Negative pressure wound therapy: violation of ethical and scientific standards

24 September 2018

About one decade after its first benefit assessment of negative pressure wound therapy (NPWT), the German Institute for Quality and Efficiency in Health Care (IQWiG) is reassessing this treatment method. However, then as now, its benefit and harm are unclear. Whereas only few studies with very limited informative value were available in 2006, over 100 clinical comparisons with several thousands of patients have been conducted since. But results have been published for only some of these studies, as not only the manufacturers of the medical devices used, but also researchers, are concealing data, thus violating ethical and scientific standards. Assessing the benefit and harm of the treatment solely on the basis of the published data could have entailed a seriously biased result. Hence, there is still no valid basis for the assessment of the benefit and harm of this treatment.

The current report deals with NPWT for wounds healing by secondary intention; wounds healing by primary intention are the subject of a second benefit assessment. In NPWT, negative pressure in the wound is used to promote wound healing, and to accelerate the healing of large wounds in particular.

Over 100 studies with several thousands of participants

The Institute has now found that a large number of further randomized controlled trials (RCTs) comparing NPWT with standard treatment have been completed since its last report. There are currently over 100 studies involving several thousands of patients, which is an unusually large number for a non-drug intervention. One would think that this would be a good starting point for a benefit assessment.

Publication bias: positive effect often overestimated

The inclusion of the results of all studies in the assessment is indispensable to be able to draw reliable conclusions. The use of only published data could lead to an overestimation of the positive effects of a medical intervention, because it is known from research that studies with "unfavourable" results are usually the ones that remain in the file drawer or are published only years later. This is referred to as "publication bias".

For this reason, IQWiG not only conducts searches in databases or registries, but also sends requests to manufacturers and authors who have reported studies in journals, trial registries or presentations, for example. "Detective work" is sometimes required to identify studies.

Agreement with sponsors to facilitate cooperation

To be able to also use the results from studies sponsored by manufacturers as completely as possible and to facilitate cooperation, the Institutes regularly offers a contract to such sponsors, which has advantages for both sides: Confidential information such as confidential business and commercial information remains protected in any case. In return, the manufacturer agrees to submit the complete data on all published and unpublished studies. IQWiG may use and publish the results and the underlying methods.

The Institute has concluded such a contract with several manufacturers of NPWT systems. This is a comprehensive agreement, i.e. irrespective of a division of the commission by type of wound (primary, secondary).

Data missing for a large proportion of relevant studies

Many of the newly searched RCTs recorded and reported usable data on so-called patient-relevant outcomes such as mortality, wound closure, pain,

complications (of treatment), length of hospital stay, or need of long-term care, and were therefore relevant for the assessment. However, there were also a large number of studies for which the results were not available, although the Institute had repeatedly requested information from the respective study investigators.

KCI does not comply with the contract

Despite several requests, the US-based manufacturer KCI Medical Devices (Acelity) provided neither a complete overview nor complete clinical study reports on all the studies for which the company is responsible. As a result, data were incomplete for half of all participants (842 of 1681). The IQWiG researchers therefore could not consider these studies for their benefit assessment of NPWT.

Standards violated also by researchers

However, there are also gaps in the remaining studies, most of them so-called investigator-initiated trials (IITs), which were, for example, initiated by university-based researchers: Regarding secondary wound healing, usable study results were missing for at least 1703 of 4251 participants in total, corresponding to 40%. Since this magnitude impedes a meaningful interpretation of the results, here too, the Institute dispensed with an assessment of benefit and harm.

Nothing is known about the researchers' motives. Their own research interests or dependencies might play a role. It is obvious at least for some of the IITs that even though the manufacturers did not act as sponsors, they were involved indirectly, e.g. by granting scholarships or by supporting the analysis of the data and the production of manuscripts (medical writing).

Concealing data harms patients and physicians

Stefan Sauerland, Head of the Department of Non-Drug Interventions, notes with frustration: "The evidence base was meagre when we conducted our first assessments. Now there are studies with several thousands of patients, but we still cannot say whether NPWT is better, equivalent, or possibly even worse than conventional wound treatment."

The reason is that both companies and researchers are concealing data. "This violates ethical and scientific standards", says Stefan Sauerland. "And they harm patients and physicians as well as the community of insured citizens, which to me, as a physician and researcher, is very disconcerting."

Registration and publication of the results must be mandatory

NPWT is an example showing that further legal regulations are required, also for studies on non-drug interventions and medical devices. Unlike in other countries such as the United States, medical devices in Europe are not subject to a central approval process. A certification by "designated bodies", which are private sector organizations, is sufficient to launch a medical device. In many cases, clinical studies have not been necessary for this, even though Europe's Medical Device Directive is a considerable improvement for the requirements of a clinical assessment. In addition, in Germany, almost all new non-drug interventions can be used in hospitals and be reimbursed by statutory health insurance funds without prior assessment of their benefit or harm. A positive benefit assessment is only required for the outpatient sector.

New legislation would have to stipulate the registration of studies on non-drug interventions or medical devices before their start and the timely publication of their results. "More progress has been made in drug studies", says Stefan Sauerland. An EU directive and the German Act on the Reform of the Market for Medicinal Products (AMNOG) have notably increased transparency regarding drugs. Stefan Sauerland is convinced: "Without similar regulations, reliable data on interventions such as NPWT will still not be available in 10 years' time."

More information:
www.iqwig.de/en/projects-resul … -intention.9654.html