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**Brief Report**

# Impact of Surreptitious Glucocorticoids in Over-the-Counter Arthritis Supplements

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## Abstract

Adrenal dysfunction due to over-the-counter (OTC) health supplements containing unlabeled glucocorticoids has been previously reported. Here, we present a case series of 12 patients at an urban safety net medical center evaluated by endocrinology for iatrogenic adrenal dysfunction, Cushing syndrome (CS) and/or adrenal insufficiency (AI), associated with use of OTC arthritis supplements surreptitiously containing glucocorticoids. There were 12 patients using OTC arthritis supplements (Artri King [n = 8], Ardosons [n = 3], Ajo Rey [n = 1]) included. The mean age was 51.6 years and 33.3% were female. Findings of CS were identified in 10/12 (83.3%) patients, including moon facies (66%), central adiposity (66%), and abdominal striae (50%). Symptoms of AI were identified in 8/12 (66.7%) patients, including nausea/vomiting (42%), fatigue (42%), and abdominal pain (33%). Of 10/12 (83.3%) patients initially needing glucocorticoid replacement therapy, 4 continue to require treatment, 3 have successfully discontinued treatment, and 3 have been lost to follow-up. The literature reviewed identified 10 cases in 7 previously published reports, which did not include consistent follow-up data on adrenal function after discontinuation of the supplement. This case series demonstrates possible presentations of CS and/or AI from glucocorticoid exposure in patients taking these OTC arthritis supplements. Including more cases than all previously published reports combined, this series expands data for cortisol levels, cosyntropin test results, and glucocorticoid replacement needs for these patients and highlights the necessity for vigilant identification of supplement sources of exogenous steroids and the recognition of possible AI when such supplements are discontinued.

**Key Words:** Cushing syndrome, Artri King, adrenal insufficiency, cortisol, glucocorticoid-induced, supplements

**Abbreviations:** AI, adrenal insufficiency; CS, Cushing syndrome; HPA, hypothalamic-pituitary-adrenal; OTC, over-the-counter.

Over-the-counter (OTC) health supplements are commonly used by patients for a variety of ailments but may contain pharmacologic components that are not stated, such as glucocorticoids, nonsteroidal anti-inflammatory drugs, and muscle relaxants. The Food and Drug Administration (FDA) released a warning about the supplement Artri King in 2022 after recognition of undisclosed glucocorticoids in this supplement [1, 2]. Patients taking this supplement have been reported to present with signs and symptoms of Cushing syndrome (CS), as well as adrenal insufficiency (AI) after discontinuation [3-9]. However, these isolated case reports offer limited and inconsistent data about the presentations of these patients, as well as the supplements' effects on cortisol levels or provocative testing, the need for steroid hormone replacement therapy, or the duration required before adequate hypothalamic-pituitary-adrenal (HPA) axis function is restored. Here, we present a case series of 12 patients evaluated for iatrogenic adrenal dysfunction, consisting of CS and/or AI, associated with taking OTC arthritis supplements that surreptitiously contained glucocorticoids. In addition, we summarize the existing reported cases related to these products in a review of the literature to provide more generalizable data.

## Methods

Clinical information was reviewed for consecutive patients who underwent endocrinology consultation for possible adrenal dysfunction and use of an OTC arthritis supplement between the years of 2022 and 2023 at a single urban safety net medical center.

Data reviewed from the electronic medical records for all patients included: patient demographics, length of supplement use, presenting symptoms and physical examination findings, cortisol testing for AI (including results of 250 mcg adrenocorticotropic hormone [1-24] stimulation testing, also known as cosyntropin testing), and initiation of glucocorticoid replacement after initial evaluation. For patients in whom glucocorticoid replacement therapy was started, duration of continued therapy was calculated as the time from initiation to last visit when treatment was continued, and the time to HPA axis recovery was calculated from initiation of treatment

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to successful discontinuation without subsequent evidence of AI. Cortisol levels were measured in the same laboratory with the Elecsys II assay. No identified cases of confirmed OTC arthritis supplement use were excluded from analysis. This study was approved by the governing Institutional Review Board.

To review the existing case report literature, a PubMed search was performed over all dates with the terms: ("*artri king*" OR "*artriking*" OR "*artri*" OR "*artri-king*" OR "*ardosons*" OR "*ajo rey*"), to identify previous published journal articles related to these products. No language restriction was applied. Reference lists from all full-text articles that were reviewed were assessed to identify additional articles. Data extraction for each citation was performed by 1 of 3 authors (K.S.W., C.R.H., or T.E.A.) and included patient characteristics, biochemical results, cosyntropin testing, and details of adrenal replacement therapy according to a standardized data collection sheet. This study is not considered human subjects research and Institutional Review Board review was not required.

Continuous data are represented as means ± SD or median (range) as appropriate based on normality assessment, and categorical data are represented as number (percentage). Statistical calculations and/or figures were produced using Microsoft Excel for Mac version 16.87 (Microsoft, Inc.), Graphpad Prism (Graphpad, Inc), and Adobe Photoshop 23.1.1 (Adobe, Inc).

## Results

### Case Series

For the 12 patients included in this case series, individual patient information is shown in Table 1. The mean age ± SD was 51.6 ± 10.7 years, 4/12 (33.3%) were female, and all patients were of Hispanic/Latinx race/ethnicity. The OTC supplements identified by the patients were called Artri King, Ardosons, and Ajo Rey, and were used for treating joint pain in all cases. The median length of supplement use prior to presentation was 6 months (range, 3-120 months). Patients were evaluated by endocrinology due to symptoms of AI or clinical evidence of CS. Symptomatic AI was diagnosed in 8/12 (66.7%) patients, with the most common presenting symptoms being nausea/vomiting (42%) and fatigue (42%) (Fig. 1A). There were 10/12 (83.3%) patients with physical examination findings of CS, including moon facies (66%), central adiposity (66%), abdominal striae (50%), dorsocervical fat pad (33%), and bruising (33%) (Fig. 1B and 1C). Hospitalization was required in 8/12 (66.7%) patients for a variety of reasons, including acute hypoxic respiratory failure, heart failure, sepsis, and airway observation. Intensive care unit admission was required in 3/12 (25%) patients.

Generally, adrenal function assessed by AM fasting cortisol level was considered suppressed if < 5 mcg/dL, sufficient when > 10 mcg/dL, and equivocal if 5 to 10 mcg/dL, although the diagnosis of individual patients was influenced by clinical judgment for each case. Some degree of AI was considered present if serum cortisol level did not reach 15 mcg/dL upon cosyntropin testing. Initial cortisol assessment, either AM or random, was performed in 11/12 patients (Fig. 2), which showed a normal cortisol level in 2 patients, AI in 4 patients (cortisol ≤ 5 mcg/dL), and an equivocal level (cortisol 5-10 mcg/dL) in 5 patients. Cosyntropin testing was performed

**Table 1. Presentation, laboratory testing, and treatment of patients**

| Patient | Age | Sex | Supplement | Cushingoid at presentation? | Symptoms of AI at presentation? | AM fasting cortisol[a] (mcg/dL) | ACTH (pg/mL) | Cosyntropin stimulation test | | | Initiation of long-term glucocorticoid therapy for AI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Baseline serum cortisol (mcg/dL) | 30-min cortisol (mcg/dL) | 60-min cortisol (mcg/dL) | |
| 1 | 58 | F | Artri King | YES | NO | *<0.2* | | | | | YES |
| 2 | 56 | M | Artri King | NO | YES | 1 | *<5* | | | | YES |
| 3 | 53 | M | Artri King | YES | NO | 1 | 20 | | | | YES |
| 4 | 60 | M | Ajo Rey | NO | YES | 4.5 | 28 | | | | YES |
| 5 | 51 | M | Artri King | YES | NO | 21.5 | | | | | NO |
| 6 | 32 | M | Artri King | YES | NO | | | | | | YES |
| 7 | 50 | F | Artri King | YES | YES | 5.5 | | | | | YES |
| 8 | 42 | M | Ardosons | YES | YES | *7.2* | 12 | 5.6 | 9.1 | 10.8 | YES |
| 9 | 36 | F | Artri King | YES | YES | *7.3* | | 6.8 | 10.3 | 10.9 | YES |
| 10 | 69 | F | Ardosons | YES | YES | 8.8 | 18 | 6.8 | 10.5 | 12.5 | YES |
| 11 | 50 | M | Arti King | YES | YES | 5.8 | | 9.5 | 15.2 | 18.4 | YES |
| 12 | 62 | M | Ardosons | YES | YES | 11.3 | | 15.2 | 18.1 | 18.2 | NO |

Abbreviations: ACTH, adrenocorticotropic hormone; AI, adrenal insufficiency; CS, Cushing syndrome; F, female; M, male.
[a]Values in italics represent random serum cortisol value not obtained as a fasting AM measurement.

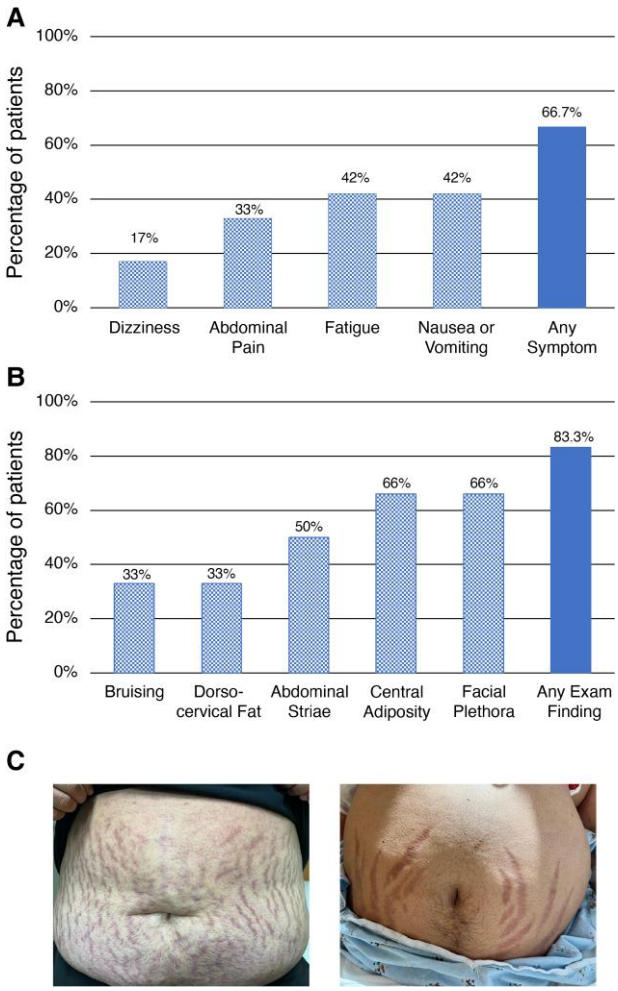


**Figure 1.** Presentations of patients taking an over-the-counter arthritis supplement who presented with adrenal dysfunction. (A) Percentage of patients who presented with different symptoms of adrenal insufficiency (shaded bars) or any symptoms of adrenal insufficiency (solid bar). (B) Percentages of patients who presented with different examination findings of Cushing syndrome (shaded bars) or any findings of Cushing syndrome (solid bar). (C) Photographs of abdominal striae highly suggestive of glucocorticoid excess in 2 patients.

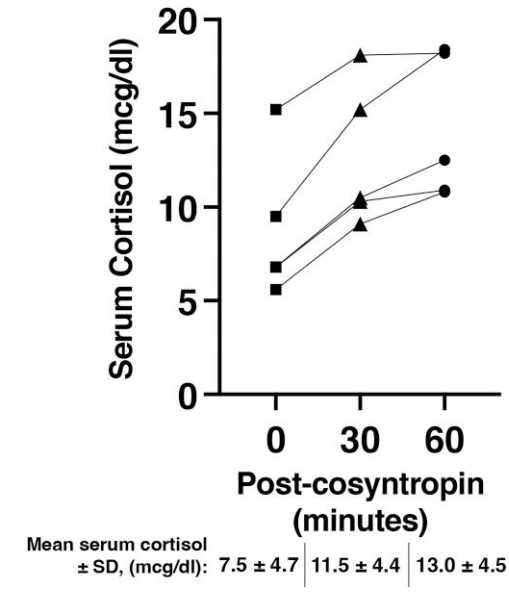


**Figure 2.** Results of cosyntropin stimulation testing. Results for 5 patients who underwent cosyntropin stimulation testing at the time of initial evaluation showing serum cortisol (mcg/dL) at baseline (time 0, black squares), 30 minutes post-cosyntropin (black triangles), and 60-minutes post-cosyntropin (black circles).

at the time of initial evaluation in 5 patients (Table 1). In 4 patients with equivocal initial cortisol level, 3 showed insufficient response suggestive of AI (cortisol level < 15 mcg/dL) (Fig. 3). The other 2 patients who underwent cosyntropin stimulation testing had appropriate response.

In total, 10/12 patients were prescribed glucocorticoid replacements to treat, or to avoid precipitating, AI (Table 1). Of the 2 patients who did not receive glucocorticoid replacement, one had a normal AM cortisol level and did not exhibit symptoms of AI while off Artri King during hospitalization. The other patient did not have symptoms of AI and demonstrated a sufficient cortisol response upon cosyntropin stimulation test (cortisol level of 18.2 mcg/dL at 60 minutes). A third patient presented with critical illness and symptoms suggestive of AI, and stress dose steroids were initiated. Subsequent cosyntropin stimulation testing for that patient showed adequate response (cortisol level of 18.4 mcg/dL at 60 minutes), and a taper to discontinuation was planned at the time of hospital discharge.

Hydrocortisone was prescribed for adrenal replacement in 6 of 10 patients who had glucocorticoid replacement initiated, with the total daily dosage ranging from 10 to 45 mg (given in 2 divided doses). The other type of prescribed glucocorticoid was prednisone. After initiation, 3 patients were successfully weaned off glucocorticoid replacement therapy after 8, 365, and 1134 days, respectively. Four patients have continued to require glucocorticoid replacement at 284, 335, 378, and 464 days post-initiation. The remaining 3 patients were lost to follow-up after the recommended initiation of glucocorticoid therapy.

## Review of the Literature

The search strategy and determination of final included records is shown in Fig. 4. There were 11 records initially obtained, of which 4 were excluded based on title and abstract assessment. Of the other 7 records that underwent full-text review, 6 reported cases were included. Two additional records were identified from reference lists, one of which contained a case report and was included, leading to 7 articles in the final review of the literature. These 7 articles [3-9] reported 10 patient cases of adrenal dysfunction due to Artri King use (Table 2). The mean age ±SD was 47 ± 15 years, 6/10 (60%) were female, and the median duration of use was 12 months with a range of 2 weeks to 36 months. Signs and/or symptoms of CS were reported in 9/10 (90%) patients, whereas any clinical evidence of AI was only reported in 2/10 (20%) patients. An initial AM fasting cortisol concentration was reported in 9/10 (90%) patients and was undetectable or < 2 mcg/dL in all of these. A cosyntropin stimulation test was performed in 4/10 (40%) patients with no patient achieving sufficient stimulation. Glucocorticoid replacement was initiated in 6/10 (60%) patients. Whether this therapy was able to be later discontinued was only

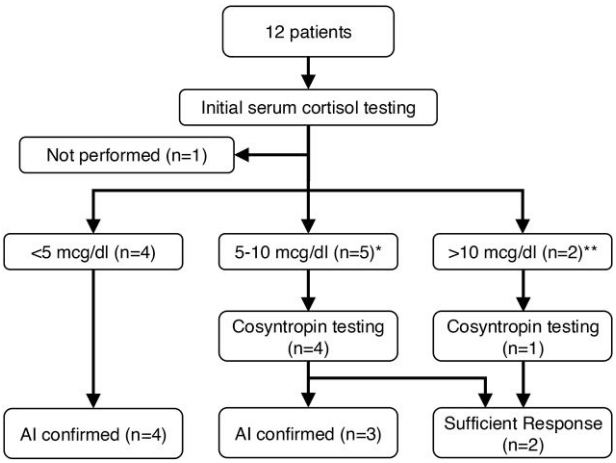


**Figure 3.** Flow diagram of diagnostic evaluation for adrenal insufficiency. Cosyntropin testing involved baseline serum cortisol assessment prior to 250 mcg adrenocorticotropic hormone (1-24) intravenously, followed by serum cortisol assessment at 30 and 60 minutes post-cosyntropin. Abbreviation: AI, adrenal insufficiency. *1 patient with initial serum cortisol of 5.5 mcg/dL had AI diagnosed clinically and received adrenal replacement without further cosyntropin testing. **1 patient with an initial serum cortisol of 21.5 mcg/dL was considered to have sufficient adrenal function and no adrenal replacement was started (also see Table 1).

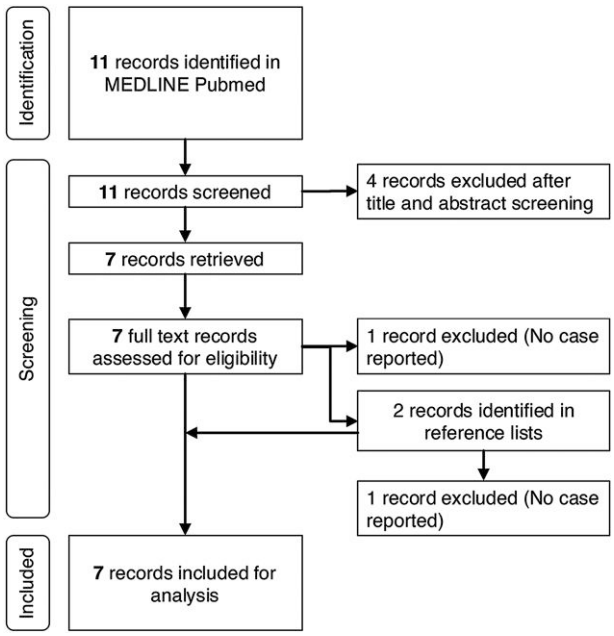


**Figure 4.** Flow diagram of literature review process.

reported in 2/10 (20%) patients. The duration of glucocorticoid replacement was only reported in 1/10 (10%) patients and was 4 months long.

## Discussion

Our case series demonstrates possible Cushing syndrome (CS) and/or adrenal insufficiency (AI) after unintentional exposure to glucocorticoids in OTC arthritis supplements, which has only previously been reported in a small number of case reports [3-9]. To date, this is the largest case series of OTC arthritis supplement users collected at a single institution. This series collected over a 2-year period offers important clinical insights. Because patients may not identify or recall a supplement, possible use of OTC medications for arthritis or other anti-inflammatory purposes should be specifically assessed in patients presenting with AI—especially with concomitant findings suggesting CS. Because the presence of CS with concomitant suppression of serum cortisol strongly suggests exposure to exogenous glucocorticoids, a urine/serum synthetic glucocorticoid screen by liquid chromatography–tandem mass spectrometry to establish the diagnosis may be essential in cases where no medication or supplement use is identified.

In addition to Artri King, we identified Ardosons and Ajo Rey as product names used by patients. Some previous case reports have found elevated dexamethasone levels in patients taking Artri King without other identified exposures to this glucocorticoid [4, 9], and laboratory analysis has shown dexamethasone as an unlabeled ingredient [1]. In contrast, betamethasone 0.75 mg is one of the labeled ingredients of Ardosons.

Compared to previously published case reports (Table 2) where every patient had an AM fasting cortisol level below the lower limit of normal, only 4 of our patients had an AM cortisol concentration confirmatory of AI with an additional 3 more found to have AI with cosyntropin stimulation testing. The reasons for these contrasting findings may include differences in the duration and/or quantity of the supplement taken, or timing of discontinuation prior to evaluation. There is also a possibility of selection bias in previously published case reports that favored more severe or remarkable presentations. Differences in cortisol assays also cannot be excluded.

In the literature review, 6/10 patients required initiation of long-term glucocorticoid therapy for AI, whereas 10/12 of our patients required initiation. Together, these data are consistent in showing that for patients on such OTC supplements, immediate discontinuation may not be possible and should not be done without considering the need for cortisol replacement. Patients generally tolerated hydrocortisone doses ranging from 10 to 30 mg in the morning and 5 to 15 mg in the afternoon/evening.

The duration of glucocorticoid replacement use was only specified in 1 of 10 patients in the reviewed literature and was 4 months long. In our series, 10 patients required glucocorticoid replacement, and only 3 have successfully been weaned off replacement therapy thus far. The general approach was to initiate a taper regimen from physiologic to twice physiologic dosing depending on the presentation. Glucocorticoid replacement tapering was largely dictated by clinical evaluation. If patients were asymptomatic after dose reduction, down titration was continued, whereas clinical symptoms (depending on severity) would lead to resumption of the previous dose or maintenance of the current dose until the next appointment.

For patients who have failed to wean off replacement glucocorticoids, the major limiting factors identified were symptoms of AI experienced when decreasing the dose, or persistently suppressed cortisol levels despite months of replacement therapy. The proposed mechanism of this is HPA axis dysfunction after prolonged exposure to exogenous glucocorticoids found in the OTC arthritis supplements [10, 11]. Prior studies have documented HPA axis recovery after a year of steroid replacement therapy and have found that

**Table 2. Summary of case reports of patients taking Artri King in existing literature**

| Citation | Age (years) | Sex | Duration of use (months) | CS at presentation | AI symptoms at presentation | AM fasting cortisol (mcg/dL) | ACTH (pg/mL) | Cosyntropin stimulation testing performed? | Post-cosyntropin cortisol (mcg/dL) | Initiation of long-term glucocorticoid therapy for AI | Ability to stop glucocorticoid replacement | Duration of glucocorticoid therapy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Mikhail 2022 | 54 | M | 12 | Y | N | uD | uD | N | n/a | N | n/a | n/a |
| Patel 2022 | 49 | F | 5 | Y | N | <0.5 | <5 | N | n/a | Y | n/r | n/r |
| Patel 2022 | 61 | F | 24 | Y | N | <1.0 | <5 | N | n/a | Y | n/r | n/r |
| Boncompagni 2023 | 52 | M | 18 | Y | Y | 1.2 | 32.2 | Y | 1.4 > 8.6[a] | Y | n/r | n/r |
| Dani 2023 | 12 | M | 10 | Y | N | n/r | n/r | N | n/a | n/r | n/a | n/a |
| Dunn 2023 | 35 | F | 36 | Y | N | <1 | <1.5 | Y | <1 > 3.2 > 3.7[b] | Y | Y | n/r |
| Saad-Omer 2023 | 40 | F | 36 | Y | N | <0.64 | 1.5 | Y | 1.6 > 1.3 > 6.5[b] | N | n/a | n/a |
| Berg 2024 | 58 | F | 12 | Y | Y | 1.0 | <2 | Y | 10.0[c] | Y | n/r | n/r |
| Berg 2024 | 55 | F | n/r | Y | N | 1.1 | n/a | N | n/a | Y | Y | 4 months |
| Berg 2024 | 59 | M | 0.5 | N | N | 0.6 | <2 | N | n/a | N | n/a | n/a |
| Aggregate data: | 47 ± 15[d] | 60% F | 12 (0.5-36)[e] | 9/10 (90%) | 2/10 (20%) | | | 4/10 (40%) | | | 2/10 (20%) | |

Abbreviations: AI, adrenal insufficiency; ACTH, adrenocorticotropic hormone; CS, Cushing syndrome; F, female; M, male; n/a, not applicable; n/r, not reported; uD, undetectable.
[a]Baseline and only 1 post-cosyntropin serum cortisol level, without specific timing, was reported.
[b]Numbers from left to right indicate baseline serum cortisol > cortisol 30 minutes after cosyntropin > cortisol 60 minutes after cosyntropin.
[c]Only 1 post-cosyntropin cortisol value reported without time point stated.
[d]Reported as mean ± SD.
[e]Reported as median (range).

up to 25% of patients initiated on long-term corticosteroids (defined in the meta-analysis as > 1 year of use) can still suffer from AI after 6 months [11-13]. In our cohort, multiple patients have taken longer than a year to demonstrate HPA axis recovery (the longest duration to date being 37 months). Although patients were counseled at follow-up visits to ensure that they did not resume the offending supplement or start taking new supplements, we cannot entirely exclude this possibility. Urine or serum synthetic glucocorticoid screening can be used as a helpful adjunct to objectively assess ongoing use of OTC supplements [14].

In the present case series, we add to the current understanding of presentations, HPA axis findings, glucocorticoid replacement dosing, and duration of therapy required, although there are limitations to these data to consider. The amount of supplement exposure—duration and dose—was estimated from the patients' report and was not able to be confirmed. As this was a retrospective assessment of the clinical care of these patients, sometimes during acute hospitalization, the diagnosis of AI based on clinical and biochemical findings was not standardized. Nevertheless, diagnostic assessments were largely in agreement with recent international recommendations for the diagnosis of glucocorticoid-induced AI [15].

In conclusion, this case series draws attention to possible CS and/or AI after unintentional glucocorticoid exposure in OTC arthritis supplements. Because patients may not identify or recall a supplement, specific assessment for the possible use of OTC medications for arthritis or other anti-inflammatory purposes should be assessed in patients presenting with AI (especially with concomitant findings suggesting CS). Given the risk of glucocorticoid excess and potential long-term HPA axis suppression and glucocorticoid replacement needs from OTC arthritis supplements, it is imperative that healthcare professionals, particularly endocrinologists, be vigilant in identifying the use of such products and informing patients about their dangers. The inclusion of glucocorticoids in OTC supplements raises serious regulatory and safety concerns that require greater public discourse for increased awareness. For patients on such supplements, immediate discontinuation may not be possible without cortisol replacement and should be done with caution.

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## Disclosures

The authors have nothing to disclose.

## Data Availability

Restrictions apply to the availability of some or all data generated or analyzed during this study to preserve patient confidentiality or because they were used under license. The corresponding author will on request detail the restrictions and any conditions under which access to some data may be provided.

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