Title: Warfarin-Drug Interactions: An Emphasis on Influence of Polypharmacy and High Doses of Amoxicillin/Clavulanate

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The objective of this study was to investigate the effect of polypharmacy and high doses of amoxicillin/clavulanate on warfarin response in hospitalized patients. This was a prospective cross-sectional observational study on 120 patients from July 2013 to January 2014. Potentially interacting drugs were classified according to their tendency of increasing international normalized ratio (INR) or bleeding risk. The 87.5% of patients prescribed high-dose amoxicillin/clavulanate (10-12 g daily) compared with 28.9% of patients prescribed a normal dose (up to 3.6 g daily) had INR values ≥4 during the hospital stay (P ≤ .001). Increased number of potentially interacting drugs that are known to increase INR was a significant predictor of having INR values ≥4 (OR, 2.5; 95%CI, 1.3-4.7), and increased number of potentially interacting drugs that are known to increase bleeding risk was a significant predictor of
experiencing bleeding episodes (OR, 3.1; 95%CI, 1.3-7.3). High doses of amoxicillin/clavulanate were associated with a higher risk of over-anticoagulation when combined with warfarin than were normal doses. Increased risk of having INR ≥ 4 and bleeding events was associated with increased numbers of potentially interacting drugs prescribed, indicating that polypharmacy is a problem of concern. Frequent monitoring of warfarin therapy along with patients’ medications is necessary to avoid complications.