

Re: A dose of humility, BMJ 20.07.2015

„Paracetamol is „no better than placebo for back pain“ (BMJ 2015).

So why not put it this way: „Placebo is as good as ...“ and make every effort to improving physician-patient-relationships (Benedetti 2013). The term placebo („Placebo Domino in regione vivorum“, Vulgata 114:9) is misleading. E.g. a placebo-control might contain the same adjuvant as the verum-group (Villa 2005/2006).

Our current knowledge of placebo-effects should have scientific implications (Benedetti 2014). We should refrain from shame-surgery or pseudo-placebo-treatments, which are still ethically accepted in Germany under certain conditions (BÄK 2010).

Treatments come with different effects:

- Specific (receptor oriented)
- Weakly specific (off target: side effect)
- Systemic: (e.g. mother-newborn-relationship, health-communication, the art of touching a patient, ...)

RCTs are perfectly designed to measure specific effects. The observation of system-effects might need longer time-periods, different designs (cmRCT? Relton 2010), and other indicators: „quality through the patient’s eyes“, less costs for further medications, behavior change, qualitative observations etc.

Systemic effects might also be induced by highly specific devices or chemical products (e.g. adjuvants targeting specific receptors, 3D-“baby-television“-ultrasound, vagus-nerve-stimulation ...). These products (designed for systemic outcomes) are less controlled than specific interventions.

Homeopathy is a good example to reflect on specific and systemic effects:

- The mortality of cholera in the 19th century was about 40%
- Specific standard treatment (blood-letting and fluid restriction) raised

the mortality rate to about 60%.

- Hahnemann reported far better results, because he diluted the specific effect to absolute zero, eliminated all side effects, let his patients drink, as much as they wanted, talked to them and refrained from bloodletting (Hahnemann 1831). Florence Nightingale went even further and concentrated herself completely on the systemic cure-effect (care without a believe-system).

The problem with homeopathy is that the physician who uses it has to be absolutely convinced that the effect is indeed „specific“. His strong belief is than mirrored by the patient, who therefore is convinced that the future will be positive. Therefore homeopathy is a belief-system which might induce systemic effects (and very weak or non-specific effects). It has no “specific” side effects, but surely can cause harm, if a specific standard treatment would work better.

In Pharmacology and in gene-technology highly-specific molecules will be designed in the near future to trigger powerful non-specific (system effects) E.g stimulation of the Toll-like Receptor to cause an immune system alert. For these substances, the usual trials do not apply, as their effects cannot be described using classic RCT. In modern vaccine-studies (in which the small antigen snippets cannot elicit an immune response), the adjuvant (causing the system response) has to appear in the verum and in the control. Therefore, in recent “placebo-controlled”-studies the zero-control does not contain „nothing“ but „something“, which can cause specific side-effects (Gøtzsche 2016). E.g.: Narcolepsy incidence 2009: ~1:10,000 Pandemrix vaccinations. (Sturkenboom 2015, Ahmed 2015)

We should study systemic effects more seriously.

There might be an evolutionary reason why a far too optimistic homo sapiens (Sharot 2011) feels pessimistic when ill, and why he needs someone to care for him, in order to let his nature do the cure (Placebo-Paradox: Humphrey 2012).

If we understand systemic effects better, we might improve health outcomes and use less specific treatments, thereby reducing costs – and the need for over-diagnosis, overtreatment and medicalization.

We need new study designs to evaluate the effects of specific pharmacological substances triggering system effects in

- cancer-treatments,
- vaccinations,
- microbiom-psycho-neuro-endocrinology,
- neuro-psychiatry,
- genetics-epigenetics ...

And we should establish long-term observations of non-specific effects e.g.

- postmarketing studies of blockbusters (eg. PPI)
- neonatal development after interventions in pregnancy (eg. flu vaccination)

References

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1459-66: „The placebo contained the same adjuvant and was visually indistinguishable from vaccine ...“