Eur J Clin Pharmacol (2009) 65:1061–1062
DOI 10.1007/s00228-009-0681-0

LETTER TO THE EDITORS

Pitfalls in patient self-management of subcutaneous drug application: removal of rubber protection caps from ready-to-use syringes

Seraina Mengiardi · Beat Goepfert · Dimitrios A. Tsakiris · Kurt E. Hersberger

Received: 22 April 2009 / Revised: 26 May 2009 / Accepted: 1 June 2009 / Published online: 18 June 2009

Sirs,

Outpatient subcutaneous therapies are becoming more and more common, such as the use of low-molecular-weight heparins (LMWH) for prophylaxis or for the therapeutic treatment of thromboembolisms, multiple sclerosis, arthritis, anemia, or female infertility. Based on reports from patients and nurses indicating that some ready-to-use syringes require a concerted effort to remove the rubber protection cap, we decided to evaluate cap removal forces of commercial LMWH pre-loaded syringes as we were unable to find an ISO-norm from such syringes nor studies on this topic.

Three methodological approaches were used: (1) self-assessment by a study population, (2) simultaneous observer's assessment, and (3) mechanical pull-off tests.

In parts (1) and (2) of our study, we analyzed Clexane (enoxaparin; old device), Fragmin (dalteparin), and Fraxiparine (nadroparin), three widely prescribed LMWH products in Switzerland. The study population included 68 persons (age range 19–86 years, median age 29 years), of whom 34 were pharmacy students, 18 were hospitalized orthopedic patients, and 16 were pharmacy customers. Persons with obvious disabilities of the upper extremities were excluded. One syringe of each brand within its expiration date was given to each of the subjects in randomized order. In part (1), subjects rated the force needed to remove the rubber protection cap using a visual analog scale (VAS). In part (2), the observer rated the effort needed to remove the cap as: (1) no effort needed, (2) effort needed, or (3) can not remove the protection cap. In part (3), the pull-off forces were investigated on a standard mechanical testing machine. The custom-designed holding fixture allowed an axial pull-off of the cap, measured in Newtons (N), at a constant speed without shear forces. In addition to the syringes used in parts (1) and (2), we enlarged the study sample with Arixtra (fondaparinux), Clexane (new device with an automatic safety system), and Sandoparin (certoparin), which meant that our study included the most important brands. Of each brand, 20 syringes within the expiration date were tested in randomized order (two different lots of ten syringes per lot).

The results of part (1) of this study revealed that the removal of the rubber protection cap was not possible in five of 204 cases involving four subjects and two brands. Figure 1a shows significant differences between the VAS scores (ANOVA $p<0.001$; Tukey-B-test $p<0.05$ for pairwise differences between the mean values) and high interquartile ranges caused by highly individual self-estimations. The observer's results from part (2) supported these findings (Fig. 1b). Measurements of the mechanical cap-pull-off forces (part 3) showed a large range of median forces (13.6–29.9 Newton) were needed to remove the rubber caps, with the highest forces needed for Fraxiparine and the old Clexane device (ANOVA $p<0.001$; Tukey-B-test $p<0.05$). Significant differences between different lots of the same brand were detected only with Fraxiparine (Fig. 1c).

S. Mengiardi (✉) · K. E. Hersberger
Institute of Clinical Pharmacy, University of Basel,
Pharmacenter, Klingelbergstrasse 50,
4056 Basel, Switzerland
e-mail: seraina.mengiardi@unibas.ch

B. Goepfert
Laboratory for Orthopaedic Biomechanics, University of Basel,
Pharmacenter, Klingelbergstrasse 50,
4056 Basel, Switzerland

D. A. Tsakiris
Division of Hematology, University Hospital Basel,
Spitalstrasse 21 / Petersgraben 4,
4031 Basel, Switzerland

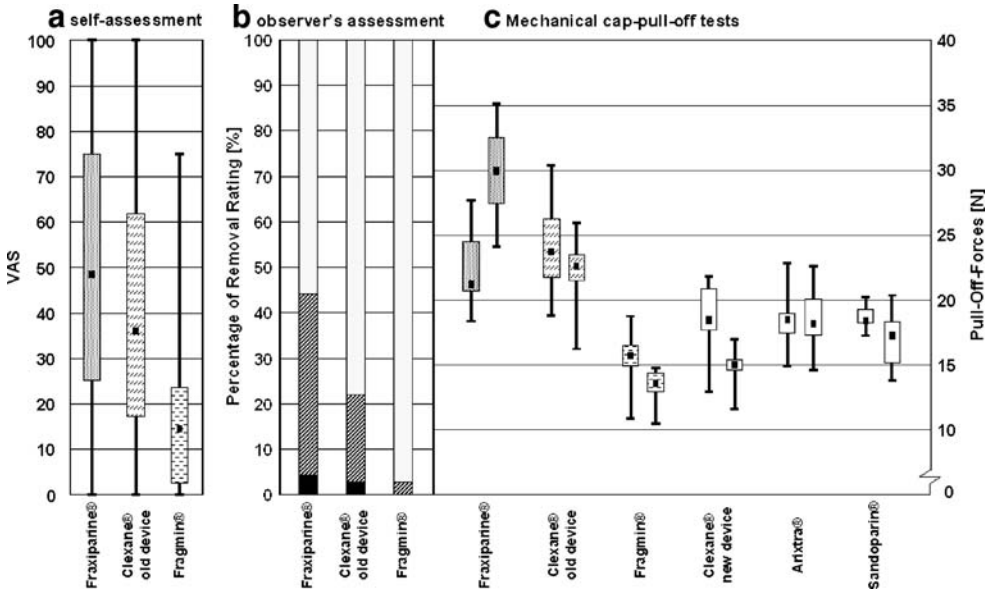

Fig. 1 Determination of the pull-off forces needed to remove the rubber protection caps from ready-to-use syringes. **a** Self-assessment using the visual analog scale: 0 = no effort/100 = enormous effort. Values are presented as the median and interquartile range (IQR): Fraxiparine 48.5 (49.75), Clexane old device 36.0 (44.5), Fragmin 14.5 (20.75). **b** Simultaneous observer's assessment using three assessments (%): *black portion of bar* person can not remove the protection cap (Fraxiparine 4.41; Clexane old device 2.94; Fragmin 0), *portion of bar with diagonal stripes* person needs to make some effort (Fraxiparine 39.71; Clexane old device 19.12; Fragmin 2.94), *open portion of bar* person needs no effort (Fraxiparine 55.88; Clexane old device 77.94; Fragmin 97.06). **c** Mechanical pull-off tests (N) performed by a standard mechanical testing machine; each *bar* indicates one lot including ten syringes. Values are given as the median and IQR

In conclusion, the mechanical cap-pull-off tests confirmed the results from self- and observer's assessments, and important differences between brands were observed. The pull-off forces correspond roughly to the force needed to hold a narrow-neck plastic flask containing 1–3 l of water by pinching the neck between a finger and thumb. Medical staff should be aware of these possibly crucial handling difficulties and their consequences for successful therapy and compliance.