# Menorrhagia in hemorrhagic disorders:

# a new, simple quantitative method for its evaluation.

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## Introduction:

Menorrhagia is a very prevalent bleeding symptom in congenital bleeding disorders (from 60 to 100%) and in patients on Oral Anticoagulants (OA), but no prospective studies are available.

## Methods:

We have validated, in a cohort of healthy women not on contraceptives (n= 85, age range 20-45y.), a novel, quantitative method for the measurement of menstrual losses (QUantitative Evaluation of Menses, [QUEM], ClinicalTrials.gov: NCTO1276964). QUEM, based on the weight measurement of the vacuum-preserved sanitary wears, was tested and compared (Bland and Altman plot) with the reference method, the Alkaline Hematin Method (AHM). In detail, each wear was collected in plastic bags and vacuum-sealed using a vacuum-sealing portable device. Collected bags were weighted, and the hematin content assessed within one month. (TAB.1)

**Table 1: Overall and day by day menstrual discharges.**

| | | Overall | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **n** | 85 | 85 | 85 | 78 | 49 | 19 | 3 |
| **AHM (mL)** | **median** | 22 | 10.0 | 6.9 | 1.8 | 0.7 | 0.4 | 0.1 |
| | **mean** | 22.9 | 10.7 | 8.6 | 3.0 | 1.3 | 0.6 | 0.1 |
| | **SD** | 14.5 | 6.2 | 6.6 | 3.3 | 1.4 | 0.5 | 0.1 |
| | **range** | 2.3.-73.6 | 1.3-33.1 | 0.1-28.3 | 0.0-15.2 | 0.0-5.4 | 0.0-2.1 | 0.0-0.2 |
| **QUEM (mL)** | **median** | 58 | 23,5 | 17,6 | 6,7 | 4,4 | 2,1 | 3,5 |
| | **mean** | 66 | 29,8 | 22,4 | 9,3 | 5,5 | 2,9 | - |
| | **SD** | 37.5 | 16,8 | 14,5 | 7,8 | 4,5 | 2,5 | - |
| | **range** | 9.5-188.4 | 3.6-79.7 | 2.2-69.4 | 0.59-36.9 | 0.12-22.7 | 0.005-9.6 | 0.4-5.0 |
| **Correlation AHM-QUEM** | **r** | 0.77 | 0.7855 | 0.8106 | 0.7032 | 0.5271 | 0.4427 | - |
| | **"p"** | P<0.0001 | P<0.0001 | P<0.0001 | P<0.0001 | P=0.0001 | P=0.0577 | - |
| | **CI** | 0.67-0.85 | 0.68-0.85 | 0.72-0.87 | 0.57-0.80 | 0.29-0.70 | -0.01-0.74 | - |

**Table 2: AHM and QUEM in menorrhagic patients**

| Menorrhagic patients | Menes duration | AHM | QUEM |
|---|---|---|---|
| - FVII deficiency | 7 | 83 | 355 |
| - On Oral anticoagulants | 7 | 109.5 | 253 |
| - FVII deficiency after treatment with FVII | 5 | 42 | 92.5 |
| - After OA withdrawal | 5 | 53.6 | 86.7 |
| - Upper reference value (x+2 SD) | 5 | 51 | 141 |

## Conclusion

**QUEM can be easily autonomously employed in an outpatient environment. Of relevance, sample stability allows multicentre studies to be performed.**

## Results:

The overall correlation (r) between QUEM and the reference method was 0.77(p<0.0001; CI 0.67-0.85) and the Bland and Altman approach showed that they were interchangeable and highly comparable. Also, a patient with a severe, congenital clotting defect (FVII deficiency, FVII<1%) and a patient on OA (INR value 2.5) complaining heavy periods, were evaluated by both methods. Menstrual discharge resulted higher than the upper range values in both conditions of impaired hemostasis, when measured with both QUEM and AHM. Further, correction of hemostasis (replacement therapy with recombinant FVIIa and withdrawal of oral anticoagulants) resulted in menstrual discharge within the range of normality, either with QUEM or AHM. (TAB.2)