Solutions to the Cockcroft-Gault Weight Debate

Due to limitations in the standard equation, many debates have formulated regarding the inability to accurately calculate the exact creatinine clearance (CrCl) value. These limitations can lead to potential drug dosing errors in various medications. A literature review of studies was conducted to determine the most accurate solution when addressing CrCl via the Cockcroft-Gault equation in obese patients. This issue of CLIPS briefly summarizes an article that advises an improved application of the standard Cockcroft-Gault equation when renally dosing obese patients. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.


Background

- Creatinine clearance (CrCl) is used to determine renal dosing in medications and is based on a patient’s individual age, weight, gender, and serum creatinine.
- The Cockcroft-Gault equation, published in 1976, has been widely accepted as the means to calculate CrCl for drug dosing from a combination of age, weight, gender, and serum creatinine. Due to its common use in clinical trials and ease of calculating, it is preferred by clinicians over the Modification of Diet in Renal Disease (MDRD) equation.
- The initial study that determined the Cockcroft-Gault equation recommended the use of ideal body weight or lean body weight for overweight patients with no evidence to support the suggestion.
- Due to an increased variance of the population’s weight and muscle distribution since the original publication of Cockcroft-Gault formula, recent studies have been performed to examine a more accurate way to apply the equation to an obese patient.
- Inaccurate calculations of CrCl can lead to an incorrect dose recommendation for renally excreted drugs (e.g., amoxicillin, gabapentin, piperacillin/tazobactam) and cause medication errors.
- This literature review is designed to formulate the optimal use of the Cockcroft-Gault equation in an obese population based on the consensus of multiple studies that focus on the limitations of the standard CrCl equation.

Methods

- A literature review was performed using PubMed MEDLINE utilizing studies from 1980 to April 2013.
- Search terms used were Cockcroft-Gault, body weight, and obesity with an English-language limit.
- The review utilized studies that were not limited to obese patients but discussed the limitations of the Cockcroft-Gault equation.

Results

- Three studies were reviewed to conclude how Cockcroft-Gault is optimally used in an obese population. Table 1 summarizes the results of each study.

CONTINUED NEXT PAGE
Table 1. Summary of Study Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>Results</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilhelm SM, et al. (2011)</td>
<td>Compared the Cockcroft-Gault equation to 24-hour measured CrCl in 1197 patients.</td>
<td>For the obese patients, TBW overestimated CrCl. ABW with a correction factor of 0.3 or 0.4 slightly overestimated CrCl with a mean not significantly different from the measured CrCl. NBW concluded less bias than ABW.</td>
<td>NBW resulted in the least bias but did not have a recorded formula to correct the patient’s weight to 70 kg in order to eliminate weight from the equation. Second to NBW was ABW with a correction factor of 0.3 or 0.4.</td>
</tr>
<tr>
<td>Meta-analysis of 13 studies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demirovic JA, et al. (2009)</td>
<td>Compared the limitations of Cockcroft-Gault equation to 24-hr measured CrCl in 54 patients with a BMI &gt;40 kg/m².</td>
<td>TBW overestimated CrCl, IBW underestimated CrCl, and ABW with 0.3 and 0.4 adjustment factors overestimated CrCl. FFW created the least bias. Estimated LBW was comparable to FFW.</td>
<td>Despite its accuracy, FFW is not likely to be used due to an extensive procedure to acquire the value. Therefore, LBW is the least biased weight calculation.</td>
</tr>
<tr>
<td>Cross-sectional study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Winter MA, et al. (2012)</td>
<td>Analysis of 3678 patients comparing the Cockcroft-Gault equation with 24-hr measured CrCl in various weight populations including three levels of obesity.</td>
<td>TBW and IBW overestimated CrCl in every obesity level. LBW underestimated CrCl. ABW with 0.4 adjustment factor was least biased.</td>
<td>ABW with an adjustment factor of 0.4 was most accurate, however, still a significantly biased calculation. Concluded that ABW was the least inaccurate.</td>
</tr>
<tr>
<td>Retrospective analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CrCl=creatinine clearance; TBW=total body weight; ABW=adjusted body weight: adjusts for the difference between TBW and IBW; NBW=no body weight; BMI=body mass index; IBW=ideal body weight; FFW=fat-free weight; bioelectric impedance analysis requires procedure; LBW= lean body weight; calculated from TBW and BMI

Conclusions
- Evaluation of studies led to no conclusive answer as to which weight calculation (e.g., TBW, ABW, NBW, LBW, IBW, or FFW) was most accurate when using Cockcroft-Gault in obese patients.
- Despite an inconclusive weight formula from these studies, a more efficient use of the Cockcroft-Gault equation in obese patients was identified.
- Due to multiple limitations and subsequently the inability to calculate an exact value from the equation, it is more reasonable to focus on changing the use of the equation rather than fixing the equation itself.
- The ultimate conclusion was found that Cockcroft-Gault is most effective in calculating a range of CrCl values which is guaranteed to include the exact CrCl value.

Summary
- In summary, using the Cockcroft-Gault equation to measure CrCl with IBW and TBW will create a minimum and maximum range of values, respectively, that will be used to further determine a renal dose of medication.
- If a calculated range of CrCl values spans over two dosing intervals, a clinician is then to use their professional judgment based on the patient’s risk versus benefit profile to determine which dosing interval should be used.

Prepared by: Mary Kyle Hall, Pharm.D. Candidate
Reviewed by: Rachel M. Slaton, Pharm.D., BCPS