CRITICAL CARE

LETTER

Benefit of low-dose aspirin and non-steroidal anti-inflammatory drugs in septic patients

Maik Sossdorf[1,2], Gordon P Otto[1,3], Janina Boettel[2], Johannes Winning[1] and Wolfgang Lösche*[1,2]

Abstract

Analyzing medical records of 979 patients with severe sepsis or septic shock provided some evidence that the use of low-dose aspirin or non-steroidal anti-inflammatory drugs (NSAIDs) was associated with decreased hospital mortality. However, the benefit was abolished when aspirin and NSAIDs were given together.

Various retrospective clinical studies have shown that pre- and in-hospital use of low-dose aspirin was associated with a reduced mortality [1-4], but there is no evidence that NSAIDs may have a similar benefit [1,5]. We studied the medical records of 979 patients with severe sepsis or septic shock who were admitted to a university hospital surgical intensive care unit (ICU). Exclusion criteria were ICU stay of less than 48 hours, age of more than 18 years, and pregnancy. The study was approved by the local ethics committee. Investigators were not required to ask patients for informed consent.

Findings

Ninety-three patients had received NSAIDs (that is, ibuprofen, diclofenac, or indomethacin) during their ICU stay. There was no difference in APACHE (Acute Physiology and Chronic Health Evaluation) II score at ICU admission, but there were significant differences in age, gender, and length of ICU stay. In-hospital mortality was about 10% lower in NSAID users in comparison with non-users (Table 1). Medication during ICU stay with low-dose aspirin, clopidogrel, or statins, all three of which are believed to have a benefit on the outcome in sepsis, is also indicated in Table 1. A model of stepwise logistic regression with in-hospital mortality as a dependent variable and age, gender, APACHE II score, and the administration of NSAIDs, aspirin, clopidogrel, and statins as independent variables indicated that administration of aspirin during ICU stay was associated with a decreased mortality indicated by an odds ratio (OR) of 0.57 (95% confidence interval 0.39 to 0.83) but that NSAIDs, clopidogrel, statins, and gender were without significant effects. However, when patients on aspirin were excluded from the analysis, NSAIDs were

Table 1. Characteristics of the patients included in the study

Variables	All patients	Without NSAIDs	With NSAIDs	*P* value[a]
Number of patients	979	886	93	
Age, years[b]	67 (56-75)	67 (57-75)	61 (49-71)	0.001
Males/Females, percentage	66.2/33.8	64.7/35.3	81.6/19.4	0.002
APACHE II score[b]	23 (16-29)	23 (16-29)	22 (17-26)	0.160
Length of stay in ICU, days[b]	13 (6-23)	12 (5-22)	25 (14-18)	0.0001
Hospital mortality, percentage	42.0	42.9	33.3	0.076
Co-medication, percentage				
Aspirin[c]	28.0	26.7	39.8	0.008
Clopidogrel	6.2	6.5	3.2	0.208
Statins	21.2	20.4	29.0	0.054

[a]Significant differences between patients without and those with non-steroidal anti-inflammatory drugs (NSAIDs); [b]values are presented as mean (range); [c]100 mg/day. APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit.

*Correspondence: wolfgang.loesche@med.uni-jena.de
[1]Clinic for Anaesthesiology and Intensive Care Medicine, University Hospital Jena, Erlanger Allee 101, D-07747 Jena, Germany
Full list of author information is available at the end of the article

also associated with a reduction of the in-hospital mortality (OR = 0.50, 0.26 to 0.94). On the other hand, the benefit of aspirin (acetylsalicylic acid) was completely abolished in those patients who also received NSAIDs (OR = 1.12, 0.55 to 2.25).

The data of the present study indicate that, given separately, both aspirin and NSAIDs may reduce mortality in patients with sepsis. The interaction between aspirin and NSAIDs needs to be considered in forthcoming trials looking for benefits of either compound in patients with sepsis. We speculate that the lack of benefit of parallel use of aspirin and NSAIDs is due to a higher bleeding risk or anti-inflammatory action or both.

Abbreviations
APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; NSAID, non-steroidal anti-inflammatory drug; OR, odds ratio.

Competing interests
The authors declare that they have no competing interests.

Acknowledgments
This study was supported by the German Federal Ministry of Education and Research within the 'Center for Sepsis Control and Care'.

Author details
[1]Clinic for Anaesthesiology and Intensive Care Medicine, University Hospital Jena, Erlanger Allee 101, D-07747 Jena, Germany. [2]Center for Sepsis Control and Care, University Hospital Jena, Erlanger Allee 101, D-07747 Jena, Germany. [3]Department of Internal Medicine, Division of Nephrology, University Hospital Jena, Erlanger Allee 101, D-07747 Jena, Germany.

Published: 8 January 2013

References

1. Eisen DP: **Manifold beneficial effects of acetyl salicylic acid and non-steroidal anti-inflammatory drugs on sepsis.** *Intensive Care Med* 2012, **38:**1249-1257.
2. Winning J, Neumann J, Kohl M, Claus RA, Reinhart K, Bauer M, Lösche W: **Antiplatelet drugs and outcome in mixed admissions to an intensive care unit.** *Crit Care Med* 2010, **38:**32-37.
3. Winning J, Reichel J, Eisenhut Y, Hamacher J, Kohl M, Deigner HP, Claus RA, Bauer M, Lösche W: **Anti-platelet drugs and outcome in severe infection: clinical impact and underlying mechanisms.** *Platelets* 2009, **20:**50-57.
4. Sanchez MA, Thomas CB, O'Neal HR: **Do aspirin and statins prevent severe sepsis?** *Curr Opin Infect Dis* 2012, **25:**345-350.
5. Bernard GR, Wheeler AP, Russell JA, Schein R, Summer WR, Steinberg KP, Fulkerson WJ, Wright PE, Christman BW, Dupont WD, Higgins SB, Swindell BB: **The effects of ibuprofen on the physiology and survival of patients with sepsis. The Ibuprofen in Sepsis Study Group.** *N Engl J Med* 1997, **336:**912-918.

doi:10.1186/cc11886
Cite this article as: Sossdorf M, *et al*.: **Benefit of low-dose aspirin and non-steroidal anti-inflammatory drugs in septic patients.** *Critical Care* 2013, **17:**402.