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Tablet splitting: risk determination, epidemiology, and measures to improve prescribing quality

Geboren am 12.04.1976 in Albstadt-Ebingen
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Promotionsfach: Klinische Pharmakologie
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Tablets are frequently split by patients on oral drug therapy, a procedure which may have several advantages. Indeed, it may promote dose flexibility, ease swallowing, or save cost. However, not all tablets (and particularly not unscored tablets) are suitable for splitting. Splitting of modified release tablets may alter the effect of a drug and thus endanger patients' health and limit effectiveness. Therefore, distinct measures have to be taken to avoid the splitting of tablets not suitable for splitting.

We aimed to assess the frequency and determinants of tablet splitting in primary care in Germany and evaluated the quality of information on divisibility in the Summary of Product Characteristics (SPCs) and in the Package Leaflets (PLs) which act as legal sources of information for health care providers and patients. In a questionnaire survey among ambulatory patients of 59 general practitioners in the German Federal State Saxony-Anhalt we collected detailed information on all drugs of patients on at least three drugs. The response rate to the first questionnaire was 82.1% and 3158 tablets of 882 patients were included in the analyses. Of all tablets, 24.1% were split (762 of 3158). Of all split tablets, 8.7% (66 of 762) were unscored and 3.8% of all split tablets were not allowed to be split (29 of 762). Hence, this study revealed that ~1% of all solid oral formulations were probably destroyed before use because they were split even though not being suitable for splitting. This high frequency of inappropriate tablet splitting could not be solely explained by lack of drugs with appropriate strength because in about two thirds a switch to more suitable drugs would have been possible. However, the SPC and PL provided only limited information about divisibility. Only 22.5% of the SPCs of the split unscored tablets contained explicit information on divisibility and only slightly more than one third of the PLs of the split brands that were not allowed to be split stated that splitting was not appropriate. At this point the reasons for tablet splitting at such a high frequency was unclear and appropriate measures for prevention were thus difficult to design. In a second survey we therefore assessed why patients split tablets and what their attitudes towards tablet splitting are. This second survey (596 responding patients; response rate 66.4%) revealed that a large majority of patients splitting tablets (94.1%) did so as a result of a prescription. These findings suggest that tablet splitting is usually initiated by a physician i.e. triggered in the prescription process. The questionnaire also tested the knowledge of the patients on this topic and revealed that over one third of the patients

erroneously assumed that all tablets may be split and that over 80% of patients expected to find the respective information in the PLs. These findings emphasise the need for proper labelling of drugs, since the majority of patients expects to find this information in the PL and only a fraction of patients is aware that some tablets are not allowed to be split under no circumstances.

Having identified a lack of information during the prescription process as a likely cause for inappropriate tablet splitting we performed a prospective 2-period intervention study to test the effect of an electronic alert system on the prescription of inappropriately split drug regimens. In a university hospital equipped with an electronic prescription system (*AiDKlinik*) inappropriate splitting was evaluated at baseline and during an intervention that provided structured information on divisibility and issued alerts for each prescription error. Electronic prescriptions of 54 wards and clinics were collected. 20031 tablets and capsules of 4727 medication regimens were eligible for analysis (baseline period: 9545 drugs; intervention period: 10486 drugs). In this study 2.7% of all tablets and capsules, an important fraction of medication regimens of our university hospital, were inappropriately prescribed to be split (21.6% of all split tablets and capsules). During the intervention period, the frequency of inappropriate tablet splitting was nearly halved ($p < 0.0001$). Over 50% of the alerts that informed physicians about inappropriate dosage regimens prompted an adjustment of the medication regimens. However, while the adjustment in most cases clearly led to an improvement of the medication regimen, in about 15% (11 of 75) the adjustments could have been further improved, possibly by concurrently suggesting more appropriate drugs to the user with the alert.

In conclusion, the splitting of tablets in primary care is a frequent habit and almost 1% of all tablets are split that must not be split. In an overwhelming majority of patients, tablet splitting was prescribed by physicians, suggesting that the rather high frequency of inappropriate tablet splitting found in this population was initiated by the physicians and not by the patients themselves. This emphasises the need for appropriate information for prescribers at the time of prescription. It also suggests that patient education on drug application and its limitations should be improved and that authorities should take measures to improve labelling.