 200 and 35000 kDa. PEGs with a low MW (<400) are usually clear viscous liquids but those with high MW (>1000) are usually opaque solids and powders. Products with a MW over 100,000 are referred to as poly(ethylene oxide) PEO [3]. Pharmaceutical products such as laxatives and bowel preparations (lavage solutions used for whole bowel irrigation prior to colorectal surgery) [4] often contain PEG 3350 or PEG 4000. PEGs are found in tablet binders, parenteral liquid preparations, suppositories and skin lubricants [1]. Also pegylation (coating the surface of nanoparticles) improves systemic drug delivery. Similarly, PEGs are present in cosmetics e.g. creams, facial products and baby wipes. MW labelling of PEGs for pharmaceuticals versus cosmetic products differs. The numerical value in cosmetic products refers to the average number of ethylene oxide units whereas in medications, it refers to the average MW calculated by multiplying the number of ethylene oxide units by its atomic mass (44 Da). For example PEG 75 is approximately the same weight as macrogol 3350 (44x75=3300) [1].

There is increasing awareness of systemic allergic reactions (SARs) to PEGs, which can vary from mild SARs to life-threatening anaphylaxis. PEG can be referred to as “a hidden allergen”. A reported death following PEG-induced anaphylaxis was reported in Dublin, Ireland. A 24-year old man was originally given a glucocorticoid injection containing PEG and developed urticaria. A year later, he was given a second glucocorticoid injection and died from anaphylaxis [5].

Our experience and that of other authors[1] has shown that PEG’s potential to cause anaphylaxis increases with higher MWs and concentration. Therefore when PEGs or macrogols are listed as drug excipients unless the MW and amount of PEG are stated it can prove frustratingly challenging to investigate suspected allergic reactions.

Four cases of anaphylaxis, as defined by the National Institute of Allergy and Infectious Disease (NIAID), and one case of an SAR (without hypotension and respiratory distress) [6] to PEG were confirmed by skin tests, the largest case series to date.

An algorithm to investigate suspected PEG-induced SARs is proposed and includes the source of reagents, skin test dilutions and methods used to grade the skin test results.

Case 1 – Skin prick tests can cause a systemic reaction

A 51-year old female with a history of contact dermatitis to cosmetics presented following anaphylaxis to medroxy-progesterone acetate (containing PEG 3350 and polysorbate 80) (Depo-Provera; Pfizer, Kent, UK) and a SAR to the laxative Moviprep (PEG 3350, ascorbic acid; potassium chloride; sodium ascorbate; sodium chloride and sodium sulphate) (Norgine, Middlesex, UK).

Within minutes of receiving medroxy-progesterone acetate she became light-headed, developed generalised pruritus, swelling of her hands and feet, profuse vomiting and profound hypotension. She received 0.5mg adrenaline IM and recovered. On another occasion, she developed generalised erythema and pruritus and mouth angioedema immediately following four sips of Moviprep and was treated with IV hydrocortisone.

Skin prick tests (SPT) were sequentially undertaken to PEG dilutions of PEG 200 (10%), 400 (10%), 3350 (50%), 4000 (10%) (Sigma-Aldrich, Dorset, UK) 20000 (10%; Santa Cruz Biotechnology, Texas, US) and Moviprep (10%; Norgine, Middlesex, UK). SPT took 15-30 minutes to develop and were strongly positive to PEG 3350 (50%) (weal 10mm/flare 30mm), 4000 (10%) (weal 8mm/flare 30mm), 20000 (10%) (weal 15mm/flare 30mm) and positive to Moviprep (10%) (weal 6mm/flare 25mm).

Following completion of all SPT; she developed facial flushing and six urticarial lesions on her neck, back and abdomen. She was treated with oral cetirizine syrup, then IV hydrocortisone and chlorpheniramine without further sequelae.

Case 2 – Allergic patients may have an individual MW threshold

A 42-year-old female developed generalised urticaria and lip angioedema after two Gaviscon Double Action tablets (sodium alginate, sodium bicarbonate, calcium carbonate and PEG 20000) (Reckitt Benckiser, Slough, Berkshire, UK). She was successfully treated with oral glucocorticosteroids and chlorpheniramine in an emergency department. She had previously tolerated Gaviscon Peppermint Liquid (sodium alginate, sodium bicarbonate and calcium carbonate) (Reckitt Benckiser, Slough, Berkshire, UK) but had never previously taken Gaviscon Double Action tablets. The only difference noted between the two medications is that Gaviscon Double Action contains PEG 20000, but the liquid version does not.

SPT and intradermal tests (IDT) to Gaviscon Peppermint Liquid (SPT undiluted; IDT 1:100) and Gaviscon Double Action tablets (SPT 25mg/ml; IDT 1:100) were negative, and she passed oral challenge to Gaviscon Peppermint Liquid. She was then challenged with two Gaviscon Double Action tablets on

another visit and within 1 hour became agitated, pruritic, and developed urticarial weals on her leg, facial flushing and cough. She immediately received IM adrenaline, IV hydrocortisone, IV chlorpheniramine, nebulised salbutamol and ipratropium bromide. Serum tryptase was normal. She tolerated an oral challenge with Movicol (potassium chloride, sodium chloride, sodium bicarbonate, PEG 3350)(Norgine, Middlesex, UK).

There was a year delay confirming the MW of PEG in the tablets from Reckitt Benckiser. During this time she had a transient ischaemic attack and was started on clopidogrel (PEG 4000)(Teva, Eastbourne, East Sussex, UK) and atorvastatin 40 mg (PEG 8000) (Ranbaxy, Hayes, UK), which she tolerated. However, she did react to bisacodyl 5mg (PEG 6000) (Dulcolax GR; Sanofi, Berkshire, UK) developing a cough, dyspnoea and pruritus which resolved with an H1-antihistamine.

SPT performed to PEG 200, 400, 3350, 4000, 20000 and polysorbate 80 (dilutions of 0.01%, 0.1%, 1% and 10%) were negative. PEG IDTs (0.01%) were also negative.

However 30 minutes after completing the IDTs she became agitated, developed a cough, urticaria on her upper extremities and hypotension (systolic 80mmHg). She was treated with IM adrenaline, IV chlorpheniramine and hydrocortisone. Her observations improved quickly and tryptase levels

measured immediately, at 1 hour and 1.5 hours were 5, 4 and 4 ng/ml respectively (baseline 3.2 ng/ml).

Case 3 – Amount of PEG exposure as well as MW determines threshold for allergic reactions

A 52-year old lady had three reactions to medications. The first occurred when she immediately developed angioedema of her face, lips and hands with dyspnoea after taking an unknown tablet (not aspirin) before coronary angiography.

The second episode occurred on day four of taking Malarone (atovaquone, proguanil hydrochloride, PEG 400 and 8000) (GlaxoSmithKline, Middlesex, UK) when she developed nausea, facial erythema, bilateral hand angioedema and dyspnoea. The third reaction followed IM methylprednisolone acetate (Depo-Medrone, PEG 3350) (Pfizer, Kent, UK), with immediate rhinitis, flushing and pruritus of her palms and feet and light-headedness. She required two doses of 0.5mg IM adrenaline, hydrocortisone and chlorpheniramine. She gave a prior history of allergic conjunctivitis to certain moisturisers (although we were unable to establish whether they contained PEG).

SPT were undertaken to methylprednisolone acetate (40mg/ml; Pfizer, Kent, UK), Malarone (250mg/ml; GlaxoSmithKline, Middlesex, UK), PEG 200 (10%), 400 (10%), 3350 (50%), 4000 (10%) and 20000 (0.001%).

SPT were positive to Malarone (250mg/ml) (weal 6mm/flare 20mm), PEG 3350 (50%) (weal 3mm/flare 6mm), 4000 (10%)(weal 4mm, flare16mm) and 20000 (0.001%) (weal 5mm,flare 30mm).

Case 4 – Fatal reactions can occur in those allergic to PEG

A twenty-year-old male presented following near-fatal anaphylaxis after taking Gaviscon Double Action tablets (PEG 20000). Thirty minutes after two Gaviscon Double Action tablets, he developed periorbital swelling and nasal congestion followed by generalised urticaria, dyspnoea and cardiac arrest in hospital. He was successfully resuscitated and taken to ICU for further monitoring.

He regularly takes mesalazine MR (PEG 6000) (Octasa, Tillotts Pharma, Lincolnshire, UK) without reaction.

SPT undertaken to PEG 400, 3350, 4000 (dilutions 0.1%, 1% and 10%), PEG 200000 (0.1%, 1%) and polysorbate 80 and poloxamer 407 (10%; Sigma-

Aldrich, Dorset, UK) were positive only to PEG 20000 at 1% dilution (weal 4, flare 16mm).

As he tolerates medications with PEG 6000 following the reaction; this was established as the threshold level and has avoided medications with PEG MW above 6000.

Case 5 – Extreme caution is advised with ST to PEG especially IDTs

A 70-year-old women had four reactions to different medications. The first occurred after taking Moviprep (Norgine, Middlesex, UK). She took three sips and immediately developed plantar and groin pruritus, dyspnoea and became lightheaded; no treatment was given.

Within thirty minutes of the first tablet of a course of penicillin, she developed plantar and groin pruritus, then generalised pruritus. She stopped the penicillin.

Her most severe reaction occurred during admission with chest pain and dyspnoea. A CT pulmonary angiogram with iohexol contrast (Omnipaque; GE healthcare, AS, Norway) was normal. She was treated for an acute coronary event with 75mg clopidogrel (Sanofi, Paris, France) and fondaparinux (Aspen, Dublin, Ireland). Ten minutes later she became flushed, developed generalised pruritus and urticaria on the trunk and groin. No treatment was

given. Two days later she had a CT angiogram and immediately after iohexol developed plantar pruritus, generalised pruritus, dyspnoea, profound hypotension (systolic 35 mmHg) and tachycardia of 200 bpm. She was treated with IM adrenaline, IV hydrocortisone, chlorpheniramine and fluids. She was successfully resuscitated and transferred to ICU for monitoring. An immediate tryptase was 32ng/ml (baseline 10ng/ml).

SPTs were undertaken to undiluted concentrations of benzyl penicilloyl-polylysine (SPT/IDT: 0.04mg/ml PPL), MD (SPT/IDT: 0.5mg/ml)(major and minor determinants of penicillin respectively) (Allergy Therapeutics, Worthing, UK) amoxicillin, (SPT: 200mg/ml, IDT: 20mg/ml; Wockhardt, Wrexham, UK) benzypenicillin (SPT: 150mg/ml, IDT: 15mg/ml; Genus, Berkshire, UK), flucloxacillin (SPT: 50mg/ml, IDT: 5mg/ml; Fresenius Kabi, Cheshire, UK) co-amoxiclav (SPT: 200mg amoxicillin, and 40mg clavulanic acid /ml, IDT: 20mg amoxicillin, and 4mg clavulanic acid /ml; Bowmed Ibisqus, Wrexham, UK), iohexol (Omnipaque SPT: 300mg/ml, IDT :30mg/ml; GE Healthcare, AS, Norway) , iodixanol (Visipaque SPT: 270mg/ml, IDT: 27mg/ml GE Healthcare AS, Norway), iopamidol (Niopam SPT: 370mg/ml, IDT 37mg/ml; Bracco, High Wycombe, UK), iomeprol (Iomeron SPT: 300mg/ml, IDT 30mg/ml; Bracco, High Wycombe, UK), PEG 4000 and 20000(SPT/IDT: 1%). All SPT were negative and therefore IDT were undertaken to these agents resulting in a positive reaction to PEG 20000 (1%). An hour after IDT she developed generalised pruritus, chest tightness and dyspnoea. She was treated with IM adrenaline and oral cetirizine and admitted overnight for observation. An immediate tryptase level was raised at 36ng/ml.

On review of each of her reactions, we concluded that PEG caused the first reaction involving Moviprep; containing PEG 3350. General practitioner (GP) summary records confirmed that the second reaction was triggered by phenoxymethylpenicillin (Sandoz, Surrey, UK) which contains PEG 6000. The third reaction following clopidogrel and fondiparanux was felt to be secondary to clopidogrel, because the Sanofi brand of clopidogrel contains PEG 6000, whereas fondiparanux does not. Lastly the reaction during CT angiogram, could have been caused by aspirin 300mg as some brands of aspirin 300mg contain PEG 6000, however the hospital was unable to confirm the brand of aspirin given to the patient. No other agent administered contained PEG and SPT and IDT to other agents were negative.

Discussion

Wenande & Garvey reviewed all the case reports of immediate hypersensitivity to PEG published between 1977 and 2016. Of the 37 cases reported, 76% met the criteria for anaphylaxis [1]. Patients report reactions to different brands of medications and some to cosmetics containing PEG.

Our cases demonstrate that each PEG-allergic subject has an individual threshold level dependent on MW in combination with the amount of PEG ingested [1]. For example, case 4 reacted to MW 20000, but tolerated medications containing PEG 6000 and was therefore advised to avoid

medications with MW above 6000. Our cases also show that investigation carries a high risk of anaphylaxis. We were unable to determine the amount of PEG contained in each of the medications that gave rise to allergic reactions but consider it likely that the amount ingested is an important factor determining whether an allergic reaction occurs as well as MW. Tablets with PEG coating may be less allergenic, as there is a smaller amount ingested.

The onset of SAR and anaphylaxis to PEG is typically rapid and severe. Common symptoms include pruritus, flushing, urticaria and angioedema. Hypotension occurs in severe cases with airway symptoms of chest tightness and dyspnoea.

Cases were listed in chronological order starting in 2016 and our method of investigation was modified after each case culminating in the algorithm and ST guideline provided.

An algorithm is proposed to diagnose PEG allergy (figure1). This includes obtaining a detailed history of medications taken, their brand and excipients and MW of PEG. In many cases it is necessary to obtain hospital and ED records to confirm time of administration of each drug, time-course of onset and resolution of symptoms and emergency treatment administered [7]. Tryptase levels should be measured within 30 minutes of the reaction and 1 to 2 hours later with a baseline reading >24 hours later [8]. It is imperative to

confirm the brand of the index drug causing each reaction to determine whether PEG is present and its MW. In addition, it is also important to take a thorough drug history, confirming usual medications (including brands) taken and tolerated to determine, where necessary, each patient's individual MW threshold.

If PEG allergy is suspected the patient should be referred to a specialist drug allergy service for SPT to PEG, as this poses a higher risk for SAR than other types of drug allergy investigation.

From our experience patients who are PEG allergic are at risk of systemic reactions to SPT (2/5 cases). This occurred with high concentrations of PEG and always with higher MWs. SPT weals develop slower than biological, and can take 30 minutes to evolve, and produce small weals at lower concentrations. Therefore skin prick testing should begin with dilute concentrations of PEG using a stepwise approach, waiting at least 30 mins before progressing to the next concentration in order to reduce the risk of a reaction. We have included guidance for SPT concentrations and MWs undertaken in our clinic (table 2).

IDTs in PEG-allergic patients who are SPT negative can cause systemic reactions (as in 2/5 of our cases who underwent IDT) and therefore should be undertaken with considerable caution by starting with low MWs at low

concentration. Patients should be formally consented, as the risk is similar to a challenge test, and cannulated prior to IDTs. IDTs should be avoided or only undertaken with special precautions in patients with cardiovascular risk, and multiple co-morbidities, older patients, as well as those who have had severe hypersensitivity reactions. Wenande &Garvey recommend that intradermals if undertaken should be undertaken at 0.01% dilution [1]. SPT and IDTs were undertaken in four control patients who were not allergic to PEG with negative results.

Patients diagnosed with PEG allergy will find it challenging to avoid PEG containing products especially if their allergic threshold is at a low MW, as this increases the number of medications to be avoided. Therefore, it is vital to only investigate for PEG allergy if there is a high index of suspicion, rather than screening large numbers of patients, as this may adversely impact the vigilance required during investigation. Establishing PEG MW thresholds provides additional valuable information allowing individual risk-assessment.

Emergency medications used to treat anaphylaxis may contain PEG. We have compiled a list of emergency anaphylaxis medications which contain PEG (table 3) and which are safe to use, however these are formulations of medications used in the UK and may differ around the world and require regular updating. As formulations change, it is important to check excipients before prescribing and not to use generic prescribing. Healthcare professionals may avoid prescribing ‘any’ medication in these patients when

they are confronted with a non-allergic emergency resulting in inequitable access to healthcare. Therefore each hospital should have a PEG-free emergency drug list, dependent on local availabilities, which should be regularly checked and updated.

Patient education is paramount; they need to be suspicious of all new medications prescribed and even new supplies of existing prescriptions. In our experience, when the diagnosis is confirmed, patients are scrupulous with new medications or brands. Patients should also be informed of their individual threshold level.

As PEG allergy is emerging, with little awareness amongst medical professionals, it is important to carefully manage these patients and prevent deaths. Emergency departments should be aware of PEG allergy and check medications prior to treating PEG allergic patients in the acute setting. Written patient information should also be provided. GPs and pharmacists should also check the brands of medications that contain PEG before prescribing or dispensing medications to PEG-allergic patients. Electronic medical record developers will need to update their software to facilitate accurate PEG allergy recording and avoidance of PEG containing drugs.

Once confirmed, details of the PEG allergy should be added to the electronic medical record, and a copy provided to the patient, and copied to the GP [7,8].

This should identify the PEG MWs to be avoided and list the medications to which the patient has reacted. It should also highlight medications containing PEG (with MWs), which should not be used to treat acute allergic reactions and a list of medications which can be used safely. The patient should be given a copy of the clinic letter so this can be presented to physicians involved in their future management.

Normally an adrenaline auto-injector is not indicated in drug allergy; as the drug is avoidable [7,8]. However, PEG is not easily avoidable and therefore we recommend prescribing an adrenaline auto-injector in conjunction with a written emergency treatment plan.

This is the largest case-series of PEG allergic patients confirmed with skin tests. PEG is a high-risk 'hidden' allergen, usually unsuspected and can cause frequent allergic reactions due to inadvertent re-exposure. Allergy investigation carries the risk of anaphylaxis and should be undertaken only in specialist drug allergy centres. Patients require detailed written information with instructions on how to keep them safe.

References

1. Wenande, E., Garvey, L.H. Immediate-type hypersensitivity to polyethylene glycols: a review. Clin Exp Allergy. 2016; 46:907–922
2. EFSA Panel on Food Additives and Nutrient Sources added to Food (EFSA ANS Panel), et al. “Refined exposure assessment of polyethylene glycol (E 1521) from its use as a food additive.” EFSA Journal 16.6 (2018): e05293.
3. Sigma Aldrich Materials Science Products Poly(ethylene glycol) and Poly (ethylene oxide). Available at: https://www.sigmaaldrich.com/materials-science/material-science-products.html?TablePage=20204110
4. Bowden TA, DiPiro JT, Michael KA. Polyethylene glycol electrolyte lavage solution (PEG-ELS). A rapid, safe mechanical bowel preparation for colorectal surgery. Am Surg. 1987;53:34-36]
5. Roseingrave L. Verdict of medical misadventure in case of fatal allergic reaction; 2017. Available at: https://www.irishtimes.com/news/crime-and-law/courts/coroner-s-court/verdict-of-medical-misadventure-in-case-of-fatal-allergic-reaction-1.3324937. Accessed December 12, 2017.
6. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF, Jr., Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report–Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol. 2006;117:391–397. doi: 10.1016/j.jaci.2005.12.1303
7. Mirakian R, Ewan PW, Durham SR, Youlten LJ, Dugué P, Friedmann PS, et al. BSACI guidelines for the management of drug allergy. Clin Exp Allergy 2009; 39:43-61
8. Dworzynski K, Ardern-Jones M, Nasser S. Diagnosis and management of drug allergy in adults, children and young people: summary of NICE guidance. BMJ2014;349:4852.

408 Figure 1: Algorithm for the investigation of suspected PEG systemic
409 allergic reactions

Table 1: Summary of investigations in 5 cases of PEG allergy and causative drugs

Case	Age /sex	Index reaction to drug	Drug(s) cause	SPT	IDT	GR to skin test	
						SPT	IDT
1	51F	anaph	Medroxy-progesterone acetate (PEG 3350, Polysorbate 80) Moviprep (PEG 3350) Cosmetic	+ 3350 + 4000 + 20k + Moviprep	ND	+ U, E, Pr	ND
2	42F	SR	Gaviscon Double Action (PEG 20k) Bisacodyl (PEG 6000)	- 200 - 400 - 3350 - 4000 - 20k	- 200 - 400 - 3350 - 4000 - 20k	-	+ anaph
3	52F	anaph	Unknown Malarone (PEG 400 & 8k) Methylprednisolone acetate (PEG 3350) Cosmetic	+ 3350 + 4000 + 20k + Malarone	ND	-	-
4	20M	Near fatal anaph; cardiac arrest	Gaviscon Double Action (PEG 20k)	+ 20k	ND	-	-
5	70F	anaph	Moviprep (PEG 3350) Phenoxy-methylpenicillin (PEG 6000) Clopidogel (PEG 6k) Aspirin (NK)	- Penicillins - RCM - 4000 - 20k	+ 20k	-	+ anaph

SPT = skin prick test; IDT = intradermal test; + = positive; - = negative; GR= generalise reaction; Anaph = anaphylaxis; SR= systemic reaction (without cardiac and airway compromise); U = urticaria, E = erythema; Pr = pruritus; ND= not done; NK= not known; RCM= radiocontrast media

k= thousands; MW=molecular weight
MW above 4000 expressed as thousands

Table 2: Skin prick testing protocol for PEGs

PEG MW	STEP 1	STEP 2	STEP 3
400	0.5%		
3350	0.1%	1%	10%
4000	0.1%	1%	10%
8000	0.1%	1%	10%
20000	0.1%	1%	10%

PEG obtained from Sigma-Aldrich, Dorset, UK (diluent phenol saline). Each step carried out sequentially with intervals of at least 30 mins

Table 3: Emergency drugs containing PEG

PEG containing drugs	**Non PEG containing emergency drugs**
Cetirizine tablets (4000)	Cetirizine syrup
Telfast tablets (400)	Chlorpheniramine tablets/syrup
Loratadine 10 mg Orodispersible Tablet (Sandoz) (Polysorbate 80)	Hydrocortisone
	Soluble/non soluble Prednioslone (excl gastro- resistant)
	Adrenaline
	Methylprednisolone
	Other forms loratadine tablets/syrup

Always check before giving rescue and new medications