

Incidence of Lipoatrophy Associated with Autoinjection Versus Manual SQ Injection of Glatiramer Acetate

Vu A. Nguyen, student; Ronald O. Bailey, M.D.; and Carina G. Sprague, LVN

Riverside Medical Clinic, Riverside, CA



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OBJECTIVES

- Compare the incidence of lipoatrophy associated with long-term use of autoinjection versus manual SQ injection of glatiramer acetate (GA) in a large clinical practice population of multiple sclerosis (MS) patients.

BACKGROUND

- The prevalence and severity of lipoatrophy with long-term GA therapy is unknown.
- In the GA prescribing information, the incidence of lipoatrophy has been reported as occurring "in approximately 2% of patients exposed to COPAXONE 20mg per ml in the 5 placebo-controlled trials compared to none on placebo and 0.5% of patients exposed to COPAXONE 40mg per ml in a single placebo-controlled trial and none on placebo."¹
- In contrast, lipoatrophy occurrence related to GA injection has been reported as high as 45% in an independent study.²
- Speculation surrounds the exact cause of lipoatrophy, although GA injection may lead to an elevation in tumor necrosis factor-alpha that causes a dedifferentiation of adipocytes in SQ tissue.

METHODS

- A total of 73 MS patients maintained on GA (mean 36 months) were given the option of use of autoject 2 (autoject 2 apparatus was provided through Shared Solutions) versus manual SQ injection.
- 40 patients (54.8%) employed autoinjection and the remaining 33 patients (45.2%) opted for the manual SQ injections.
- Both groups were followed with clinical examination and serial photographs at three month intervals over 3 years.
- All patients were counseled on proper injection site rotation and methods at each visit.

RESULTS

- A total of 46 patients (63%) taking GA developed lipoatrophy over a 3-year interval. Thirty-five (88%) out of the 46 patients developed lipoatrophy with the use of autoject 2.
- Lipoatrophy occurrence was predominantly in women. Multiple injection sites were often involved in the same patient.
- In some patients lipoatrophy occurred in the first 3 months of GA therapy and was severe enough to cause the patient to switch to another MS disease modifying therapy.
- Lipoatrophy was permanent, at times severely disfiguring, and was often associated with some psychological impact.
- Four case vignettes of the 35 patients developing lipoatrophy with autoject 2 use are presented along with photographs.

Figures 1a and 1b

Case 1. 32 year old woman with relapsing-remitting (RR) MS, EDSS 2.5, who was taking GA by autoinjection for 4 years.

Note marked disfiguring lipoatrophy in tissue above the area of the triceps muscle bilaterally. Lipoatrophy began one year after the start of GA autoinjection.

Figure 1a.

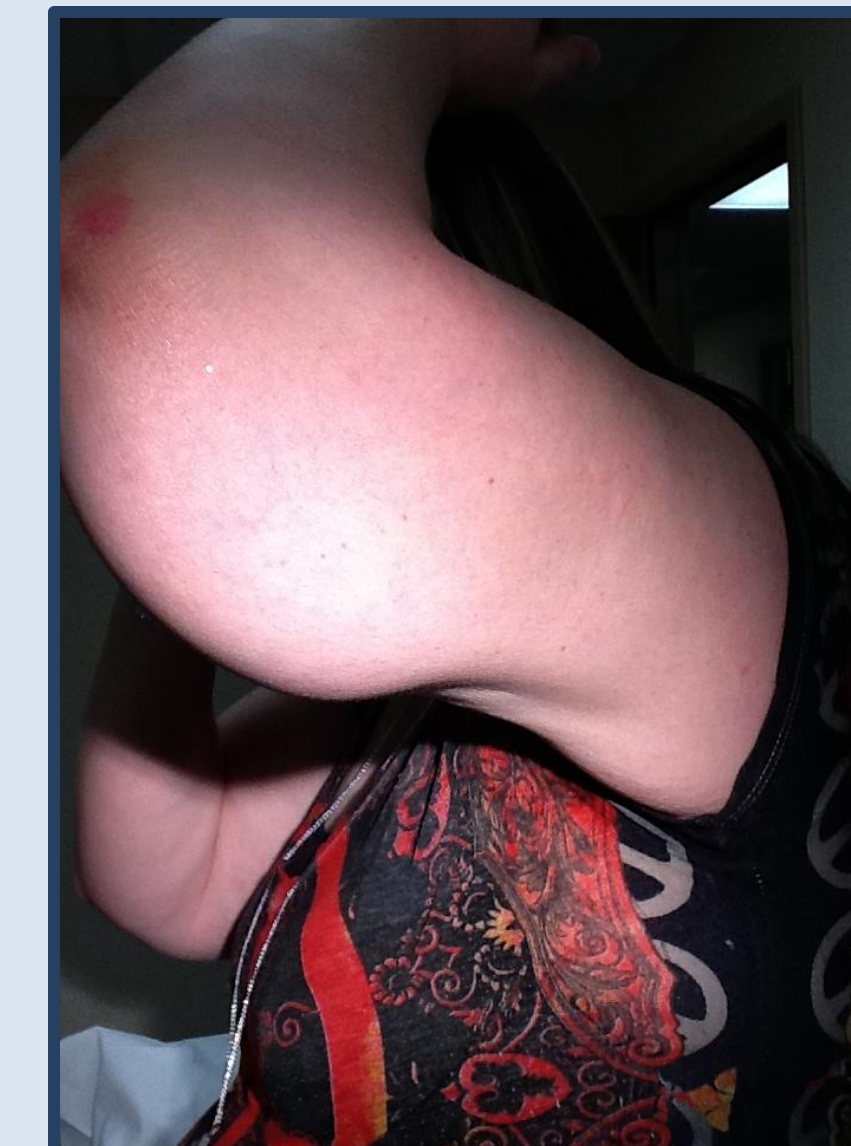


Figure 1b.



Figure 2a.



Figure 2b.



Figures 2a and 2b

Case 2. 44 year old woman with RRMS, EDSS 3.0, who had been on GA by autoinjection for 3 years.

Note multiple indentations in the posterior arms. Lipoatrophy began in the 3rd month of use of GA autoinjection.

Figures 3a, 3b and 3c

Case 3. 52 year old woman with RRMS, EDSS 3.5, who had been taking GA for 4 years using autoject 2.

Note multiple areas of lipoatrophy in the posterior right arm, and right thigh which worsened over time. Lipoatrophy began in 6 months after start of GA autoinjection.

Figure 3a.



Figure 3b.



Figure 3c.

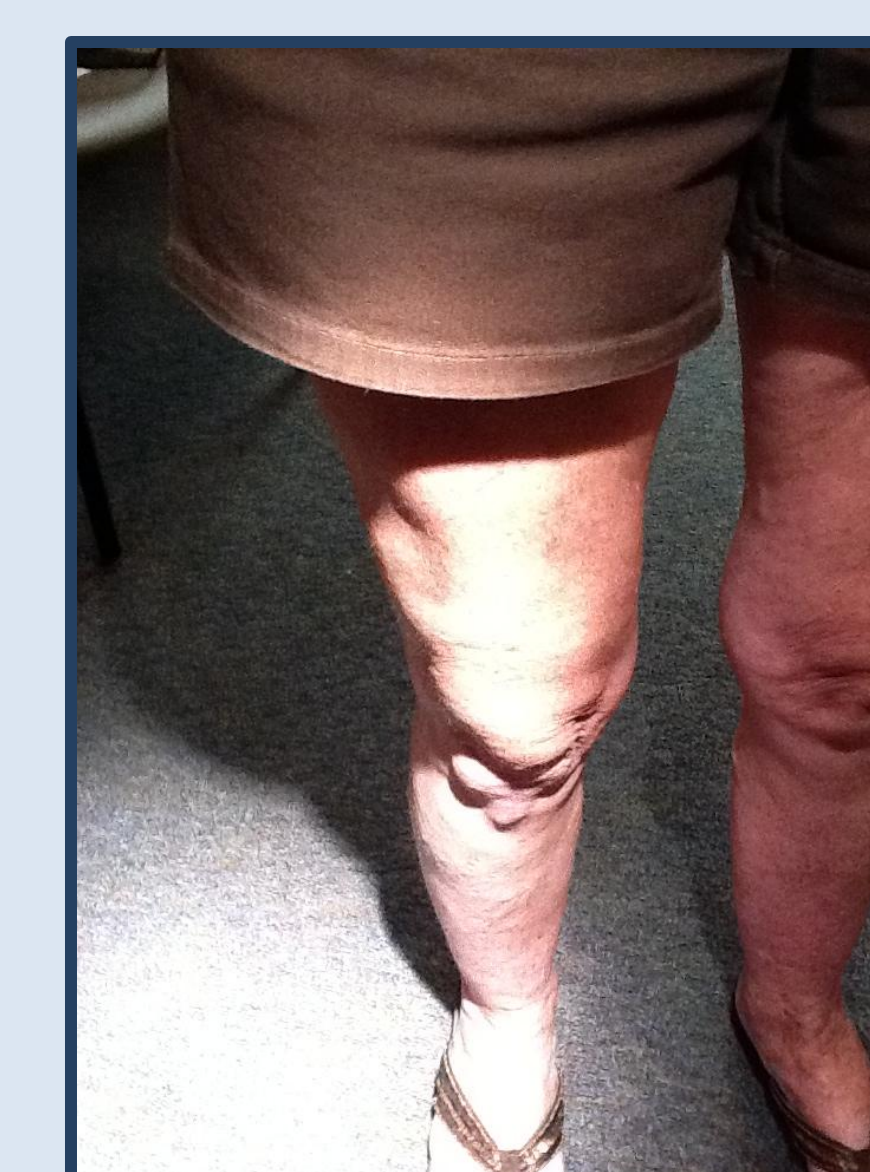
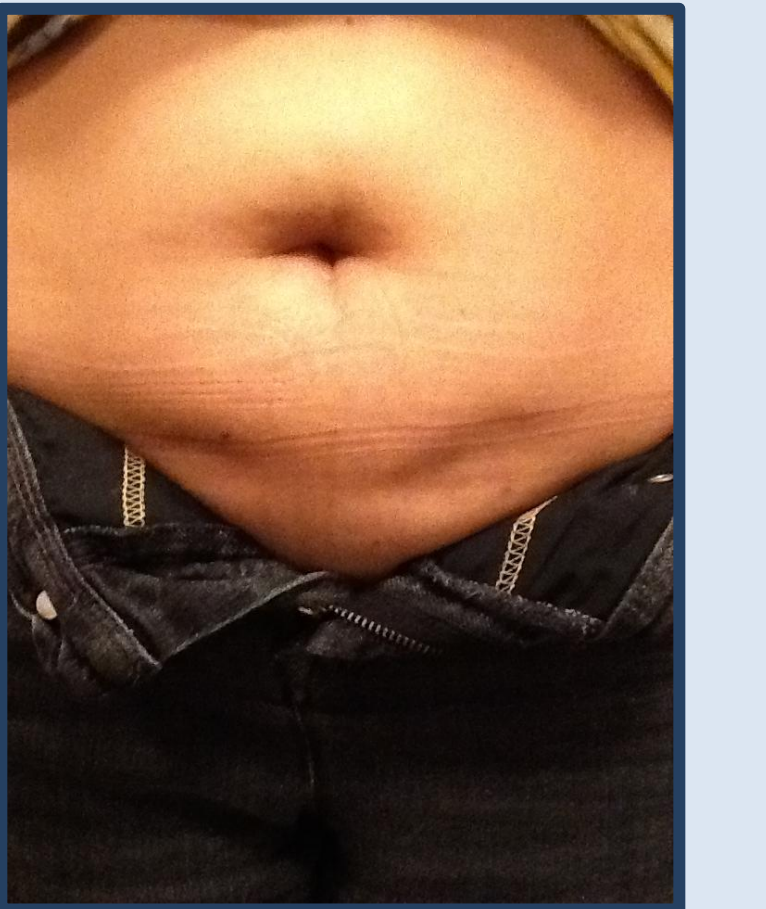


Figure 4

Case 4. 48 year old woman with RRMS, EDSS 3.0, who had been taking GA by manual SQ injection for 2 years.

Note dimpling of lower abdomen at sites of GA injection. Lipoatrophy began in the 4th month after the start of GA autoinjection.

Figure 4.



CONCLUSIONS

- Lipoatrophy can be severely disfiguring and is invariably permanent.
- The occurrence of lipoatrophy was highest in the autoinjection group, was substantively higher than previously reported and was often the solitary factor in prompting patients to switch to another MS agent.
- Lipoatrophy occurrence was found predominantly in women.
- A heightened risk of lipoatrophy is an inherent autoimmune problem and may not necessarily be mitigated by vigilant injection site rotation irrespective of the methodology of GA administration.
- The psychological consequences may be significant.

REFERENCES

- Copaxone® (glatiramer acetate) prescribing information. TEVA Pharmaceuticals, January 2014.
- Edgar CM, Burnet DG, Fento P, et al. Lipoatrophy in Patients with Multiple Sclerosis on Glatiramer Acetate. Can.J. Neurol. Sci. 2004; 31: 58-63

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