Colchicine Brand Switching in FMF Patients: A Therapeutic Strategy

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ABSTRACT

In July of 2009 the U.S. Food and Drug Administration enacted new regulation of colchicine under the "Unapproved Drugs Program." Like other old drugs that were on the market before the existence of the FDA, colchicine had never been subjected to FDA-required safety and efficacy trials. One company elected to put colchicine through the FDA's approval protocol and when approval was granted in 2009 the FDA announced a ban on five unapproved brands of colchicine on the market and gave proprietary rights to one approved brand. Sudden brand changes following this regulation led to a therapeutic crisis for FMF patients and coincidentally revealed unrecognized patterns of response to different brands of colchicine.

An effort was undertaken to document and characterize the brand specific response of individual FMF patients participating in FMF support groups on the internet and determine the potential of multiple brand exposure for improving the effectiveness of colchicine by reducing intolerance and resistance rates. An online survey of FMF patients participating in patient support groups on Facebook and Yahoo was conducted. Patients residing in the U.S. were asked to report each brand of colchicine they had ever taken and to indicate for each brand whether their response was satisfactory; unsatisfactory, but kept taking it; or unsatisfactory and discontinued it.

40 FMF patients reported taking 11 brands of colchicine; a total of 101 individual/brand trials. Of 31 patients taking 2 or more brands, 3 brands was the average tried. FMF patients revealed a highly idiosyncratic response to different brands of colchicine. Adverse responses and ineffectiveness were common for all brands ranging from 81% (FDA approved brand) to 30% (FDA banned brand). A critical finding was that all 9 patients discontinuing a brand for ineffectiveness ("colchicine resistance") had a satisfactory response to another brand. Despite the frequency of intolerance or ineffectiveness to individual brands, patients exposed to 2 or more brands had a satisfactory response to at least one brand.

Conclusions: Intolerance and ineffectiveness (i.e. "colchicine resistance") are not characteristics of FMF patients but are idiosyncratic brand responses. Most FMF patients could achieve a satisfactory therapeutic response to colchicine if three independent brands were available to them. Wider availability of brand options are needed for all FMF patients. Before resorting to higher-risk drugs, FMF patients should demonstrate intolerance/ineffectiveness to 3 brands of colchicine. This is a clinically simple therapeutic strategy, but the greater challenge is the maze of regulations governing the importance of pharmaceuticals across national borders.

Colchicine brands taken by 40 FMF patients and their responses to each brand

	1	2	3	4	5	6	7	8	9
Case #	U.S. approved	U.S. banned A	U.S. banned B	U.S. banned C	U.S. banned D	U.S. banned E	Canadian	Israeli	Turkish
1									
2									
3									
4									
5									
6									
7*									
8									
9									
10*									
11*									
12									
13									
14									
15									
16*									
17									
18									
19									
20									
21									
22		had taken another brand rated as satisfactory but could not identify it							
23									
24*									
25*									
26									
27*									
28									
29									
30									
31									
32									
33									
34*									
35*									
36*									
37*									
38									
39*									
40									

satisfactory | unsatisfactory, kept taking | unsatisfactory, discontinued

*cases age <15 years

References

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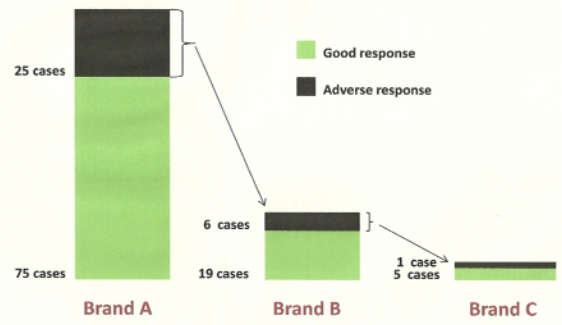
Hypothetical Algorithm for Colchicine Brand Switches Necessary for a Good Clinical Outcome in 100 FMF Patients

(assuming 75% good outcome for all brands)



Results: shown in the table, illustrate how the transition from five brands of colchicine (brands # 2-6) to a single brand (brand # 1) became a therapeutic crisis.

- Of brands that were taken by 10 or more patients, the FDA "approved" brand had the lowest percent of patients with a satisfactory response (14.2%) and the highest percent of patients who discontinued due to adverse response (52.4%) including 2 patients who received hospital treatment.
- By contrast, 70.6% of patients taking "banned" brand A , 63.6% taking "banned" brand B, and 78.6% taking the Canadian brand, reported a satisfactory response; while 9.0%, 27.3% and 21.4% of patients taking banned brands A and B, and the Canadian brand, respectively, discontinued due to adverse response.
- Of 30 total instances of discontinuation due to adverse response, ineffectiveness of the brand was cited in 9 instances, suggestive of cases that might be classified as "colchicine-resistant."
- Finally, in every case of adverse response to the FDA-approved brand, patients reported having had a satisfactory response to at least one other brand, either banned in the U.S. or a foreign brand.

Conclusion: Although observed in the U.S., the principle of idiosyncratic brand response applies to all FMF patients, with whom we share a common need for global access to colchicine. Achieving this goal will offer a renewed opportunity for FMF patients to realize the full therapeutic potential of colchicine.