Drug & Poison Information Center—Faculty of Pharmacy—Tanta University

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Breakthrough: Targeting Cancerous Tumors with Precision Using Nanorobots

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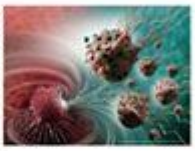

Researchers from Polytechnique Montréal, Université de Montréal and McGill University have achieved a spectacular breakthrough in cancer research. They have developed new nanorobotic agents capable of navigating through the bloodstream to administer a drug with precision by specifically targeting the active cancerous cells of tumors. This way of injecting medication ensures the optimal targeting of a tumor and avoids jeopardizing the integrity of organs and surrounding healthy tissues. As a result, the drug dosage that is highly toxic for the human organism could be significantly reduced. The research was done on mice, which were successfully administered nanorobotic agents into colorectal tumors.

These legions of nanorobotic agents were actually composed of more than 100 million flagellated bacteria -- and therefore self-propelled -- and loaded with drugs that moved by taking the most direct path between the drug's injection point and the area of the body to cure. The drug's propelling force was enough to travel efficiently and enter deep inside the tumors.

When they enter a tumor, the nanorobotic agents can detect in a wholly autonomous fashion the hypoxic zones and deliver the drug to them.

This hypoxic zone is created by the substantial consumption of oxygen by rapidly proliferative tumor cells. Hypoxic zones are known to be resistant to most therapies, including radiotherapy. To move around, bacteria used rely on two natural systems. A kind of compass created by the synthesis of a chain of magnetic nanoparticles allows them to move in the direction of a magnetic field, while a sensor measuring oxygen concentration enables them to reach and remain in the tumor's active regions.

By harnessing these two transportation systems and by exposing the bacteria to a computer-controlled magnetic field, researchers showed that these bacteria could perfectly replicate artificial nanorobots of the future designed for this kind of task.

This innovative use of nanotransporters will have an impact not only on creating more advanced engineering concepts and original intervention methods, but it also throws the door wide open to the synthesis of new vehicles for therapeutic, imaging and diagnostic agents.

Chemotherapy, which is so toxic for the entire human body, could make use of these natural nanorobots to move drugs directly to the targeted area, eliminating the harmful side effects while also boosting its therapeutic effectiveness.

Source:

- ***Felfoul O, Mohammadi M, Taherkhani S, et al. Magneto-aerotactic bacteria deliver drug-containing nanoliposomes to tumour hypoxic regions. Nat Nanotechnol. 2016 Aug 15. doi: 10.1038/nnano.2016.137.***

Stop ACE Inhibitors, ARBs before Non-cardiac Surgery

VISION study is an international prospective cohort study which was conducted at 12 centers in eight countries in Asia, Australia, Europe, and North and South America from 2007 to 2011 to evaluate the effect of Withholding *versus* Continuing Angiotensin-converting Enzyme (ACE) Inhibitors or Angiotensin II Receptor Blockers (ARBs) before Non-cardiac Surgery on the cardiovascular outcomes.

Methods:

- Authors analyzed data from 14,687 patients (including 4,802 ACE inhibitor/ ARB users) at least 45 yr old who had inpatient noncardiac surgery from 2007 to 2011.
- Using multivariable regression models, the authors studied the relationship between withholding ACE inhibitors/ARBs and a primary composite outcome of all-cause death, stroke, or myocardial injury after noncardiac surgery at 30 days, with intra-operative and postoperative clinically important hypotension as secondary outcomes.

Results:

- Of the 4802 patients taking ACE inhibitors or ARBs, 1245 (26%) stopped 24 hours before surgery and 3551 (74%) did not.
- The composite end point was met by 150 patients who stopped taking their medications and by 459 of those who continued (12.0% vs 12.9%).
- Patients who stopped medications were less likely than those who did not to meet the composite outcome (adjusted relative risk [aRR], 0.82; 95% confidence interval [CI], 0.70 - 0.96; $P = .01$).
- Those who stopped were also at lower risk for intraoperative hypotension than those who did not (aRR, 0.80; 95% CI, 0.72 - 0.93; $P < .001$).

- Patients with intraoperative hypotension were more likely to meet the composite outcome than those without (aRR, 1.23; 95% CI, 1.03 - 1.47; $P = .03$), as were those with postoperative hypotension (aRR, 2.01; 95% CI, 1.72 - 2.33; $P < .001$).

Conclusions: Withholding ACE inhibitors/ARBs before major non-cardiac surgery was associated with a lower risk of death and postoperative vascular events. A large randomized trial is needed to confirm this finding. In the interim, clinicians should consider recommending that patients withhold ACE inhibitors/ARBs 24 h before surgery.

Sources:

- ***Anesthesiology 2016 from the American Society of Anesthesiologists. From http://anesthesiology.pubs.asahq.org/article.aspx?articleid=2572372***
- ***Stop ACE Inhibitors , ARBs Before Noncardiac Surgery . From http:// www.medscape.com/viewarticle/871421***

Case Reports from the Egyptian Pharmaceutical Vigilance Center (EPVC)

Case reports from Sohag-Toxic level dose with Digoxin

The Egyptian pharmaceutical Vigilance regional center in Sohag has received 14 Individual Case Safety Reports (ICSRs) of toxicity with Digoxin administration and was manifested by nausea and vomiting in few cases. Seven of them for adult female patients, five for adult male patients, one for infant three months age and one for child male patient ten years old.

All of the adult patients had administered Digoxin tabet as (0.25 mg per day) and both the infant and the child had administered Digoxin injection as (0.01 mg/ kg per day) not for long time (from a week to 6 months). Then their automatic analysis showed Digoxin level above **2 ng** (toxic level); and since the normal level between (0.7 ng – 2 ng), then their physician stopped the administration of Digoxin.

Upon search, it was found that:

Digoxin toxicity: is indicated by nausea, vomiting, visual disturbances, and cardiac arrhythmias. Advanced age, low body weight, impaired renal function and electrolyte abnormalities predispose to toxicity.

Interpret the serum digoxin concentration in the overall clinical context, and do not use an isolated measurement of serum digoxin concentration as the basis for increasing or decreasing the LANOXIN dose.

Serum digoxin concentrations may be falsely elevated by endogenous digoxin-like substances. If the assay is sensitive to these substances, consider obtaining a baseline digoxin level before starting LANOXIN and correct post-treatment values by the reported baseline level.

Blood should be taken 6 hours or more after the last dose of digoxin. There are no rigid guidelines as to the range of serum concentrations that are most efficacious but most patients will benefit, with little risk of toxic symptoms and signs developing, with digoxin concentrations from 0.8 ng/ml (1.02 nmol/L) to 2.0ng/ml (2.56nmol/L). Above this range toxic symptoms and signs become more frequent and levels above 3ng/ml (3.84nmol/L) are quite likely to be toxic.

However, in deciding whether a patient's symptoms are due to digoxin, the patent's clinical state together with the serum potassium level and thyroid function is important factors. Other glycosides, including metabolites of digoxin, can interfere with the assays that are available and one should always be wary of values, which do not seem commensurate with the clinical state of the patient.

Source:

Egyptian Pharmaceutical Vigilance Center (EPVC) newsletter. October 2016, vol. 7, issue 10.

What Should You Know about Antibiotic Resistance???

What is antibiotic resistance?

Antibiotic resistance is the ability of bacteria or other microbes to resist the effects of an antibiotic.

It occurs when bacteria change in some way that reduces or eliminates the effectiveness of drugs, chemicals, or other agents designed to cure or prevent infections. The bacteria survive and continue to multiply causing more harm.

Why are bacteria becoming resistant to antibiotics?

Every time a person takes antibiotics, sensitive bacteria are killed, but resistant germs may be left to grow and multiply.

Repeated and improper uses of antibiotics are primary causes of the increase in drug-resistant bacteria. Smart use of antibiotics is the key to controlling the spread of resistance.

How do bacteria become resistant to antibiotics?

Antibiotics kill or inhibit the growth of susceptible bacteria. Sometimes one of the bacteria survives because it has the ability to neutralize or escape the effect of the antibiotic; that one bacterium can then multiply and replace all the bacteria that were killed off.

In addition, bacteria that were at one time susceptible to an antibiotic can acquire resistance through mutation of their genetic material or by acquiring pieces of DNA that code for the resistance properties from other bacteria. The DNA that codes for resistance can be grouped in a single easily transferable package. This means that bacteria can become resistant to many antimicrobial agents because of the transfer of one piece of DNA.

What about antibacterial-containing products?

An essential part of preventing the spread of infection in the community and at home is proper hygiene. This includes hand-washing and cleaning shared items and surfaces. Antibacterial-containing products have not been proven to prevent the spread of infection better than products that do not contain antibacterial chemicals.

Although a link between antibacterial chemicals used in personal cleaning products and bacterial resistance has been shown in vitro studies (in a controlled environment), no human health consequence has been demonstrated. More studies examining resistance issues related to these products are needed.

How can I prevent antibiotic-resistant infections?

1. Talk with your healthcare provider about antibiotic resistance:
   - Ask whether an antibiotic is likely to be beneficial for your illness
   - Ask what else you can do to feel better sooner.
2. Do not take an antibiotic for a viral infection like a cold or the flu.
3. Discard any leftover medication once you have completed your prescribed course of treatment.
4. Take an antibiotic exactly as the healthcare provider tells you. Complete the prescribed course of treatment even if you are feeling better.
5. Do not take antibiotics prescribed for someone else.
6. If your healthcare provider determines that you do not have a bacterial infection, ask about ways to help relieve your symptoms.

Source:
Antibiotic Resistance . From http://www.rxlist.com/antibiotic_resistance-page2/drugs-condition.htm#resistance

Ten key points for the appropriate use of antibiotics in hospitalized patients

(*Proposed by the Antibiotic Stewardship and Resistance Working Groups of the International Society for Chemotherapy***)**

1. Get appropriate microbiological samples before antibiotic administration and carefully interpret the results, in the absence of clinical signs of infection, colonization rarely requires antimicrobial treatment.

2. Avoid the use of antibiotics to 'treat' fever: use them to treat infections, and investigate the root cause of fever prior to starting treatment.

3. Start empirical antibiotic treatment after taking cultures, tailoring it to the site of infection, risk factors for multidrug-resistant bacteria, and the local microbiology and susceptibility patterns.

4. Prescribe drugs at their optimal dosing and for an appropriate duration, adapted to each clinical situation and patient characteristics.
5. Use antibiotic combinations only where the current evidence suggests some benefit.
6. When possible, avoid antibiotics with a higher likelihood of promoting drug resistance or hospital-acquired infections, or use them only as a last resort.
7. Drain the infected foci quickly and remove all potentially or proven infected devices: control the infection source.
8. Always try to de-escalate/streamline antibiotic treatment according to the clinical situation and the microbiological results.
9. Stop unnecessarily prescribed antibiotics once the absence of infection is likely.
10. Do not work alone: set up local teams with an infectious diseases specialist, clinical microbiologist, hospital pharmacist, infection control practitioner or hospital epidemiologist, and comply with hospital antibiotic policies and guidelines.

Source: Levy Hara G, Kanj SS, Pagani L, et al. Int J Antimicrob Agents. 2016 Sep;48(3):239-46. doi: 10.1016/j.ijantimicag.2016.06.015. Epub 2016 Jul 25.

Editorial board

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