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The Role of Traditional Medicine in Antibiotic Resistance

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Annotation: Antibiotics can undoubtedly save millions of lives, but at the same time, they can also cause harm, even to future generations, if used improperly! This once again raises the issue of the rational use of antibacterial agents and highlights the fact that, despite all efforts, there is a lack of knowledge in the global medical community about the potentially harmful aspects of antibiotic therapy. Ethiopian colleagues report on the irrational use of antibiotics, far from WHO recommendations, predominantly in injectable forms.

Keywords: traditional medicine, infection, antibiotics, anti-bacterial agents, antibiotic resistance, children.

According to research, antibiotics are often prescribed empirically—most commonly crystalline penicillin, gentamicin, and ampicillin—sometimes involving up to five types per patient. These prescriptions frequently address diagnoses such as pneumonia, sepsis, and meningitis. Pediatricians from Australia have similarly reported significantly higher antibiotic prescriptions for young children compared to other countries. Similar data exists for Russia and other CIS countries, indicating widespread antibiotic usage. For example, in Ukraine, the official vaccination rate for children does not exceed 29%, far below the required 95% for herd immunity, according to WHO.

Parental misconceptions further exacerbate the problem. A Lebanese study surveying 1,037 parents revealed that 40% still view antibiotics as beneficial for common colds, 36.2% expect faster recovery, and 37.9% mistakenly believe antibiotics treat viral infections. Additionally, one in five parents reduces the dosage if the child's condition improves. These findings highlight the lack of awareness about proper antibiotic use among parents.

A systematic review of parental knowledge in 20 countries over 20 years showed better understanding in higher socioeconomic groups in developed economies, where detailed physician explanations improved adherence to recommendations. Written instructions for parents have proven even more effective in promoting rational antibiotic use.

The growing popularity of "natural medicine" further complicates pediatric care. Surveys reveal that over half of Russians trust "folk medicine," though many confuse traditional Chinese remedies, homeopathy, and phytomedicines. Globally, the trend towards "natural medicines" has spurred organizations like the American Medical Association and the American Academy of Pediatrics (AAP) to issue statements. In 2017, the AAP updated its guidelines on integrative pediatrics, recognizing the increasing use of complementary methods, such as dietary supplements and yoga, in treating over 10% of children in the U.S., including those with chronic illnesses.

While certain practices like yoga have demonstrated benefits for children with ADHD, inflammatory bowel diseases, or juvenile arthritis, other methods lack regulation and rigorous evaluation. For example, some Ayurvedic medicines contain toxins or heavy metals, and "natural" homeopathic teething remedies have been found to contain toxic levels of belladonna, causing severe poisoning in children.

Inadequate regulation of dietary supplements and herbal products poses additional risks. For instance, St. John’s Wort interacts with anticoagulants, calcium channel blockers, and antidepressants, while herbal products like ginkgo biloba and cranberry may increase bleeding risks when combined with warfarin or aspirin. The National Center for Complementary and Integrative Health recommends against using such products in children and pregnant women due to the lack of safety studies.

Pediatricians urgently need comprehensive resources on the risks and benefits of alternative treatments. These tools are vital to educating parents, many of whom believe plant-based products are inherently safe. Distinguishing between proven phytomedicines and potentially harmful "natural remedies" is critical to ensuring child safety and effective care.

Indeed, such research exists, and evidence-based medicine has accumulated a significant body of work on a different class of plant-derived medicinal products. These phytomedicines are derived from raw materials grown in ecologically clean areas, with their harvesting, storage, and therapeutic formulation adhering strictly to Good Manufacturing Practices (GMP). While examples of truly high-quality phytopharmaceuticals are rare, they demonstrate that evidence-based principles can indeed apply to plant-based medicines.

Years ago, the concept of phytoniring—the combined use of high-quality natural plant materials and advanced pharmaceutical technologies—was proposed. Advocates of this approach invested considerable effort in proving the high efficacy and safety of their products through experimental and clinical studies. These studies aimed to establish the role of modern phytomedicines in mono- or combination therapy for common pediatric conditions where antibiotics are often overused by doctors and parents alike.

Notably, phytomedicines have been developed to treat acute conditions or prevent exacerbations of chronic diseases affecting the upper and lower respiratory tracts and ENT organs, such as rhinitis, sinusitis, otitis, and bronchitis. For example, significant antiviral effects were demonstrated in studies on the phytomedicine BNO1010-1016, 1085 (a combination of extracts from gentian root, primrose and elderflower, sorrel herb, and vervain), marketed under the name Sinupret. This preparation, available in liquid and tablet forms, inhibited influenza, parainfluenza, adenoviruses, rhinoviruses, and respiratory syncytial (RS) viruses by 30–80%. Additionally, it exhibited strong anti-inflammatory activity in a carrageenan-induced inflammation model.

The phytomedicine also demonstrated a pronounced dose-dependent anti-inflammatory effect comparable to indomethacin in terms of both exudate formation and mucosal infiltration by polymorphonuclear neutrophils. These experimental findings were later confirmed in clinical studies involving a large cohort of over 3,100 children aged 2 years and older with rhinosinusitis. The studies showed high efficacy of the drug, with very good or good results in 88% of cases and moderate results in 7%. The benefits included rapid relief from nasal congestion and the resolution of facial or headache symptoms in children aged 2–6 and 12 years.

An important advantage of this phytomedicine is its ability to reduce pathogenic bacterial colonization. This makes it effective in preventing respiratory viral infections (RVIs), even among young athletes—a particularly valuable feature in light of ongoing doping controversies involving Russian athletes.

The phytomedicine O 1030/1035 (marketed as Tonsilgon), available in the form of drops, syrup, tablets, and dragees, combines extracts from oak bark, marshmallow root, walnut leaves, dandelion herb, yarrow, horsetail, and chamomile flowers. It has demonstrated strong immunomodulatory effects in in vitro tests. These effects include significant enhancement of phagocytosis processes, activation of natural killer cells, increased cytolytic activity, and stimulation of interferon production by the tonsils.

In in vivo studies, this phytomedicine was shown to reduce the frequency of respiratory viral infection (RVI) episodes in frequently ill children and to alleviate the severity of viral infections associated with nasopharyngitis and tonsillitis.

Finally, regarding the phytomedicine BNO 1202/1205 (marketed as Bronchipret), designed for treating pediatric illnesses accompanied by cough, particularly bronchitis: this medication combines liquid extracts of thyme and ivy leaves (in drops or syrup form) and tablets with extracts of thyme, ivy leaves, and St. John's wort flowers. Several studies have demonstrated that using this medication can reduce the duration of illness and decrease the frequency of antibiotic prescriptions for children with prolonged coughs lasting over two weeks.

Moreover, a multicenter randomized double-blind placebo-controlled trial (E-BRO-PCT) with three study arms (antibiotic + placebo, placebo + phytomedicine, and antibiotic + phytomedicine) evaluated the efficacy and safety of this medication for treating acute bronchitis in children. The findings confirmed that phytotherapy is justified in all cases: patients with acute viral bronchitis benefit most from monotherapy with the phytomedicine, while those with acute bacterial bronchitis benefit from a combination of phytomedicine and antibiotics.

Given ongoing debates, particularly in pediatrics, regarding the necessity of antibiotics for acute bronchitis, a Cochrane systematic review was revisited in 2017. This review included 17 studies with 5,099 participants, once again demonstrating the limited evidence supporting routine antibiotic use in such cases.

Considering the above findings and the promising preliminary results of a new study comparing the effectiveness of a phytomedicine for urinary tract sanitation with fosfomycin in over 700 patients, a new concept of "empirical" treatment is emerging. This approach emphasizes treating acute respiratory tract infections (e.g., acute bronchitis), ENT disorders (e.g., acute sinusitis), or urinary tract infections (e.g., acute cystitis) without antibiotics. Instead, it advocates for the use of phytomedicines with proven efficacy for these clinical scenarios, ensuring absolute safety.

Under this new paradigm, empirical therapy would no longer imply the automatic, thoughtless use of antibiotics. Instead, it would align with its original intent: treatment initiated in cases of an uncertain diagnosis, where the therapeutic response (ex juvantibus) confirms the suspected condition.

Acute bronchitis, sinusitis, or cystitis will often resolve within a few days without antibiotics when treated with empirical monophytotherapy, as their etiology is most often viral, as noted above. If symptoms persist, these few days would be sufficient to obtain results from microbiological tests conducted at the onset of illness, allowing for the prescription of targeted antibacterial therapy.

This approach ensures that treatment is both effective and safe. Moreover, it significantly reduces the frequency of irrational antibiotic use, ultimately leading to a decline in antibiotic resistance.

The widespread use of antibiotics in practical healthcare, especially modern highly effective representatives, has saved millions of lives. At the same time, today, antibacterial drugs are considered a group frequently causing adverse reactions (ARs). Given the clinical significance of

antibiotics, it is essential to carefully study the risks associated with antibacterial therapy, enabling the development of recommendations for their safe and rational use.

A common misconception among many healthcare professionals and the public is the belief that if a drug is approved for use, it has been thoroughly studied, and its safety is fully reflected in the instructions. Currently, it is established that pre-registration preclinical and clinical studies identify and investigate only about 50% of ARs of a new drug. Therefore, to determine the true safety profile of all medications, including antibiotics, continuous pharmacovigilance of the drug's use in clinical practice is necessary.

Smyth and colleagues analyzed a review of publications on adverse reactions (ARs) in children. The study included 102 observational studies conducted in over 30 countries worldwide. The highest number of ARs requiring hospitalization in children was associated with the use of antibacterial and anticonvulsant drugs. The same drug groups were also responsible for the majority of ARs reported during the children's hospital stays.

In outpatient treatment, the most common drugs causing ARs in children were nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics. Among individuals over the age of 65, antibiotics also ranked among the leading causes of ARs, second only to cardiovascular medications.

Allergic reactions are dose-independent (type B according to the WHO classification), meaning that even low doses can trigger severe adverse reactions (ARs) such as anaphylactic shock, Lyell's syndrome, Stevens–Johnson syndrome, and others. Unlike ARs caused by the pharmacological effects of drugs (type A, dose-dependent), allergic reactions cannot be predicted during the initial prescription of a drug and, therefore, cannot be entirely avoided or prevented.

To reduce the likelihood of developing an allergic reaction, it is crucial to thoroughly collect the patient’s medication history, paying particular attention to previously used antibacterial drugs and whether any ARs occurred during their use. When prescribing treatment to patients with a history of hypersensitivity reactions, it is important to consider the potential for cross-allergies to antibiotics of the same class.

Since prolonged use of high-dose antibiotics is more likely to sensitize the body than short-term prophylactic use (e.g., in surgery), unnecessarily prolonged courses of antibacterial treatment should be avoided. The likelihood of an allergic reaction significantly increases when multiple highly reactive drugs are used simultaneously. For instance, procaine (novocaine), often used as a solvent for antibiotics, can itself cause allergic reactions.

Here are some data on the hepatotoxic effects of antibacterial agents. A detailed analysis of drug-induced liver injury cases recorded in Spain over a 10-year period (a total of 461 cases) revealed that systemic antibiotics were the most common cause of drug-induced hepatitis and liver failure, accounting for 21% of cases. Notably, 59 cases (13%) were linked to the use of amoxicillin/clavulanate.

An analysis of spontaneous adverse drug reaction reports from the WHO Pharmacovigilance database (VigiBase) identified erythromycin, ceftriaxone, and minocycline among the 15 drugs most frequently associated with hepatotoxic reactions in children and adolescents under 18 years of age.

It is believed that the most frequent hepatotoxic reactions occur with antimicrobial agents such as amoxicillin/clavulanate and co-trimoxazole. The incidence of such side effects is significantly lower for antibiotics from the macrolide, fluoroquinolone, and tetracycline groups.

Traditionally, macrolides are considered one of the safest groups of antibacterial drugs. The frequency of hepatotoxic effects (primarily cholestatic hepatitis) associated with erythromycin does not exceed 3.6 cases per 100,000 prescriptions. The likelihood of hospitalization due to drug-induced liver injury is 2.28 per 1 million patients receiving a 10-day course of therapy. However,

an increasing number of researchers question whether these low figures accurately reflect the actual situation.

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