Topical Corticosteroid Abuse: A Japanese Perspective

22

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Abstract

Abuse of topical steroids has been a problem in Japan since at least the 1990s due in a large part to the nature of the National Health Insurance (NHI) system and the "drug price margin" issue. The Atopic Dermatitis Treatment Guidelines published in 2000, which emphasise the safety of topical steroids, do not discuss potential adverse effects such as red skin syndrome.

Keywords

Drug price margin • Overprescribing • Lawsuit • Media • Guidelines

Learning Points

1. Topical steroid abuse in Japan started in 1980s related with overprescribing by doctors.
2. Japanese authoritative dermatologists got involved in lawsuits and discussion about side effects of topical steroids became taboo.
3. Guidelines are not successfully functioning for preventing side effects of topical steroids such as Red Skin Syndrome.

22.1 Topical Steroids Available Over the Counter in Japan

Mild to potent topical steroids are available over the counter (OTC) in Japan. They are sold in stores where a pharmacist or registered sales clerk is permanently stationed. (Registered sales clerks need to pass an examination to obtain a qualification.) When selling OTC topical steroids, education is provided to the customer, unless the customer advises the pharmacist (or clerk) that such education is not necessary.

22.2 Precautions on the Package Inserts of OTC Topical Steroids

The following is an example of the precautions given to people buying OTC topical steroids in Japan:

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This medication is used to treat skin disorders, so please do not use it as make-up or aftershave. If you are using high doses or using the product for a long period of time, you may develop acne or skin breakouts (pimples), reddening of the facial skin, facial swelling, dryness or roughness of the skin and increased hairiness. Therefore, please take particular caution when using them on the face. In addition, please do not use this product unnecessarily after symptoms have improved.

How to use topical steroids correctly when self-medicating:

*Please apply the correct quantity to the affected region. Under normal circumstances apply twice daily; however, if symptoms are severe, apply three times daily.

*Once symptoms improve reduce frequency of use.

*Please do not use for more than 1 week.

*If your skin does not improve in 5–6 days, or if your symptoms worsen, the diagnosis may be incorrect. Self-medication is no longer appropriate. Please stop using the topical steroid and discuss your condition with your doctor, pharmacist or registered sales clerk.

*If you have used topical steroids over an extensive area on the trunk that exceeds the area of 2–3 palms, self-medication is no longer appropriate. Please discuss your condition with your doctor, pharmacist or registered sales clerk.

What is an appropriate amount of topical steroid to use?

The "finger-tip" unit is useful in guiding topical steroid use. 0.5 g of topical steroid is approximately the amount of topical steroid squeezed from a tube from the tip of an adult's index finger to the first crease in the finger. This amount should cover an area about the size of two adult palms. Using this as a guide, you can compare the area of the affected region and determine the amount of topical steroid recommended.

22.3 Prescription of Topical Steroids by Doctors in Japan

Doctors prescribing topical steroids in Japan do not necessarily have dermatological training. While doctors must examine patients before issuing a prescription, there is no legal obligation to provide an explanation about the medication's use or discuss its potential side effects. Some doctors may give patients detailed information, whereas others will provide virtually zero patient education. Some doctors may prescribe topical steroids where there is limited clinical indication for this treatment.

22.4 National Health Insurance System and Drug Price Margins Influence on Topical Steroid Prescriptions in Japan

In 1961 a National Health Insurance (NHI) system was introduced in Japan. Employees are covered by corporate insurance. Retirees and people who are self-employed are covered by citizen's health insurance which is provided by the local government. Cover is extended to families also. Insurers pay for 70–90% of the cost of medical consultations, investigations or medications. In 2013, the mean annual insurance premium paid by NHI patients was 70,000 Yen, while the medical benefits per patient averaged 300,000 Yen. Thus, the patient premium only partially offsets the cost of the programme which is largely paid for by the Japanese taxpayer.

Overservicing is rife in Japanese hospitals and private consulting rooms. There is a tendency to readily prescribe topical steroids even for minor skin conditions such as insect bites or benign self-limiting rashes.

The "drug price margin" is a unique issue in Japan. At present, medical practices are run separately from pharmacies. However, up till 1990, pharmacies were usually located within medical

practices and run by the same company. This, in addition to the fact that patients experienced little out of pocket costs, meant overprescribing was rampant due to a push to increase company profits.

The drug price margin refers to the difference between the wholesale cost of the drug and the retail price for the patient. In the NHI system, the retail price of drugs is controlled at a national level at the time of the drug's approval. However, the wholesale price can be negotiated by the drug manufacturers and the pharmacy. Greater sales of drugs resulted in larger hospital profits, and thus in the 1970s and 1980s, overprescribing became a problem in Japan. This problem is becoming less of an issue now that pharmacies and medical practices are separate from one another.

Japan's total expenditure on topical steroids from 1992–1996 (source IMS Japan)

1992	39,256
1993	37,274
1994	35,257
1995	34,366
1996	33,252

Unit: 1,000,000 Yen

The table above clearly shows spending on topical steroids decreased steadily once the link between medical practices and pharmacies was removed.

22.5 The Media and Topical Steroid Use in Japan

Due to the issues with the NHI system and the previous drug price margin, overprescribing of medications was a hot topic in the Japanese media in the 1980s and 1990s. In 1992, the "News Station", a popular show in Japan, discussed the issue of overprescribing topical steroids. Dr. Takehara criticised the show repeatedly for their negative attitude towards the use of topical steroids. His views were widely published in newspaper articles, magazines, books and journals. He was particularly scathing towards the broadcaster of this programme for closing the programme with the line: "We know that, in the end, these topical steroids are drugs that will be used to the bitter end". However, the comment had actually been made by a pharmacology professor. Dr. Takehara later coauthored the Japanese Dermatological Association's atopic dermatitis guidelines.

22.6 Medical Malpractice Claims Regarding Topical Steroid Prescribing

Patients in Japan have sued over the management of their dermatological condition. The Kawasaki Steroid lawsuit [1] became famous. In this case, the patient experienced rosacea-like dermatitis to her face secondary to topical steroid use. Topical steroids had been prescribed over several years by multiple doctors in different medical facilities. The patient ultimately lost the case. Here is an extract of the expert opinion provided by Dr. Kawashima from Tokyo Women's Medical University:

> It is easy for dermatologists to diagnosis atopic dermatitis if they focus on the itching, the characteristic skin eruption and the chronic clinical course. We believe misdiagnosis of this condition by a dermatologist with sufficient training is very unlikely. However, from the latter half of 1975, an increase in the number of patients with conspicuous facial erythema was observed and a diagnosis of atopic dermatitis was possible by considering skin eruptions at other sites. There is no consensus in determining whether facial lesions are (a) side effects of topical steroids, (b) the concomitant presence of atopic dermatitis and side effects or (c) symptoms of atopic dermatitis. We need to make clinical decisions based on the patient's history—including drug use history, current symptoms and examination findings. At that time, this facial erythema was suspected to be rosacea-like dermatitis, which was commonly seen in patients who had used topical steroids like make-up to healthy skin, but the facial skin eruptions in this condition and those in rosacea-like dermatitis are different. The former are eczematous lesions, while the latter are a mixture of

acne and pustules and characterised by a burning sensation rather than itching. Most of the facial symptoms seen in this patient were of atopic dermatitis and we believe they should be considered to represent a case of atopic dermatitis.

Dr. Kawashima determined that "as there were no acne like pustules, we cannot diagnose this case as rosacea-like dermatitis and it should not be considered to be the result of an adverse effect of topical steroids". Currently, rosacea is commonly believed to present in two variants, one that is mainly erythema and the other that is erythema mixed with pustules [2]. Although there were some doubts with the expert testimony from Dr. Kawashima, it highlighted the difficulty of differentiating between the side effects of topical steroids and the primary condition (i.e. atopic dermatitis). Due to this fact, the ruling went in favour of the doctors.

22.7 Advocacy for Topical Steroid Withdrawal by Both Doctors and Alternative Health Practitioners

Under these conditions, Japanese doctors such as Dr. Tamaki [3], Dr. Sato [4] and Dr. Fujisawa began educating the public about the problems caused by overuse of topical steroids. Dr. Enomoto also reported several cases of patients with a history of long-term topical steroid use where they had ceased topical steroids and went on to experience marked systemic symptoms despite normal adrenocortical function [5]. This was the first report of systemic symptoms caused by the withdrawal of topical steroids. Dr. Hara and others published books aimed at the general public educating about the dangers of topical steroids overuse.

Meanwhile many "traditional" or alternative practitioners are treating "steroid withdrawal" in Japan. Topical steroid withdrawal does not generally require medical intervention unless complicated by infection. This is because the biggest factor in resolution of symptoms is time. As a result these traditional practitioners are able to generate a client load and income by "treating" these patients. Traditional practitioner management has at times been counterproductive and deceitful. Some topical medications contained steroids despite being promoted to patients as a traditional (and steroid free) Chinese medication.

Thus management of steroid withdrawal in Japan has been a mixed bag since the 1990s.

22.8 The Development of the Japanese Dermatological Association Guidelines for Atopic Dermatitis

As a result of the above issues, guidelines for atopic dermatitis management in Japan were required for dermatologists, paediatricians and allergy medicine doctors. The Ministry of Health, Labour and Welfare (MHLF), in the interest of controlling health expenditure, has promoted the use of clinical guidelines.

However, as these guidelines were developed by doctors such as Dr. Kawashima and Dr. Takehara who have a history of taking a "pro topical steroid" stance, the guidelines contain little information about adverse effects of topical steroids and do not suggest precautions to avoid these. Instead, the guidelines serve to emphasise the safety of topical steroid treatment and promote strategies to counter so-called patient steroid phobia. Dr. Furue, who was chair of the committee who wrote the guidelines, went on to use a grant from MHLW to create a website campaigning introducing the phrase "standard treatment" and recommended all Japanese doctors strictly adhere to the guidelines. In Japan, most doctors feel compelled to follow this "standard treatment" and, reassured by these guidelines, do not consider potential side effects of topical steroids or the risks of topical steroid overuse.

22.9 Lessons from the Japanese Situation

Steps to reduce topical steroid overuse in Japan include the improvement of package inserts with OTC topical steroids and restriction of sales

without a prescription. Neighbouring countries, especially in Southeast Asia, could potentially benefit from implementing similar measures. However, even with these strategies, the problem of topical steroid overuse remains in Japan. It is also difficult to differentiate atopic dermatitis from the adverse effects of topical steroid overuse. It does not help that terms such as red skin syndrome and topical steroid rebound are rejected by the Japanese Dermatological Association and are even considered taboo. There are concerns that if this condition was more widely recognised, there would be difficulties with prescribing topical steroids, which is currently a very common treatment. Calling patients steroid phobic is easier than dealing with the possibility that topical steroid overuse may have resulted in a problem for the patient.

However, now that Internet use has become widespread, it is evident that there are many patients around the world with symptoms fitting with red skin syndrome that state stopping topical steroids ultimately resulted in clinical improvement. Some of these patients may have had an exacerbation of a primary disease and healed with time, while others may genuinely have had severe side effects of topical steroid use similar to those cases reported by Enomoto. We cannot continue to ignore this problem.

In the future, there will be new drugs available for the treatment of atopic dermatitis. It may be beneficial for the drug companies promoting them to highlight the potential adverse effects of topical steroids so as to gain a market advantage. However, dermatologists must never forget first principles, namely, the treatment for contact dermatitis is the avoidance of irritants and allergens and the fact that atopic dermatitis can clear spontaneously and does not always require medical management. Treatment has financial implications for large drug companies and governments, but the doctor must always act in the best interests of their patient.

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