www.medicalacademic.co.za

Bringing you medical news that matters

SPECIALIST FORUM

Vol. 23 • No. 11 • November 2023

Wound care

Antimicrobial resistance

Allergology

Allergic rhinitis pathology, symptoms and impact on QoL

JOIN
PfizerPro
TODAY

Pfizer
for Professionals

JOIN the growing PfizerPro community

and access exclusive resources for registered Healthcare Professionals

SIGN UP TODAY

and get instant access to simple, agile and responsive content that is aimed at improving patient outcomes and keeping you informed.

How to sign up:

1. Visit **pfizerpro.co.za**
2. Click "**Register**" to create your account.

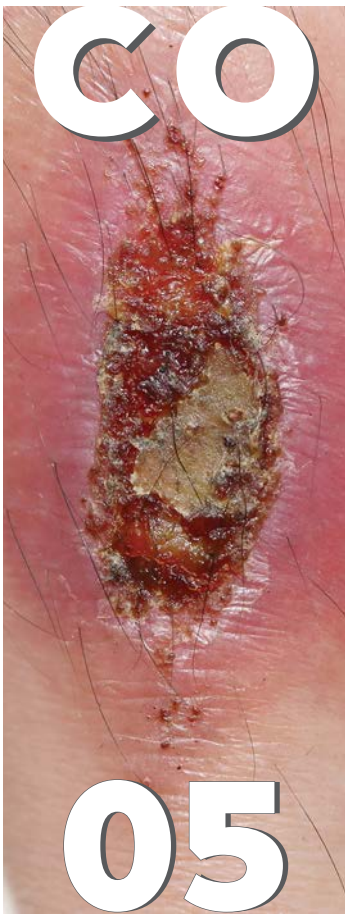
Or **scan** to sign up

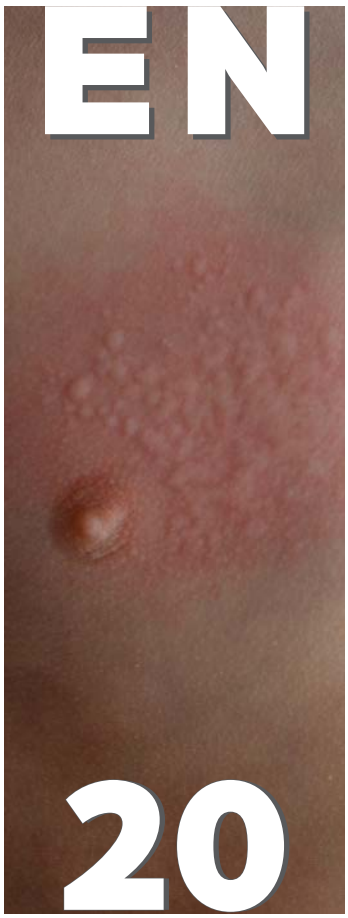
To report an adverse event, please contact ZAF.AEReporting@pfizer.com. If you wish to contact Pfizer for any other purpose, please use contact details below.

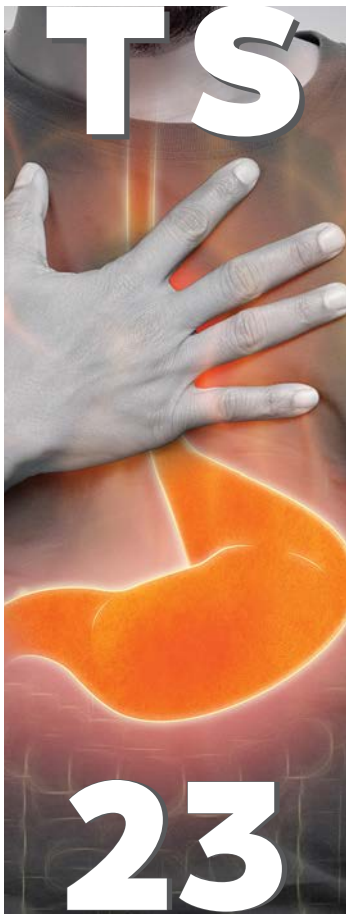
+27 11 320 6000 or 0860 734 937 (SA). Monday to Friday 09h00-17h00.

PP-UNP-ZAF-0159

CONTENTS







EDITORIAL
GUEST EDITORS: **Claire Rush**
Conrad Strydom
SUB EDITOR: **Gill Abrahams**
LAYOUT & DESIGN: **Allison McCallum**

ADVERTISING
ADVERTISING EXECUTIVE
Charissa Piek | 063 281 1205
Charissa.Piek@newmedia.co.za

DISTRIBUTION & SUBSCRIPTIONS
Felicity Garbers
Felicity.Garbers@newmedia.co.za

PUBLISHING TEAM
GENERAL MANAGER: **Dev Naidoo**
HEAD OF COMMERCIAL: B2B & OWNED BRANDS: **Johann Gerber**
Johann.Gerber@newmedia.co.za
PRODUCTION MANAGER: **Angela Silver**
ART DIRECTOR: **David Kyslinger**

CONTACT
Johannesburg Office: Ground Floor, 272 Pretoria Avenue, Randburg 2194

Postal Address:
PO Box 784698,
Sandton, Johannesburg, 2146
T +27(0)11 877 6111 F +27(0)11 713 9024

www.medicalacademic.co.za

PRINTING
Printed by CTP Printers

COVER PRICE
Specialist Forum per issue R80,00 VAT Incl.
ISSN: 2218-8282

Published by New Media, a division of Media24 (Pty) Ltd

MANAGEMENT TEAM
CEO: NEW MEDIA: **Aileen Lamb**
COMMERCIAL DIRECTOR: **Maria Tiganis**
STRATEGY DIRECTOR: **Andrew Nunneley**
CHIEF FINANCIAL OFFICER: **Venette Malone**
CEO: MEDIA24: **Ishmet Davidson**

HEAD OFFICE
8th floor, Media24 Centre, 40 Heerengracht, Cape Town 8001
PO Box 440, Green Point, Cape Town 8051
Tel: +27 (0)21 406 2002
www.newmedia.co.za

Photo credit: Shutterstock.com

The ever-evolving landscape of medicine

Dear Reader

I have been a 'guest editor' for this issue while René recovers from surgery.

In this issue, we acknowledge World Antimicrobial Awareness Week and the pressing concern of antimicrobial resistance (AMR) within the field of wound care. Recognising the paramount importance of preserving the skin and gut's normal flora, we emphasise the preference for narrow-spectrum antimicrobial agents in minimising AMR's impact.

Recent statistics underscore the gravity of AMR, with its disease burden rivalling or surpassing that of HIV and malaria combined, resulting in about 4.95 million deaths in 2019. Furthermore, a recent study demonstrates antimicrobial stewardship programmes substantial reduction in antibiotic consumption by nearly 30%.

Chronic obstructive pulmonary disease continues to be a leading global cause of mortality, and its diagnosis remains a complex challenge.

It is that time of year when many patients are suffering from allergic rhinitis (AR). We examine its pathology, symptoms and impact on quality of life (QoL), which, as a sufferer, I can attest is huge.

We look at new treatment options for AR, with a focus on combining montelukast and levocetirizine.

Differentiating between anaphylaxis and urticaria could mean the difference between life and death. They exhibit comparable clinical characteristics and are linked by shared immune-mediated pathways.

Gastro-oesophageal reflux disease (GORD) is associated with considerable reductions in QoL and work productivity, as well as increased healthcare use. Proton pump inhibitors are currently the most effective treatment for GORD. However, there are limitations associated with these drugs in terms of patients' response. Despite these limitations, long-lasting acid control is possible.

Due to the complexity of diabetes therapy algorithms, insulin treatment protocols often seem like a minefield of right, wrong or indeterminate choices. Nonetheless, effective management requires precision on the part of clinicians.

November is National Diabetes Month and this year's focus is on taking action to prevent diabetes health problems. Nonetheless, effective management requires precision on the part of clinicians.

Testosterone has been described as 'the most misunderstood molecule in medicine'. Testosterone therapy is hugely significant for men with testosterone deficiency or hypogonadism. While many people are aware of the role of testosterone in male sexual desire and muscle mass, the broader medical community often overlooks its vital importance in addressing various general medical conditions.

We hope you find this issue informative and relevant to your practice, and as always, we remain committed to providing valuable insights to aid you in your medical journey.

Regards

Claire Rush

Guest editor

Photo credit: Shutterstock.com

Antimicrobial resistance

a growing challenge for wound care

Wounds, whether minor or severe, can affect organs, tissues, and the surrounding structures like subcutaneous tissue, muscles, tendons, nerves, blood vessels and bone. When the epidermis and connective tissues are harmed, the body's ability to protect itself from the environment is compromised, and the regeneration of a functional epidermis (and other skin layers) is essential.

Infections, especially those caused by bacteria, are the biggest challenge to wound healing and have a particularly negative effect on chronic wounds. Even though bacteria are normally present on healthy skin and in wounds, a critical number of bacteria or the formation of biofilms can delay the healing process to a considerable degree.

Despite advances in wound care, bacterial and fungal infections remain among the most common and painful conditions, often leading to significant death and illness. Currently, *Staphylococcus aureus*, methicillin–resistant *Staphylococcus aureus* (MRSA), and *Pseudomonas aeruginosa*

are the most common bacteria found in infected wounds.

Stages of the healing process

The healing process is a meticulously coordinated series of events that involve both resident and migrating cell populations, extracellular matrix components, and soluble mediators. This intricate process can be divided into five distinct phases.

Haemostasis is the initial phase, during which a fibrin clot forms to prevent blood loss through vasoconstriction and to protect against microbial contamination. Simultaneously, the inflammatory phase begins, marked by the recruitment of neutrophils, monocytes/macrophages, and lymphocytes. Neutrophils engulf bacteria, cleanse the wound through proteases and antimicrobial peptide secretion, and produce reactive oxygen intermediates.

Monocytes differentiate into macrophages, facilitating the removal of apoptotic neutrophils and other cells, while also secreting cytokines and growth factors. Lymphocytes contribute with specific responses to combat microbes; B-lymphocytes produce antibodies, and T-lymphocytes secrete cytokines involved in cytolytic activity.

The migration and proliferative phases follow, as fibroblasts migrate to the wound site and differentiate into myofibroblasts, producing extracellular matrix components like fibronectin, hyaluronic acid, collagen, and proteoglycans. These components are integral to extracellular matrix production, the formation of new blood vessels, and re-epithelisation.

The final stage, called maturation or remodelling, marks the conclusion of the wound healing process, in which all processes activated after the injury come to a halt.

Advanced wound dressings

Conventional wound dressings are passive barriers that protect wounds from infection and contamination. Advanced wound dressings, on the other hand, are active participants in the healing process, delivering therapeutic compounds to the wound site. These compounds can aid in the removal of dead tissue, promote tissue growth, and prevent or treat infections.

Antimicrobial dressings are a particularly valuable tool for managing local infections. They deliver high concentrations of antibiotics directly to the wound site, where they can effectively kill bacteria and prevent the development of biofilms. For example:

- Gentamicin-impregnated dressings can be used to treat diabetic foot ulcers.
- Silver sulfadiazine dressings are useful for treating burn wounds.
- In the treatment of chronic wounds that have been colonised by bacteria and biofilms, cadexomer iodine dressings have demonstrated efficacy.

Dressings that have a physical mode of action

Non-antibiotic treatments for wound infection play a crucial role in promoting Antimicrobial Stewardship (AMS) practices. Cleansing lotions with surfactants effectively remove debris and microbial loads by reducing surface tension. These surfactants aid in cleaning wounds by loosening dried exudate and devitalised mucous membrane, facilitating a cleaner wound bed.

Addressing the challenge of bacterial load in chronic wounds, dressings with a physical mode of action provide an alternative approach. Unlike antibiotic-based treatments, these dressings pose no risk of bacterial resistance development, ensuring effectiveness in wound bioburden management.

Additionally, dressings coated in fatty acid derivatives irreversibly bind to bacteria, limiting their activity. This unique mechanism allows for prophylactic use and is particularly beneficial for unclean, colonised, or infected wounds. By utilising treatments that do not rely on antibiotics, antimicrobials, or antiseptics, healthcare practitioners contribute to AMS practices, aligning with the emphasis on responsible and sustainable wound care.

Commonly used antibiotics

Antimicrobial dressings utilise a limited range of antibiotic classes, including aminoglycosides, beta-lactams, glycopeptides, quinolones, sulphonamides, and tetracyclines, each employing diverse mechanisms to disrupt vital bacterial processes.

- Beta-lactams and glycopeptides target bacterial cell wall synthesis.
- Penicillins, carbapenems, and cephalosporins, known as beta-lactam antibiotics, block penicillin-binding proteins, crucial for cell wall construction.
- Glycopeptide antibiotics like vancomycin hinder peptidoglycan synthesis by binding to peptidoglycan within the cell wall, restraining transglycosylases and PBPs. This compromises cell wall integrity and may lead to cell lysis.
- Sulphonamides focus on the bacterial folate pathway essential for growth. Acting as folic acid mimics, they competitively bind to bacterial enzymes, disrupting DNA, RNA, and protein synthesis.
- Aminoglycosides and tetracyclines act as protein synthesis inhibitors by binding to the 30S ribosomal subunit, obstructing aminoacyl-tRNA recruitment to the ribosome and hindering new protein production.
- Quinolones inhibit nucleic acid synthesis by targeting topoisomerase II and topoisomerase IV, enzymes vital for DNA topology maintenance. Quinolones transform topoisomerases into chromosome-fragmenting enzymes, leading to bacterial cell death.

Antimicrobial resistance

Drug-resistant wound infections are a growing threat to wound healing. The primary factor contributing to the emergence of antimicrobial resistance is the inappropriate use of antimicrobial agents, raising concerns about the proliferation of superbugs or multi-drug resistant strains.

Notably, approximately half of infections associated with bacteria such as *Escherichia coli*, *Klebsiella pneumoniae*, *S. aureus*, and *P. aeruginosa* have exhibited resistance even to potent antimicrobials like third generation cephalosporins. A fundamental prerequisite for the judicious prescription of antimicrobials is a comprehensive understanding of the criteria for wound infections, the causative pathogens, and their prevalent susceptibility patterns.

Given the established efficacy of wound debridement and irrigation, the initial approach to managing infected wounds should generally not involve prescribing antibiotics. Systemic antibiotics are warranted when the infection appears to be spreading through subcutaneous soft tissues, in cases of ascending limb infection, or when severe sepsis is a concern.

To minimise the impact of individual antibiotics on the normal flora of the skin and gut, preference should be given to narrow-spectrum agents. Empirical treatment with systemic antibiotics should be adapted based on wound culture results, and topical antibiotics have proven effective in managing patients with infected wounds. SF

References available in the online issue

Cutimed® Sorbact®

Effectively prevents and treats wound infection[1,2]

93 % of wounds were healed or improved[1]

- Sorbact® Technology dressings reduce the bioburden in wounds[3]
- Effective against the Top 5 WHO (World Health Organisation) pathogens, as shown in vitro.[4]
- Can be used during the entire wound healing process.[2]

References:

[1]Chadwick P & Ousey K. Bacterial-binding dressings in the management of wound healing and infection prevention: a narrative review. J Wound Care. 2019;28(6):370-382.
[2]Kammerlander G et al. An investigation of Cutimed Sorbact as an antimicrobial alternative in wound management. Wounds UK. 2008;4:10-18.
[3]Mosti G et al. Comparative study of two antimicrobial dressings in infected leg ulcers: a pilot study. J Wound Care. 2015;24(3):121-127.
[4]Husmark J et al. Antimicrobial effects of bacterial binding to a dialkylcarbamoyl chloride-coated wound dressing: an in vitro study. J Wound Care. 2022;31:560-570.

essity

Name and business address: BSN Medical PTY (LTD) an Essity Company. Co. Reg. No. 2001/003941/07. 30 Gillitts Road, Pinetown, 3610. Tel. No. +27 31 710 8111. Customer Specific Enquiries: +27 31 710 8038/8005. Email: medical.za@essity.com, www.essity.com. Further information available on request from Essity. 23_BSN167

Cutimed®
Your Power to Heal

ASPs reduce antibiotic consumption by almost 30%

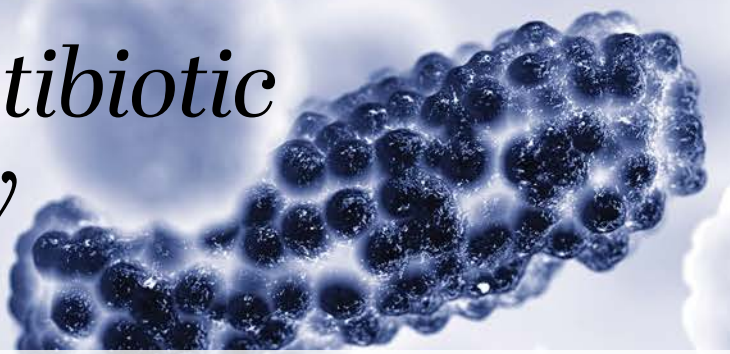


Photo credit: Shutterstock.com

Antimicrobial resistance (AMR) is a pressing global issue, spreading at an alarming rate. Recent estimations reveal that AMR's disease burden equals or exceeds that of HIV and malaria combined, causing about 4.95 million deaths in 2019.

If not effectively addressed, AMR could lead to an annual death toll of 10 million people by 2050 and cost the world economy a staggering $100 trillion. To combat AMR, antimicrobial stewardship programmes (ASPs) have been instituted in various healthcare settings to optimise antimicrobial use, slow down resistance, ensure patient safety, and reduce healthcare costs. Current research demonstrates that ASPs can decrease total antibiotic consumption in hospitals by 19% and restrict the usage of certain antimicrobials by 27%. However, the effectiveness of ASPs in low- and middle-income countries (LMICs), where antimicrobial use is disproportionately high compared to high-income countries (HICs), remains underexplored.

In a recent study by Zay *et al* (2023), the authors synthesised existing evidence regarding the connection between ASPs and global antibiotic consumption. They gathered data from multiple sources, including *PubMed, Web of Science,* and *Scopus* databases, covering studies from 1 August 2010, to 1 August 2020. Additional studies were incorporated from the references of previous systematic reviews. The study selection criteria included original research studies exploring the impact of ASPs on antimicrobial consumption across different healthcare settings and income levels. Animal and environmental studies were excluded. The researchers followed the Preferred Reporting Items in Systematic Reviews and Meta-Analyses guidelines and used multilevel random-effects models to assess the association of targeted ASPs with antimicrobial consumption. They also employed the Effective Public Health Practice Project quality assessment tool to evaluate study quality. The main outcome measures included the proportion of patients receiving antibiotic prescriptions and defined daily doses per 100 patient-days.

The study encompassed 52 research papers, involving a total of 1 794 889 participants. Among these studies, 40 were conducted in HICs, and 12 in LMICs. The analysis revealed that ASPs were linked to a 10% reduction in antibiotic prescriptions and a 28% decrease in antibiotic consumption (rate ratio, 0.72; 95% CI, 0.56–0.92). Notably, ASPs were associated with a 21% reduction in antibiotic consumption in paediatric hospitals and a 28% reduction in World Health Organization (WHO) Watch group antibiotics. These findings are promising, suggesting that ASPs are effective in reducing antibiotic consumption in both hospital and non-hospital settings. However, the assessment of ASPs' impact in resource-limited settings remains limited, underscoring the need for further research on strategies to curtail antibiotic use in LMICs.

The meta-analysis results indicate that ASPs successfully reduced antibiotic prescriptions by 10% and lowered antibiotic consumption rates by 28%. This reduction was observed across various antibiotic classes, except for penicillin, which are not always targeted by ASP interventions and, in some cases, are even encouraged. ASPs also played a crucial role in reducing antibiotic consumption of WHO Watch list antibiotics, which are at a high risk of promoting bacterial resistance. Given the growing use of Watch antibiotics worldwide, these results offer hope that protecting these drugs through appropriate ASPs is attainable.

Subgroup analyses revealed that ASPs were particularly effective in reducing antibiotic prescriptions in paediatric care, where antibiotic use is known to be notably high. In contrast, prescriptions for other patient groups, such as inpatients, outpatients, and nursing home residents, were generally smaller and often not statistically significant. Additionally, the analysis indicated that ASPs in HICs were associated with a 6% reduction in antibiotic prescriptions, echoing previous findings.

A study conducted in 47 small hospitals in South Africa did not report quantitative estimates of consumption, but it found that introducing pharmacist expertise in a setting with limited infectious disease resources had substantial consequences for antibiotic use and consumption. While the present study tried to also analyse the outcome of specific ASP components, the currently available data are not sufficient to assess the relative effectiveness of each component.

Nevertheless, the study identified only four studies conducted in LMICs, raising concerns about the generalisability of these results. The limited number of studies from LMICs and the mixed findings emphasise the need for additional research on the implementation of ASPs in such settings. Challenges in LMICs include limited access to antibiotics, scarce diagnostics, and weak adherence to treatment, making it imperative to explore how to implement ASPs effectively without compromising the quality of patient care. Although this study aimed to analyse the outcomes of specific ASP components, the current data are insufficient to assess the relative effectiveness of each component.

In conclusion, ASPs have demonstrated their ability to reduce antibiotic consumption, not only in hospital settings but also in non-hospital environments. These findings are especially encouraging as they extend to WHO Watch group antibiotics with a high risk of resistance. Given that overuse and misuse of antibiotics are the primary drivers of AMR, reducing antimicrobial consumption through ASPs is a critical step toward mitigating this global health threat. SF

References available in the online issue

IV antibiotic range

imipenem/ cilastatin

SEPENCIL
500 mg IMIPENEM/CILASTATIN
POWDER FOR SOLUTION FOR INFUSION

meropenem

MEROJECT
MEROPENEM POWDER FOR INJECTION 500 mg • 1 g

teicoplanin

DYNA TEICOPLANIN
200 mg • 400 mg
Sterile powder & solvent for injection

ertapenem

INVABEX
ERTAPENEM **1 g**
POWDER FOR SOLUTION FOR INJECTION / INFUSION

For further product information contact **PHARMA DYNAMICS**
Email info@pharmadynamics.co.za **CUSTOMER CARE LINE** +27 21 707 7000

DYNA TEICOPLANIN 200, 400 mg. Each vial contains 200, 400 mg teicoplanin respectively. S4 A43/20.1.1/0573, 0575. **DYNA TEICOPLANIN SOLVENT.** Each ampoule contains 3,2 ml water for injection. S4 A43/34/0574. **INVABEX.** Each vial contains 1 g ertapenem. S4 52/20.1.1/0811. **MEROJECT 500 mg, 1 g.** Each vial contains meropenem trihydrate equivalent to meropenem anhydrous 500 mg, 1 g respectively. S4 A42/20.1.1/0280, 0281. **SEPENCIL 500 mg.** Each vial contains imipenem monohydrate equivalent to imipenem 500 mg and cilastatin sodium equivalent to cilastatin 500 mg. For full prescribing information, refer to the professional information approved by SAHPRA. **CCA422/10/2023**

pharma dynamics
EFFECTIVE AFFORDABLE HEALTHCARE

www.pharmadynamics.co.za

November 2023 | Vol. 23 No. 11
www.medicalacademic.co.za

Photo credit: Shutterstock.com

Probiotics: *game changer for infant wellness*

Probiotics like *Lactobacillus reuteri* have a significant impact on infantile colic, a condition that affects up to 20% of newborns.

Colic, characterised by excessive crying in infants, affects 10% to 25% of babies and their parents. Its exact cause is unknown. This condition causes significant stress, often associated with prolonged and inconsolable crying in infants under five months of age. While colic tends to resolve on its own, parental stress due to the crying has been linked to delayed bonding and, in severe cases, child abuse or shaken baby syndrome.

A systematic review by Simonson *et al,* demonstrates that probiotics are effective in treating infantile colic. Oral probiotic administration to breastfed infants led to a significant reduction in crying time by at least 50% compared to a placebo. The evidence also supports the safety, cost-effectiveness, and efficacy of probiotics in reducing colic symptoms.

The exact cause of colic remains uncertain, with various theories proposed, including issues related to attachment, infant temperament, food intolerances, gastrointestinal nervous system hyperstimulation, intestinal gas, and physiological immaturity in infants. Researchers are increasingly exploring the possibility of an altered gut microbiome as a contributing factor to colic symptoms.

Probiotics, like *Lactobacillus reuteri,* have been explored as a treatment for infant colic. *L. reuteri,* a natural human gut coloniser, may correct gut flora imbalances, reduce inflammation, and alleviate colic symptoms. Its effects on the intestinal epithelium involve inhibiting pathogenic bacteria growth, immune system modulation, anti-inflammatory actions, and reducing visceral pain through direct interaction with enteric nerves. These actions collectively contribute to the potential relief of colic symptoms in infants.

A study involving 162 clinically healthy infants aged less than five months meeting the Rome-IV diagnostic criteria for infantile colic showed that treatment with probiotics resulted in fewer days with colic and increased parental satisfaction with the improvement in their child's attitude, attentiveness, activity level, and oral intake. All the babies responded well to the lactase treatment, and no significant side effects were recorded.

Probiotic drops are easily accessible options for treating colic, and those with vitamin D3 are especially beneficial. In a study by Narang *et al,* a clinically significant decrease in the duration of crying and fussing was observed in children who received lactase drops added to milk formula or breast milk before feeding, as compared to those who received a placebo during the entire four-week treatment period.

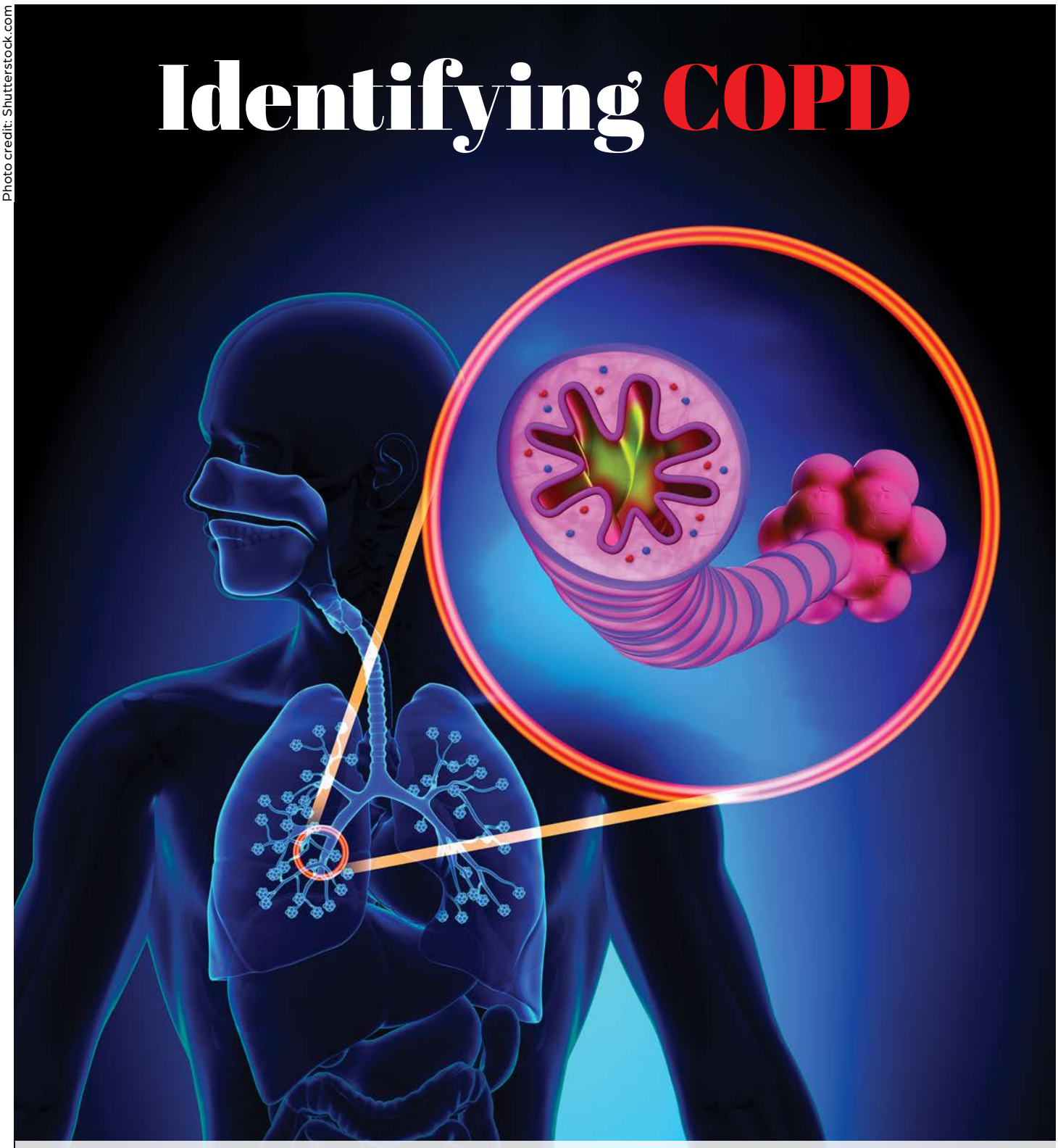
Notably, *L. reuteri* is the most extensively studied probiotic and has proven effectiveness in treating colic. Probiotic supplements containing *Bifidobacteria, Lactobacillus* GG, and mixed strains also reduced colic symptoms in breastfed infants.

It's important for healthcare professionals to inform parents that infantile colic is generally a self-resolving condition and supportive strategies like swaddling, soothing music, pacifiers, tummy time, and avoiding overstimulation or overfeeding can help. Clinicians should also stress the importance of seeking support from friends and family and provide clear guidance against striking or shaking a baby, and rule out other potential causes of infant fussiness, such as hunger, infection, trauma, constipation, or reflux.

References available in the online issue

Photo credit: Shutterstock.com

Identifying COPD



Chronic obstructive pulmonary disease (COPD) is one of the most prevalent causes of mortality globally, yet it is not always straightforward to diagnose.

COPD is a widespread respiratory ailment marked by functional and structural transformations primarily triggered by extended exposure to harmful inhaled particles. COPD is a major global cause of death, with a rising prevalence.[1] It presents with symptoms such as breathlessness, chronic productive cough, and mucous overproduction.[1]

COPD is a multifaceted disease influenced by both genetic and environmental factors, and its complications (triggered by infections and environmental factors) often require additional treatment, making it a critical health concern.[2]

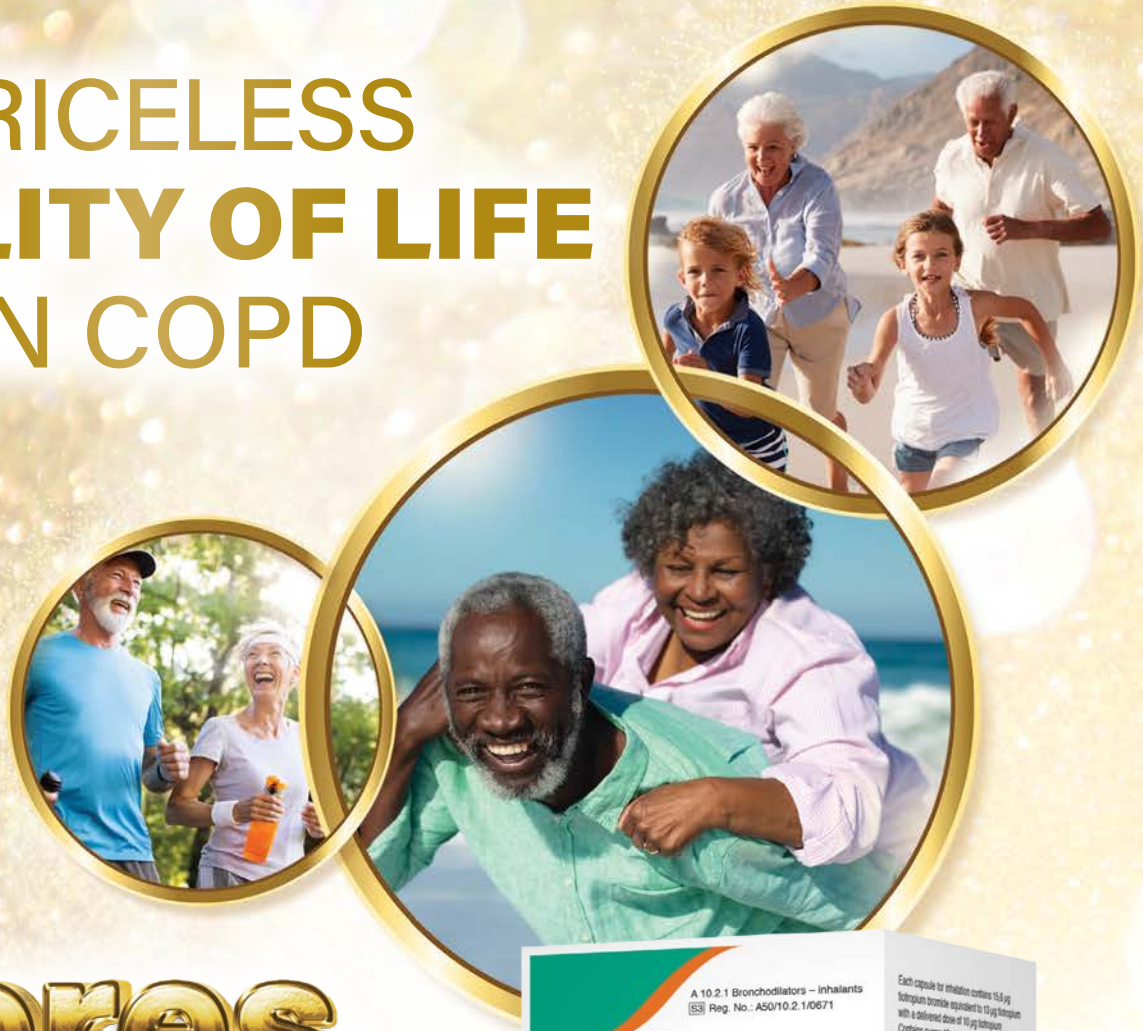
There are many endotypes of COPD, which necessitates the classification of patients into distinct subgroups based on biological differences, such as the extent of bacterial colonisation or the presence of eosinophilic inflammation.[2]

Our current understanding of these COPD subtypes is limited, necessitating further research to enable more precise, individualised treatments rather than a one-size-fits-all approach.[2]

Why treat COPD?

COPD poses a significant burden on patients and society due to its natural

PRICELESS
QUALITY OF LIFE
IN COPD



Tiores

- Clinically proven to reduce exacerbations and related hospitalisations[1]
- Improves effectiveness of pulmonary rehabilitation[1]
- Improves symptoms and health status[1]
- Once-daily dosage[2]

Dosage:
Inhale the contents of one capsule once daily, at the same time each day, using the Zephir inhaler[2]

Patients will receive a new device each month

Tiores
Tiotropium bromide

Priceless quality of life in COPD

References: 1. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease (2023 Report) [Internet]. 2023 p.57, [cited 2023 Mar 12]. Available from: https://goldcopd.org/wp-content/ uploads/2023/03/GOLD-2023-ver-1.3-17Feb2023_WMV.pdf 2. Tiores Professional Information November 2020.

S3 **TIORES.** Reg. no.: 50/10.2.1/0671. Each capsule for inhalation contains 15,6 µg tiotropium bromide equivalent to 13 µg tiotropium with a delivered dose of 10 µg tiotropium. For full prescribing information refer to the professional information approved by the South African Health Products Regulatory Authority. Date of publication: November 2020. **Applicant**: Forrester Pharma (Pty) Ltd, Tel: (021) 943 0600. **Marketed by:** Glenmark Pharmaceuticals South Africa (Pty) Ltd, 2nd Floor, Building D, Stoneridge Office Park, 8 Greenstone Place, Greenstone, Edenvale, Gauteng, 1609. Tel: (011) 564 3900. www.glenmarkpharma.co.za. TIORD03/23.

glenmark RESPIRATORY
Glenmark, touching the lives of patients for over three decades

SIYAENZA

progression, which reduces daily activities, leads to exacerbations, and contributes to work and social isolation, often resulting in psychological conditions like anxiety and depression.[3]

These factors collectively lower the health-related quality of life and increase mortality compared to the general population.[3] COPD frequently coexists with various comorbidities, some independently arising, and others linked causally or through shared risk factors, such as age, smoking, and systemic inflammation.[3]

Common comorbidities include bronchiectasis, cardiovascular disease, chronic kidney disease, dyslipidaemia, diabetes, hypertension, lung cancer, mental disorders, osteoporosis, obstructive sleep apnoea, and skeletal muscle dysfunction.[3] Notably, heart failure is a significant predictor of mortality in COPD patients, doubling the risk of death according to some research.[3]

Subtypes of COPD

The Body mass index–Obstruction–Dyspnoea–Exercise–capacity (BODE) index is a tool often used to identify individuals with COPD who are at increased risk of mortality.[4] However, the BODE index does not take into account the underlying pulmonary morphologic abnormalities that are associated with COPD.[4]

Identifying COPD subtypes that integrate these abnormalities with associated pulmonary dysfunction and risk of mortality could provide insights into potentially modifiable disease pathways and protein biomarkers of disease.[4] The most commonly used guidelines for the subclassification of COPD types are the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.[5]

According to GOLD, traditional COPD was categorised into spirometric stages 1–4.[5] Those lacking airflow obstruction (forced expiratory volume in 1 second [FEV1]/forced vital capacity [FVC] ≥0.70) and FEV1 ≥80% predicted) were designated as GOLD 0. Those with FEV1/FVC ≥0.70 and FEV1 <80% predicted were labelled as having preserved ratio-impaired spirometry (PRISm).[5]

Patients with COPD who develop pneumonia may present with symptoms that are like those of a COPD exacerbation

How do you know it's COPD?

The diagnosis of COPD can be challenging, and given its lifelong nature, it is important for clinicians to carefully consider alternative diagnoses.[3] This involves a thorough assessment of the patient's clinical history, characteristics, exposures, and spirometry results.[3] It is important not only to distinguish between obstructive lung diseases (such as asthma, bronchiectasis, and COPD) but also to recognise restrictive lung disease and heart failure, which can sometimes mimic or coexist with COPD.[3]

Historically, the reversibility of airflow obstruction after bronchodilator administration was used to distinguish between asthma and COPD.[3] However, it is now recognised that significant reversibility (defined as an increase in FEV1 of ≥12% and ≥200 mL from baseline) or an increase in FVC of ≥10% can also occur in COPD, even in the absence of features suggestive of asthma.[3] Furthermore, the degree of reversibility can vary within the same patient over time.[3]

To definitively exclude asthma and diagnose COPD, a substantial improvement in FEV1 with normalisation of the FEV1/FVC ratio after bronchodilator administration or after four to 12 weeks of inhaled corticosteroid therapy is required.[3] Patients with COPD who develop pneumonia may present with symptoms that are like those of a COPD exacerbation.[3] While the treatment of these two conditions is generally similar, the duration of antibiotic therapy for pneumonia may be longer in practice.[3]

A diagnosis of COPD is possible in any patient who complains of dyspnoea, chronic cough or sputum production, a history of recurrent lower respiratory tract infections and/or a history of exposure to risk factors for the disease but FVC manoeuvre during spirometry showing the presence of a post-bronchodilator FEV1/FVC <0.7 is needed to establish the diagnosis of COPD.[5] The FEV1 also serves to determine the severity of airflow obstruction (GOLD grades 1, 2, 3, and 4, or mild, moderate, severe, and very severe).[5]

Conclusion

At present, COPD management is primarily focused on alleviating symptoms and minimising the risk of future exacerbations. However, the severity of COPD symptoms, and the possibility of mistaking the condition for any number of other diseases, demands that clinicians actively seek to identify COPD in patients with a history of risk factors and current symptoms. SF

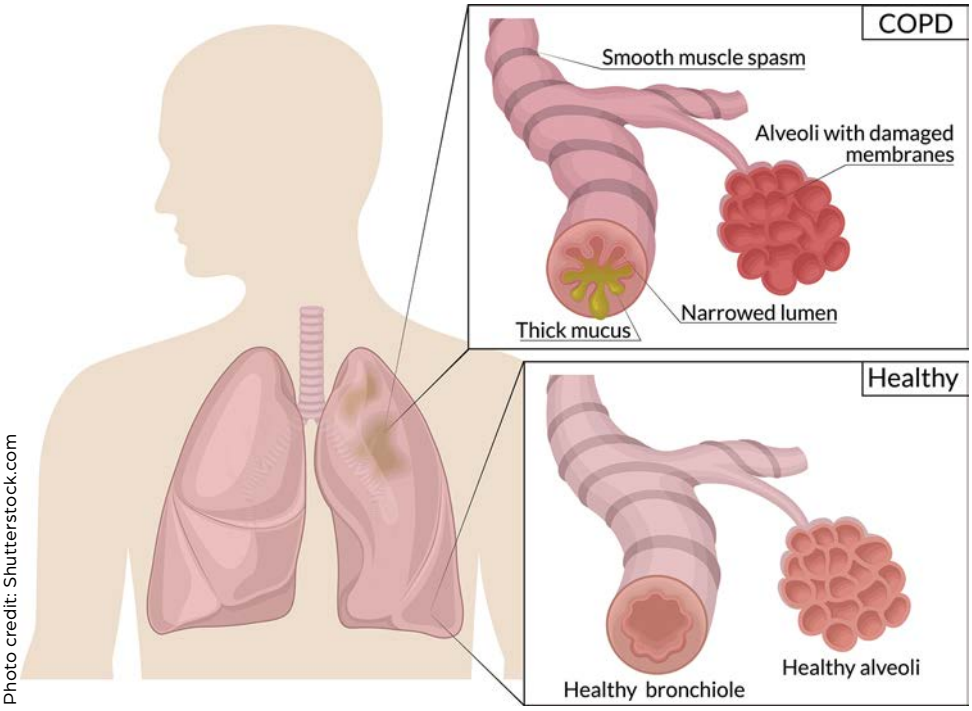


Photo credit: Shutterstock.com

References available in the online issue

Photo credit: Shutterstock.com

Allergic rhinitis pathology, symptoms and impact on QoL

Allergic rhinitis (AR) is an atopic disease presenting with symptoms of sneezing, nasal congestion, clear rhinorrhoea, and nasal pruritis. It is an immunoglobulin E (IgE)–mediated immune response that is against inhaled antigens in the immediate phase, with a subsequent leukotriene–mediated late phase.

The allergic response is classified into early and late-phase reactions. In the early phase, AR is an IgE-mediated response against inhaled allergens that cause inflammation driven by type 2 helper (Th2) cells. This initial response occurs in 5–15 minutes of exposure to an antigen, resulting in the degranulation of host mast cells. This releases a variety of synthesised mediators, including histamine, which is one of the primary mediators of AR.

Histamine induces sneezing via the trigeminal nerve and plays a role in rhinorrhoea by stimulating mucous glands. Other immune mediators, such as leukotrienes and prostaglandins, are also implicated as they act on blood vessels to cause nasal congestion.

Four to six hours after the initial response, an influx of cytokines, such as interleukins (IL)–4 and IL–13, from mast cells occurs, signifying the development of the late-phase response. These cytokines then facilitate the infiltration of eosinophils, T-lymphocytes, and basophils into the nasal mucosa and produce nasal oedema, resulting in congestion.

Non-IgE-mediated hyperresponsiveness can develop due to eosinophilic infiltration and nasal mucosal obliteration. The nasal mucosa becomes hyperreactive to normal stimuli (such as tobacco smoke and cold air) and causes symptoms of sneezing, rhinorrhoea, and nasal pruritis.

Epidemiology

The prevalence of AR based on physician diagnosis is approximately 15%. However, the prevalence is estimated to be as high as 30% based on patients with nasal symptoms. AR is known to peak in the second to fourth decades of life and then gradually decline. AR is one of the most common chronic paediatric disorders. According to data from the *International Study for Asthma and Allergies in Childhood*, 14% in the 13–14-year age group and 8% in the 6–7-year age group display symptoms of rhinoconjunctivitis linked to AR. Seasonal AR seems to be more common in the paediatric age group, whereas chronic rhinitis is more prevalent in adults.

A systematic review from 2018 estimated that 3% of adults had missed work, and 36% had impaired work performance due to AR. Economic evaluations have shown that indirect costs associated with lost work productivity account for most of the cost burden for AR.

Risk factors for developing AR include a family history of atopy, male sex, a presence of allergen specific IgE, and a serum IgE greater than 100 IU/mL before age six. Studies in young children have shown a higher risk of AR in those with an early introduction to foods or formula and/or heavy exposure to cigarette smoking in the first year of life.

According to Akhouri *et al* (2023), although many recent studies have evaluated the link between pollution and the development of AR, no significant correlation yet exists. Interestingly, there are several factors identified that may have a protective effect on the development of AR. The role of breastfeeding in the development of AR is often debated, but it is still recommended due to its many other known benefits and no associated harms. There is no evidence that pet avoidance in childhood prevents AR. However, it is hypothesised that early pet exposure may induce immune tolerance. There is a growing interest in the 'farm effect' on the development of allergies, and a meta-analysis of eight studies showed a 40% lower risk in subjects who had lived on a farm during their first year of life.

Patient examination

Taking a thorough, detailed history is an essential part of the evaluation of AR, and questions should focus on the types of symptoms, the time, duration, and frequency of symptoms, suspected exposures, exacerbating/alleviating factors, and seasonality. Patients with intermittent or seasonal AR have symptoms of sneezing, rhinorrhoea, and watery eyes, while patients with chronic AR often complain of postnasal drip, chronic nasal congestion, and obstruction. These patients will often have a family history of AR or a personal history of asthma. Patients with intermittent rhinitis may report triggers such as pollens, animal dander, flooring/upholstery, mould, humidity, perfumes, and/or tobacco smoke.

Patients may display mouth breathing, frequent sniffling and/or throat clearing, transverse supra-tip nasal crease, and dark circles under the eyes (allergic shiners). Nasal supratip crease is more common in children. Anterior rhinoscopy typically reveals swelling of the nasal mucosa and thin, clear secretions. The inferior turbinates may take on a bluish hue, and cobblestoning of the nasal mucosa may be present. Whenever possible, an internal endoscopic examination of the nasal cavity should be conducted to assess for nasal polyps and structural abnormalities. Pneumatic otoscopy can be used to assess for eustachian tube dysfunction, which can be a common finding in patients with allergic rhinitis. Sinuses may be tender to the touch in patients with chronic symptoms. Check these patients carefully for signs of asthma or dermatitis and question them regarding aspirin sensitivity.

Prognosis

Prevalence of AR seems to peak in adolescence and gradually decreases with age. In a longitudinal study, after 23 years, almost 55% of patients showed symptom improvement, with 41.6% of those being symptom-free. Patients who had an onset of symptoms at a younger age were more likely to show improvement. The severity of AR can vary over time and depends on various factors such as location and season.

Effects on QoL

Quality of life (QoL) is reduced with this condition due to the direct effects of its primary symptoms on the patient's life. AR also tends to cause sleep disorders, fatigue, impaired memory, and depression, all of which contribute to a reduced QoL. According to the Allergic Rhinitis Impact on Asthma guidelines, the QoL in patients with rhinitis dictates their rhinitis classification. For instance, sleep disorders are only associated with the moderate to severe form of rhinitis and not with its mild form.

The assessment of QoL has become a major area of interest for clinical research. Questionnaires have been developed to assess the effect of clinical management and of reducing the symptoms of chronic diseases on the patients' daily life. They are also used to determine the effect of particular methods of treatment on controlling the disease. The rhinoconjunctivitis quality of life questionnaire (RQLQ) was prepared by Juniper and Guyatt in 1991 to assess the QoL in patients with rhinoconjunctivitis.

Various studies were performed to assess QoL of AR patients. Shariat *et al* evaluated the QoL in AR patients. Their study showed that the severity of the disease adversely affects the patients' QoL. A study conducted in Brazil (2009) showed that AR has adverse effects on psychological and physical health in children.

Clinical findings

Rhinorrhoea was the most prevalent symptom among the participants. Other main symptoms of AR included itchy nose, nasal congestion and watery eyes (82%, 70% and 69%, respectively).

Sinusitis was the most common (29%) concomitant disease of AR asthma (12%). A poor sense of smell (7%) and a poor sense of taste (3%) were other concurrent conditions.

Regarding the RQLQ, among the total of 146 patients, the QoL was mildly affected in 38% and severely influenced in 62% of patients. QoL was reduced significantly in patients with severe intermittent allergic rhinitis ($p<0.05$). No significant relationships were observed between quality of life and gender ($p<0.456$). A significant relationship was found between QoL and severity of the disease ($p=0.000$).

The results of the study showed, in the majority of patients, that their QoL had been affected by problems caused by AR, including general sleep problems, morning symptoms, and practical problems during wake time. In the studies conducted by Shariat *et al*, Hubert Chen *et al*, and Monico Mit *et al*, more than 60% of the patients suffered from sleep problems and problems when awake. The authors found that patient QoL was affected by severe sleep problems (and problems during wake time) in 62% of the patients.

Patients with severe permanent or intermittent disease had a poorer QoL since the severity of the disease and associated symptoms tended to affect the patients' physical and mental well-being, making their life more difficult. These observations are consistent with those from studies conducted by Shariat *et al*, which showed that patients with a more severe type of the disease have a poorer QoL.

Complications

Chronic rhinosinusitis can be a complication of AR. It is characterised by nasal inflammation with symptoms of nasal congestion or discharge, lasting for longer than three months. Chronic rhinosinusitis may also show nasal polyps, which form as a result of chronic inflammation of the paranasal sinus mucosa. Nasal polyps are typically benign and present bilaterally. Unilateral nasal polyps should raise concerns for malignancy. The incidence of nasal polyps in the general population is approximately 4% and is more common in males. Treatment options include topical steroids and saline irrigation. Surgical removal is reserved for patients who do not respond to medical therapy.

Sensitisation to allergens in AR can alter the immunological parameters of the adenoids, resulting in adenoid hypertrophy. Eustachian tube dysfunction commonly manifests in patients with AR and presents as ear fullness, otalgia, and ear-popping. Approximately 10%–40% of patients with AR also have concurrent asthma, and some studies suggest asthma is more common in moderate-to-severe persistent rhinitis. Many studies have demonstrated AR to be an independent risk factor for asthma, especially in patients diagnosed with AR during infancy. Some other associated complications include otitis media with effusion, persistent cough, and eosinophilic oesophagitis.

Occupational AR and QoL impact

Maoua *et al* evaluated QoL and work productivity and activity impairment among patients with allergic occupational rhinitis (OR).

Patients with allergic OR do not only complain of clinical problems related to their symptomatology, but also of problems related to their occupation, such as inability to continue work, indication of allergen eviction and possible job loss. These professional changes can also interact with QoL. In the literature, several studies have evaluated the QoL in patients with occupational asthma but only few studies explored QoL in patients with OR.

In this study, female workers had more impaired QoL scores. Housekeeping activities may explain a part of these findings. Women are generally cumulating efforts at work and at home and are exposed to household products that can aggravate rhinitis symptoms, impacting QoL.

These findings were similar to those reported by Shariat *et al* conducted in 2011 among 110 patients with non-occupational AR.

Other studies mainly focused on the impact of exposure cessation on QoL. Van Wijk *et al* concluded that work cessation had beneficial effects on improving the QoL of patients with OR. Power *et al* found that among their study population of 29 patients allergic to latex, 90% noted that the total suppression of the allergen resulted in disappearance of the effects of nasal and ocular symptoms on their QoL.

Several other studies showed an impairment of work productivity and activity among patients with AR. Studies of Bousquet *et al* showed an absenteeism ranging from 0 to 4%, a presenteeism ranging from 18%–23%, a work productivity loss from 18%–26% and an overall activity impairment ranging from 20%–27%.

Absenteeism and presenteeism varies from one country to another due to cultural, socioeconomic, and health insurance factors. Compared to other diseases, AR seemed to have more negative impact on work productivity and activity than hypertension and diabetes, and only depression caused more impairment than AR in the study of De la Hoz Caballer.

There are associations between QoL and work productivity among patients with AR. Even if absenteeism rates seem to be moderate, work productivity is clearly reduced because of important presenteeism percentages.

Identification of factors such as age, gender and QoL impairment could help to identify workers with higher risk of productivity and activity impairment. A rigorous application of preventive measures and a medical control of the disease should reduce the burden of allergic occupational rhinitis and improve QoL and work productivity.

Conclusion

AR can adversely affect sleep quality, mood, and daily activities in patients. Given the significant effects of these symptoms on the patients' QoL, making an early diagnosis of the disease is the first step to overcoming it. The subsequent steps are reducing environmental allergens and taking measures to prevent the incidence of concomitant diseases, such as asthma and sinusitis. SF

References available in the online issue

Ryaltris® 665 mcg 25 mcg

(olopatadine hydrochloride and mometasone furoate monohydrate nasal spray)

FAST RELIEF, LASTING COMFORT™

Comprehensive Sustained Relief [1,2]

- Rapid symptom relief within 15 minutes
- Better quality of life (QoL) vs monotherapy
- Dual benefits of olopatadine and mometasone
- Statistically significant improvements in ocular and nasal symptoms
- Well tolerated

References: 1. Patel P, Salaptek AM, Tantry SK. Effect of olopatidine-mometasone combination nasal spray on seasonal rhinitis symptoms in an environmental exposure chamber study. American College of Allergy, Asthma & Immunology. 2019;122(2):160-166.e.1. **2**. Gross GN, Berman G, Amar NJ, et al. Efficacy and safety of olopatadine-mometasone combination nasal spray for the treatment of seasonal allergic rhinitis. Ann Allergy Asthma Immunol, 2019;122:630-638.

S2 RYALTRIS® (Nasal spray). Reg. no. 53/21.5.1/0457. Each spray delivers 600 µg olopatadine (as olopatadine hydrochloride) and 25 µg mometasone furoate (as mometasone furoate monohydrate). Contains the preservative benzalkonium chloride 0,02 % w/w. Sugar free. For full prescribing information refer to the professional information approved by the South African Health Products Regulatory Authority. Date of revision: 18 February 2022.

HCR: Glenmark Pharmaceuticals South Africa (Pty) Ltd. 2nd Floor, Building D, Stoneridge Office Park, 8 Greenstone Place, Greenstone, Edenvale, Gauteng, 1609. (Office) +27 11 564 3900. www.glenmarkpharma.com.
ZAR/04/2023/11018

Glenmark, touching the lives of patients for over three decades

Glenmark
A new way for a new world

Photo credit: Shutterstock.com

New treatment options for AR: Combining montelukast and levocetirizine

Allergic rhinitis (AR) is a significant global health challenge, and its effective management can be a formidable task. Despite several decades of available symptomatic treatments, there has been limited improvement in patient quality of life and symptom burden.

AR is initiated by exposure to allergens such as pollen, mites, and animal dander, leading to the activation of antigen-specific immunoglobulin E (IgE) receptors on mast cells and basophils in predisposed individuals. The allergic response comprises an early and late-phase reaction. The early phase involves mast cell degranulation, leading to rapid-onset nasal and ocular symptoms, primarily due to histamine release. This phase also triggers inflammation, increasing vascular permeability, and causing tissue oedema.

The late-phase reaction, which occurs hours after allergen exposure, involves the recruitment of various inflammatory cells and the release of multiple mediators, perpetuating the inflammatory response. This phase leads to nasal congestion, a distressing symptom for AR patients. Nasal and ocular symptoms significantly impact patients' quality of life and daily functioning.

Existing pharmaceutical options

Current pharmacological management of AR involves symptomatic relief using antihistamines, corticosteroids (oral or nasal), nasal decongestants, and leukotriene receptor antagonists. First-generation antihistamines are no longer recommended due to their central nervous system side effects and cardiac toxicity. Newer-generation antihistamines, such as cetirizine, loratadine, and desloratadine, offer enhanced efficacy and safety profiles. Intranasal antihistamines like olopatadine, levocabastine, and azelastine ensure targeted drug delivery to the nasal mucosa.

Corticosteroids act as the first-line pharmacotherapy by suppressing immune cell infiltration in AR and are effective for both mild and moderate-severe cases. Combination therapies, such as intranasal H1 antihistamines with intranasal corticosteroids, have demonstrated superior outcomes compared to oral H1 antihistamines plus intranasal corticosteroids. Leukotriene receptor antagonists like montelukast have shown efficacy in reducing night-time symptoms, especially when used in combination with H1 antihistamines. Nasal decongestants provide relief from nasal congestion symptoms by reducing mucosal swelling, but overuse can lead to rebound congestion (rhinitis medicamentosa), which can be treated with intranasal corticosteroids.

New research on combination therapy

Panchal *et al* (2021) conducted a Phase III, multicentre, randomised, double-blind study to evaluate the efficacy, safety, and tolerability of a fixed-dose combination (FDC) of montelukast 10mg and levocetirizine 5mg compared to either montelukast 10mg or levocetirizine 5mg alone in patients with seasonal allergic rhinitis (SAR). The study included various efficacy measures, including daytime nasal symptoms score, night-time symptoms score, daytime eye symptom score, patient's global evaluation, physician's global evaluation, and rhino-conjunctivitis quality-of-life score.

Results showed that the FDC group had a statistically significant improvement in daytime nasal symptoms score compared to the monotherapy groups. The FDC also demonstrated superiority in secondary efficacy endpoints, such as night-time symptoms score, daytime eye symptoms score, and rhino-conjunctivitis quality-of-life scores. The FDC of montelukast and levocetirizine was found to be safe and well-tolerated, with most adverse events being mild and unrelated to the study medication.

In another study by Mahatme *et al* (2016), the efficacy, safety, and cost-effectiveness of montelukast-levocetirizine and montelukast-fexofenadine combinations were compared in patients with AR. Results indicated a significant reduction in the total nasal symptom score in both groups, with the montelukast-fexofenadine group showing a more pronounced reduction. However, the cost-effectiveness ratio favoured the montelukast-levocetirizine combination.

Conclusion

The combination of montelukast and levocetirizine has emerged as an effective treatment option for AR, offering enhanced symptomatic relief compared to monotherapy. This combination not only improves symptoms but also enhances the quality of life of AR patients. Furthermore, combining montelukast with levocetirizine demonstrates cost-effectiveness, making it a practical choice for patients who may have affordability concerns with more expensive alternatives.

In the management of AR, healthcare providers should consider not only the clinical efficacy but also the economic feasibility of treatment options. The combination of montelukast and levocetirizine appears to strike a balance between efficacy and affordability, making it a valuable addition to the arsenal of treatments for AR. SF

References available in the online issue

JOINING THE DOTS

Two-fold treatment made simple

Glemolev

Montelukast • Levocetirizine dihydrochloride

Levocetirizine (second-generation antihistamine) **and montelukast** (leukotriene receptor antagonist)[1]

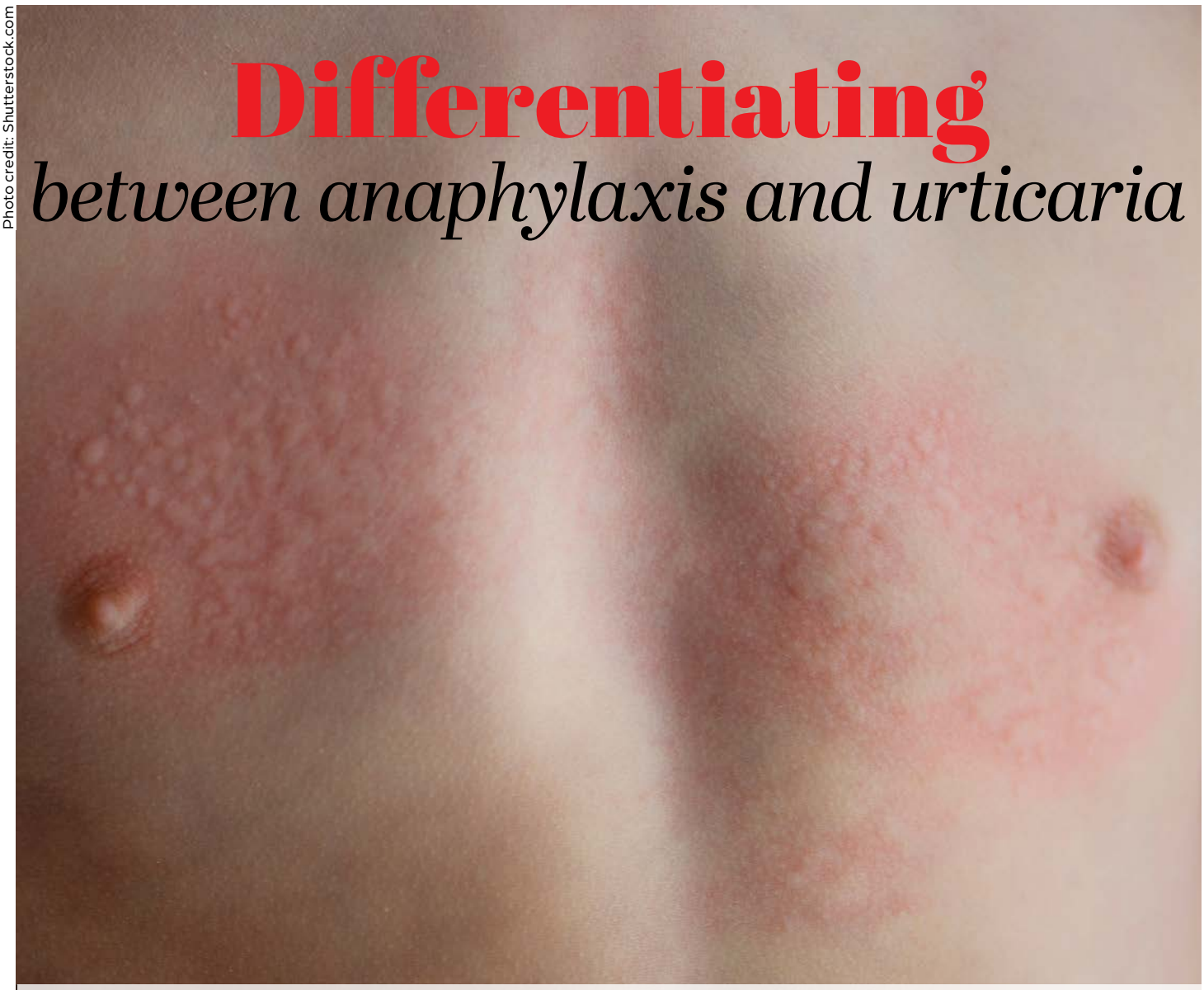
- **Levocetirizine & montelukast** combat both early and late-phase seasonal allergic rhinitis. [2,3]
- **Montelukast** targets the underlying inflammation, while **levocetirizine** provides **symptom relief** by blocking histamine. [1,2]

glenmark
A new way for a new world

References: 1. Mahatme MS, *et al*. Comparison of efficacy, safety, and cost-effectiveness of montelukast-levocetirizine and montelukast-fexofenadine in patients of allergic rhinitis: A randomized, double-blind clinical trial. *Indian J Pharmacol*. 2016;**48**(6):649-653. **2.** Bjermer L, *et al*. The complex pathophysiology of allergic rhinitis: scientific rationale for the development of an alternative treatment option. *Allergy Asthma Clin Immunol*. 2019;**15**:24. **3.** Panchal S, *et al*. Evaluation of efficacy and safety of montelukast and levocetirizine FDC tablet compared to montelukast and levocetirizine tablet in patients with seasonal allergic rhinitis: a randomized, double blind, multicentre, phase III trial. *Int J Otorhinolaryngol Head Neck Surg*. 2021;**7**(1):83-90. S3 **GLEMOLEV®** (film-coated tablets). Reg. No.: 49/5.7.1/0551. Each film-coated tablet contains montelukast sodium equivalent to montelukast 10 mg and levocetirizine dihydrochloride 5 mg. Contains sugar: 83,60 mg lactose monohydrate. For full prescribing information, refer to the Professional Information approved by the medicines regulatory authority. Date of publication: 28 October 2022. **HCR:** Glenmark Pharmaceuticals South Africa (Pty) Ltd. 2nd Floor, Building D, Stoneridge Office Park, 8 Greenstone Place, Greenstone, Edenvale, Gauteng, 1609. Tel: +27 11 564 3900. www.glenmarkpharma.co.za. 10/23/45562

Photo credit: Shutterstock.com

Differentiating between anaphylaxis and urticaria



Urticaria and anaphylaxis exhibit comparable clinical characteristics and are linked by shared immune-mediated pathways.

Urticaria manifests as a collection of fleeting, surface-level, itchy welts that appear in a pale or pink hue. They can exhibit a redness flare in their vicinity. These welts may appear in small quantities or be widespread and numerous. Their dimensions can range from a few millimetres to several centimetres. The distinctive feature of urticaria is its rapid and ever-changing nature.

Tryptase as a diagnostic marker for anyphylaxis

Tryptase serves as a marker of mast cell activation, primarily found in mast cells and to a lesser extent in basophils, with the α and β isoforms being biologically significant. During anaphylaxis, serum tryptase becomes detectable 30 minutes after symptom onset, peaking between 60 to 90 minutes, then declining after two hours, returning to baseline within 24 to 48 hours.

Thus, blood samples for tryptase measurement should be collected within 1–4 hours of the reaction, with a follow-up baseline measurement 24–48 hours later. Generally, baseline tryptase levels above 8ng/ml are considered elevated, but a precise cut-off for diagnosis is challenging, necessitating an individualised calculation based on the formula 1.2 x baseline +2ng/ml.

Tryptase levels tend to be higher and more persistent in anaphylactic reactions to intravenous drugs and insect venom than with oral triggers like food. Elevated tryptase correlates with hypotension. However, normal tryptase levels do not rule out anaphylaxis due to suboptimal sensitivity, influenced by the absence of α-tryptase genes in about 27% of the population. An alternative criterion for diagnosis is a 20% increase above baseline +2ng/ml within four hours of an allergic reaction.

Each individual welt emerges and vanishes within a 24 hour period, but the appearance of new welts implies that the entire episode may persist for a longer duration. Patients typically maintain good overall health, although during severe outbreaks, they may experience systemic symptoms like lethargy, malaise, and indigestion.

Anaphylaxis is characterised by a life-threatening decrease in blood pressure, breathing difficulties, or both. It may also exhibit additional symptoms such as widespread redness, itching, and the development of urticaria. True anaphylaxis is the result of an allergic reaction triggered by allergen-specific immunoglobulin (IgE). In contrast, anaphylactoid reactions present in a similar manner but do not involve IgE.

Anaphylaxis and urticaria

Anaphylaxis occurs when allergen cross-links with membrane-bound specific IgE antibodies, leading to immediate histamine

RUPANASE PAF* AWAY THEIR ALLERGIES.[3,4]

SUSTAINED **24 HR-ACTION** FOR EQUAL RELIEF OF **DAY & NIGHT** AR§ SYMPTOMS[2]

DUAL-ACTION **RUPANASE®** BLOCKS **HISTAMINE** FOR RELIEF OF **DAYTIME SNEEZING, RUNNY, ITCHY & BLOCKED SYMPTOMS,** AND **PAF*** FOR RELIEF OF **NASAL CONGESTION** AT **NIGHT**[2-6]

- **Once-daily 24 hour relief**[2,7,8]
- **Non-drowsy**[8]
- Starts to work **from the first dose**[9]
- Relieves chronic urticaria symptoms **from the first week**[10]

*platelet activating factor

§Allergic Rhinitis

†based on once a day dosing

References: 1. South African Medicine Price Registry. Database of Medicine Prices, 01 November 22 [online]. [cited 2022 Nov 17]; Available from URL: http://www.mpr.gov.za/. **2.** Marmouz F, Giralt J, Izquierdo I, et al. Morning and evening efficacy evaluation of rupatadine (10 and 20 mg), compared with cetirizine 10 mg in perennial allergic rhinitis: a randomized, double-blind, placebo-controlled trial. J Asthma Allergy 2011;4:27–35. **3.** Picado C. Rupatadine: pharmacological profile and its use in the treatment of allergic disorders. Exp Opin Pharmacother. 2006;7(14):1989-2001. **4.** Ridolo E, et al. Rupatadine for the treatment of allergic rhinitis and urticaria: a look at the clinical data. Clin Invest 2014;4(5):453-461. **5.** Smolensky MH, Lemmer B, Reinberg AE. Chronobiology and chronotherapy of allergic rhinitis and bronchial asthma. Adv Drug Deliv Rev 2007;59:852–882. **6.** Alfaro V. Role of histamine and platelet-activating factor in allergic rhinitis. J Physiol Biochem 2004;60(2):101-112. **7.** Valle M, et al. PD39 - Application of population pharmacokinetic modeling and simulation in the design of the optimal dose regime of rupatadine in children 2-5 year old children. Clin Transl Allergy 2014;4(Suppl 1):P39. **8.** RUPANASE Junior approved professional information, June 2020. **9.** Potter P, et al. Rupatadine oral solution in children with persistent allergic rhinitis: A randomized, double-blind, placebo-controlled study. Pediatr Allergy Immunol. 2013;24(2):144-150. **10.** Potter P, et al. Rupatadine is effective in the treatment of chronic spontaneous urticaria in children aged 2–11 years. Pediatr Allergy Immunol. 2016;27(1):55-61.

Scheduling status: S2 **Proprietary name (and dosage form):** RUPANASE 10 Tablets. **Composition:** Each tablet contains 12.80 mg rupatadine fumarate equivalent to Rupatadine 10 mg base. Contains sugar: lactose monohydrate 61.1 mg per tablet. **Registration number:** 46/5.7.1/0119. **Name and business address of applicant:** iNova Pharmaceuticals (Pty) Ltd, **Co. Reg. No.** 1952/001640/07, 15e Riley Road, Bedfordview. **Tel. No.** 011 087 0000. www.inovapharma.co.za. For full prescribing information, refer to the professional information as approved by the SAHPRA (South African Health Products Regulatory Authority) available at www.inovapharma.co.za. Further information is available on request from iNova Pharmaceuticals. 21828L. IN4808/23

inova pharmaceuticals

release from preformed mast cell granules. This activation prompts the synthesis of other mediators like leukotrienes, with their cumulative effect developing over four to six hours, potentially causing late reactions after the initial immediate response subsides. Clinically similar reactions can be induced by substances that directly activate mast cells, even without specific IgE presence.

Urticaria and angioedema can manifest together or as components of an anaphylactic reaction, yet either condition can also occur independently, and not all cases are attributed to IgE mechanisms. Anaphylaxis, on the other hand, is a sudden, life-threatening systemic reaction with diverse causes, clinical presentations, and levels of severity. It arises from the rapid release of mediators by mast cells and basophils and can even lead to fatalities.

Anaphylaxis, urticaria, and angioedema share common pathogenic mechanisms involving vasodilation and increased capillary permeability. The symptoms of anaphylaxis can vary based on age, with young children often experiencing vomiting and cough, while older children may have symptoms like chest tightness, dizziness, hypotension, and cardiovascular collapse.

Anaphylaxis can affect anyone, but those with personal or family histories of atopic disease are at a higher risk. Anaphylaxis linked to IgE antibodies, known as type 1 hypersensitivity, represents the most severe form of immediate allergic reaction, requiring prior exposure to the allergen for IgE antibodies to form and trigger anaphylaxis.

Treatment options

The primary treatment for acute anaphylaxis involves administering 1:1.000 epinephrine (0.01mg/kg, up to 0.5mg) intramuscularly in the anterolateral thigh, repeatable every five to 15 minutes if necessary. There are no absolute contraindications for epinephrine use, and its prompt administration is crucial to prevent progression to severe anaphylaxis and potential fatality. It's important to note that epinephrine is not recommended for the management of urticaria.

Airway protection, cardiovascular support with intravenous fluids, and b-adrenergic agonists like albuterol are essential. Antihistamines can help control urticaria and itching but are not first-line treatment. Limited evidence supports the use of corticosteroids, as they do not reduce the risk of biphasic reactions. Patients should be monitored for four to eight hours, with longer monitoring for asthmatic patients, those with severe anaphylaxis history, or those requiring multiple epinephrine doses.

Idiopathic anaphylaxis presents a challenge, often requiring continuous steroid treatment for patients with repetitive attacks. Patients experiencing frequent urticaria and angioedema attacks may find relief from regular preventive use of non-sedating, long-acting antihistamines, even at doses higher than typically recommended.

For nocturnal symptoms, sedating antihistamines like chlorphenamine and hydroxyzine are options. Cimetidine, with its unique immunosuppressive properties, is considered but offers limited benefit. Doxepin is potent but very sedating, while mirtazapine is effective with fewer side effects. Long-term steroid use should be avoided. For angioedema without urticaria, antihistamines may help, but tranexamic acid (up to 1g four times a day) can provide better results.

Conclusion

While urticaria primarily involves skin manifestations, anaphylaxis is a more widespread and severe systemic reaction, which can include urticaria as one of its symptoms. Therefore, urticaria can be considered one of the signs or symptoms of anaphylaxis, but they are not the same condition, and a differential diagnosis is required. SF

References available in the online issue

Long-lasting *acid control is possible*

Photo credit: Shutterstock.com

Gastro-oesophageal reflux disease (GORD) is associated with considerable reductions in quality of life and work productivity, as well as increased healthcare use. Proton pump inhibitors (PPIs) are currently the most effective treatment for GORD. However, there are limitations associated with these drugs in terms of patients' response.[1]

Erosive esophagitis, caused by gastroesophageal reflux, is a common medical problem. Therapy for erosive oesophagitis primarily focuses on the pharmacological reduction of gastric acid secretion. Decreasing the acidity of gastric juice improves reflux symptoms and facilitates oesophagitis healing.[2]

Proton pump inhibitors

The PPI, introduced in 1989, reflected a major medical therapeutic breakthrough in the treatment of peptic ulcers and GORD, resulting in more rapid healing of the lesions and symptom relief. A PPI is a prodrug which is activated by acid.[3]

PPIs have about one hour of elimination half-life. The area under the plasmic concentration curve and the intragastric pH profile are very good indicators for evaluating PPI efficacy. Omeprazole was the first PPI introduced into the market, followed by pantoprazole, lansoprazole and rabeprazole. Though these PPIs share the core structures benzimidazole and pyridine, their pharmacokinetics and pharmacodynamics are a little different.[4]

Dexlansoprazole has shown the best control of the intragastric pH among the present PPIs. Overall, PPIs made significant progress in the management of acid-related diseases and improved health-related quality of life.[4]

Because PPIs have a relatively short half-life and not all pumps are activated, it takes about three days to reach steady state inhibition of acid secretion as a balance is struck between covalent inhibition of active pump, subsequent stimulation of inactive pumps after the drug has been eliminated from the blood and *de novo* synthesis of new pumps.[4]

The target for treatment of many acid-related disorders is reduction of gastric acid secretion. PPIs are widely used to reduce acid secretion in patients with GORD.[1]

Clinical limitations

While PPIs are widely regarded as the gold-standard of GORD treatment, there are several clinical limitations to some PPIs. PPIs are associated with limited ability to fully relieve the discomfort of GORD, particularly at night. Studies show that only 23% of patients felt that their pain and discomfort was completely controlled with PPIs at night and 94% continued to experience breakthrough symptoms. This resulted in 49% of respondents using adjunctive medications to control discomfort. An estimated 45% of respondents found that treatment for nocturnal pain was unsatisfactory. Approximately 38% of patients taking PPIs had breakthrough symptoms, and an overwhelming 65% of these patients experienced them at night.[1]

According to Goh *et al* (2016), The active ingredient in a PPI must be present in high concentrations when the proton pumps are stimulated before and during a meal. As PPIs are acid labile, they need protection from degradation in the stomach by enteric coating or buffering. PPIs are rapidly absorbed and subsequently eliminated, leading to a short plasma half-life and ultimately restricting their administration to before meals to achieve their full effect.[1]

As pre-meal dosing is not always convenient, this may lead to poor adherence. However, participants reported good adherence to the prescribed therapies in terms of frequency of administration (87%), timing of medication (87%), and mealtimes (88%).[1]

Dexlansoprazole

Dexlansoprazole is the R-enantiomer of the PPI lansoprazole, a racemic mixture of R-lansoprazole and S-lansoprazole. The R-enantiomer is associated with three to five times times greater maximum concentration (Cmax), area under the plasma concentration-time curve, and time to maximum concentration values than the S-enantiomer, and smaller total body clearance values, so it has greater systemic exposure than lansoprazole and a longer elimination half-life than S-lansoprazole.[1]

Dexlansoprazole is the first PPI with a dual delayed release formulation designed to provide two separate releases of medication to extend the duration of effective plasma drug concentration. Dexlansoprazole has been shown to be effective for healing of erosive oesophagitis, and to improve patient well-being by controlling 24 hour symptoms. Dexlansoprazole has also been shown to achieve good plasma concentration, regardless of administration with or without food, providing flexible dosing.[1]

The dual delayed release formulation of dexlansoprazole results in a plasma concentration-time profile with two peaks.[1]

The pharmacodynamic impact of the second peak is that PPIs work only on activated H+, K+-ATPase enzyme (proton pumps), of which 70%-80% are activated after a meal, leaving 20%-25% inactivated. These can still be activated and lead to acid secretion. Additionally, these proton pumps have a half-life of about 50 hours, meaning that about 25% of the pumps are produced daily at about 1% per hour. These newly produced H+, K+-ATPase enzyme (proton pump) can then also produce acid.[1]

Dual delayed release formulation

The dual delayed release technology in dexlansoprazole uses two types of enteric-coated granules with different pH-dependent dissolution profiles to provide an initial drug release in the proximal small intestine, at a pH of about 5.5, followed several hours later by another drug release at more distal regions of the small intestine, at a pH of ≥6.75.[1]

Dexlansoprazole therefore produces a dual-peaked pharmacokinetic profile, as opposed to the single peak seen with conventional PPIs. Dexlansoprazole increases the mean intragastric pH and the duration that intragastric pH is >4 over a 24 hour period. The optimal dose range is 30-90mg, and the two doses currently approved for clinical use are 30mg and 60mg.[1]

Dexlansoprazole is the first PPI with a dual delayed release formulation designed to provide two separate releases of medication. In January 2009, the American Food and Drug Administration approved dexlansoprazole for the treatment of heartburn associated with symptomatic non-erosive GORD, healing of erosive oesophagitis and maintenance of healed erosive oesophagitis at doses of 30mg and 60mg once daily.[1]

GORD is associated with considerable reductions in quality of life and work productivity

As Frye *et al* (2015) explained that the R-enantiomer is subsequently associated with decreased clearance compared to the S-enantiomer. However, this is not the sole mechanism that extends the effect of dexlansoprazole modified release (MR), as the elimination half-life of dexlansoprazole is like other PPIs (approximately 1-2 hours). It is the delivery system, rather than the inherently slower hepatic clearance, that prolongs the plasma residence time of dexlansoprazole MR. The dual delayed-release technology incorporates two distinct sets of enteric-coated granules that are designed to offer two distinct, pH-dependent releases of drug.[5]

The gelatine capsule containing the granules dissolves in the stomach, and the first set of granules (~25% of the drug dose) is released into the proximal duodenum (pH 5.5). This results in an early rise in plasma concentration (one to two hours), similar to other PPIs. The remaining granules (75%) are designed to be released in the distal small intestine (pH 6.75), resulting in a second concentration peak at four to five hours after ingestion. This delivery system provides a prolonged duration of acid suppression and helps to limit the necessity for more than once-daily dosing.[5]

A randomised, open-label, two-period crossover study compared the pharmacodynamic effects of single-dose dexlansoprazole MR 60mg and esomeprazole 40mg on 24 hour intragastric pH in healthy adult subjects showed the average 24 hour intragastric pH following a single dose of dexlansoprazole MR was higher compared to a single dose of esomeprazole (58% vs 48%; P=0.0003). The most important difference was noted in the second half of the day, presumably due to the longer duration of action of dexlansoprazole MR.[5]

Chiang *et al* (2019) compared the clinical efficacy of single doses of dexlansoprazole (modified-release 60mg) and esomeprazole (40mg) after 24-weeks follow-up in patients with mild erosive oesophagitis. Patients displaying complete symptom resolution (CSR) by the end of initial treatment (eight weeks) were switched to on-demand therapy until the end of 24 weeks.[2]

The GERD Questionnaire scores at 4-, 8-, 12-, 16-, 20-, and 24-week posttreatment were less than the baseline score. The CSR, rate of symptom relapse, days to symptom resolution, sustained healing rate of erosive esophagitis, treatment failure rate, and the number of tablets taken in 24 weeks were similar in both groups. The esomeprazole group had more days with reflux symptoms than the dexlansoprazole group (37.3±37.8 vs 53.9±54.2; P=0.008). In the dexlansoprazole group, patients exhibited persistent improvement in the GERDQ score during the on-demand period (week eight vs week 24; P<0.001) but not in the esomeprazole group (week 8 vs week 24; P=0.846).[2]

This study suggests that the symptom relief effect for GERD after 24 weeks was similar for dexlansoprazole and esomeprazole. Dexlansoprazole exhibited fewer days with reflux symptoms in the 24 week study period, with better persistent improvement in the GERDQ score in the on-demand period.[2]

Conclusion

Since PPIs were introduced, considerable progress has been made in the management of acid-related diseases.

The average 24 hour intragastric pH following a single dose of dexlansoprazole MR was higher compared to a single dose of esomeprazole (58% vs 48%; P=0.0003).

The most important difference was noted in the second half of the day, presumably due to the longer duration of action of dexlansoprazole MR.[5] SF

References available in the online issue

DEXILANT®
dexlansoprazole
30 MG | 60 MG DELAYED RELEASE CAPSULES

The first once-a-day PPI with novel dual delayed release technology.[1,2]

24 hour heartburn free days are achievable.[1,2]

Rapid Release[1]

Modified Release[1]

One capsule daily[1]

At last... a chemical entity your patients can start on once-daily and stay on once-daily.[1,2]

PPI = Proton Pump Inhibitor

REFERENCES:
1. Dexilant Professional Information. Takeda (Pty) Ltd, South Africa; August 2021. **2.** Metz DC, Howden CW, Perez MC, *et al.* Clinical trial: dexlansoprazole MR, a proton pump inhibitor with dual delayed release technology, effectively controls symptoms and prevents relapse in patients with healed erosive oesophagitis. *Aliment Pharmacol Ther* 2009;29:742-754.

S4 **DEXILANT®** 30 mg modified-release capsules, hard. Reg. No. 48/11.4.3/0695. Each capsule contains 30 mg of dexlansoprazole.

S4 **DEXILANT®** 60 mg modified-release capsules, hard. Reg. No. 48/11.4.3/0696. Each capsule contains 60 mg of dexlansoprazole.

For full prescribing information refer to the professional information approved by the medicines regulatory authority. TAKEDA (Pty) Ltd. Reg. No.: 1982/011215/07. Building A, Monte Circle, 64 Montecasino Boulevard, Fourways, 2191, South Africa. Tel: +27 (0) 11 514 3000. Fax: +27 (0) 11 514 3001. Marketed by Adcock Ingram Limited. Reg. No. 2007/019928/07. Private Bag X 69, Bryanston, 2021, South Africa. Tel +27 (0) 11 635 0000. www.adcock.com. C-APROM/ZA/DEXI/0051

Takeda

adcock ingram prescription

Insulin

choices, choices, choices...

Photo credit: Shutterstock.com

Due to the complexity of diabetes therapy algorithms, insulin treatment protocols often seem like a minefield of right, wrong or indeterminate choices. Nonetheless, effective management requires precision on the part of clinicians.

Diabetic treatment must be based on a thorough understanding of the underlying mechanisms of the disease. Therefore, the only treatment for type 1 diabetes (T1DM) is the injection of insulin or insulin analogues. Insulin resistance is the predominant feature in the early stages of type 2 diabetes (T2DM), but this disease is much more complex.

The timely initiation and titration of insulin is a challenge for many healthcare professionals involved in the treatment of T2DM. The failure to do so when clinically indicated is a multifactorial problem with significant consequences for patients, including an increased risk of microvascular complications.

Barriers to insulin initiation and intensification include the inconvenience of the treatment regimen, needle phobia, and fear of hypoglycaemia. These barriers can be compounded by patient factors such as poor health literacy, lack of social support, and financial constraints. Healthcare professionals play a vital role in addressing these barriers through patient education, individualised support, and shared decision-making.

Basal insulin and analogues

Optimal basal insulin therapy entails an insulin analogue that mimics the natural basal endogenous insulin secretion profile, ensuring consistent and efficacious glycaemic control. Basal insulin analogues produced through recombinant DNA technology represent a significant advance over Neutral Protamine Hagedorn (NPH)

Use a new needle with every injection

Use needles once only

- Less painful injections – research has shown that injection pain increases in proportion to needle re-use.[1]
- Repeated use of needles amplifies the risk of needle contamination.[1]
- Reduced damage to the skin – research has shown that repeated use of the needle can increase skin inflammation at the injection site.[1]

Did you know?

Pen needles are sterile and designed for single use only.[2] This special symbol on every box of pen needles mean use once only.

1. Misnikova I.V. et al. The risks of repeated use of insulin pen needles in patients with diabetes mellitus. Journal of Diabetology 2011 ; 1:1-5
2. Frid A., New Insulin Delivery Recommendations. Mayo Clinic Proceedings. Sept. 2016. 91(9): 1231-1255

bdandme.bd.com

Becton Dickinson (Pty) Ltd, Reg. No. 1995/005042/07, 20 Woodlands Drive, The Woodlands Office Park, Building 6(G), Woodmead, 2191, Johannesburg, South Africa, Tel +27 (010) 201 7400, BD75850, Expiry Date: 30 September 2024.

CE 0050

BD

insulin, an intermediate-acting insulin still in use today despite its requirement for twice-daily dosing and relatively high risk of hypoglycaemia.

The first generation of basal insulin analogues, namely insulin glargine 100 units/mL (Gla-100) and insulin detemir 100 units/mL, offered near 24 hour glucose-lowering effects with minimal variability in insulin action and a lower hypoglycaemia incidence than NPH insulin.

The newer second-generation basal insulin analogues, insulin glargine 300 units/mL (Gla-300) and insulin degludec 100 units/mL (IDeg U100) or 200 units/mL (IDeg U200), exhibit extended durations of action and evenly distributed activity profiles. They are associated with reduced hypoglycaemia rates and maintain HbA1C control comparable to earlier basal analogues. Additionally, they offer the convenience of once-daily dosing and decreased interindividual variability.

Despite the advent of insulin analogues, improved insulin regimens, enhanced injection devices, promotion of early insulin initiation, and continuous titration algorithms, many individuals with T2DM continue to struggle with inadequate glycaemic control.

Basal plus

To enhance glycaemic control, individuals with suboptimal control on a basal insulin regimen can transition to a basal-plus insulin approach. This entails adding a short- or rapid-acting insulin before the largest meal or the one causing the most post-meal glucose spikes. Insulin doses are titrated based on self-monitoring glucose levels before subsequent meals.

Gradually, additional insulin doses are introduced for meals associated with post-meal hyperglycaemia, ultimately forming a complete basal-bolus regimen. Concurrently, oral agents, excluding metformin, are gradually phased out to simplify the regimen.

Barriers to insulin initiation and intensification include the inconvenience of the treatment regimen, needle phobia, and fear of hypoglycaemia

When to initiate insulin

Indications for insulin therapy in non-pregnant adults encompass various scenarios related to T2DM. This includes initiating insulin treatment at the time of diagnosis or during any stage when there is evident metabolic decompensation. Such decompensation can be characterised by several factors, including significant weight loss due to catabolism, fasting plasma glucose levels that exceed 14mmol/l, consistently elevated random glucose levels surpassing 16.5mmol/l, HbA1C levels exceeding 10%, and the presence of persistent ketogenesis, ketoacidosis, or a hyperosmolar non-ketotic state.

For stable patients who are not experiencing metabolic decompensation, insulin becomes a viable treatment option under different circumstances. It should be considered when these individuals struggle to achieve or maintain adequate glycaemic control despite the use of two or more alternative anti-diabetic agents. These guidelines help guide healthcare professionals in determining when insulin therapy is appropriate for non-pregnant adults with T2DM.

What influences patient choice?

For patients with T2DM who cannot or are unwilling to adhere to basal plus/basal-bolus regimens, premixed insulin is the best option. Patient-reported outcomes (PROs) should be assessed before and during treatment to ensure patient-centred care. PROs include quality of life, satisfaction, diabetes-related distress, anxiety and depression, coping skills, and the quality of communication between the healthcare provider and patient.

A patient's overall health is a critical factor in determining the suitable insulin formulation. Analogue insulins hold an advantage due to their lower hypoglycaemia risk compared to human insulins. For those with busy, unpredictable lifestyles, the flexibility to align insulin administration with the main daily meal enhances convenience and adherence.

IDegAsp is a valuable choice for initiating insulin therapy in several scenarios. This includes drug-naïve patients displaying hyperglycaemic symptoms, individuals with high-carb diets, those with elevated HbA1c levels, and concerns about post-meal blood sugar spikes. It's also an option when oral anti-diabetic medications (single, dual, or triple therapies) prove ineffective.

Consistent meal schedules are vital for achieving glycaemic goals. Yet, dietary patterns may vary based on work obligations and religious practices, like Ramadan, which can affect glycaemic control and insulin usage in individuals with diabetes. During religious fasting, premixed insulin analogues, known for their efficacy and lower hypoglycaemia rates, are preferred over premixed human insulins. IDegAsp may be the favoured choice for individuals fasting during Ramadan, highlighting the importance of risk assessment and counselling for these individuals. SF

How does insulin work?

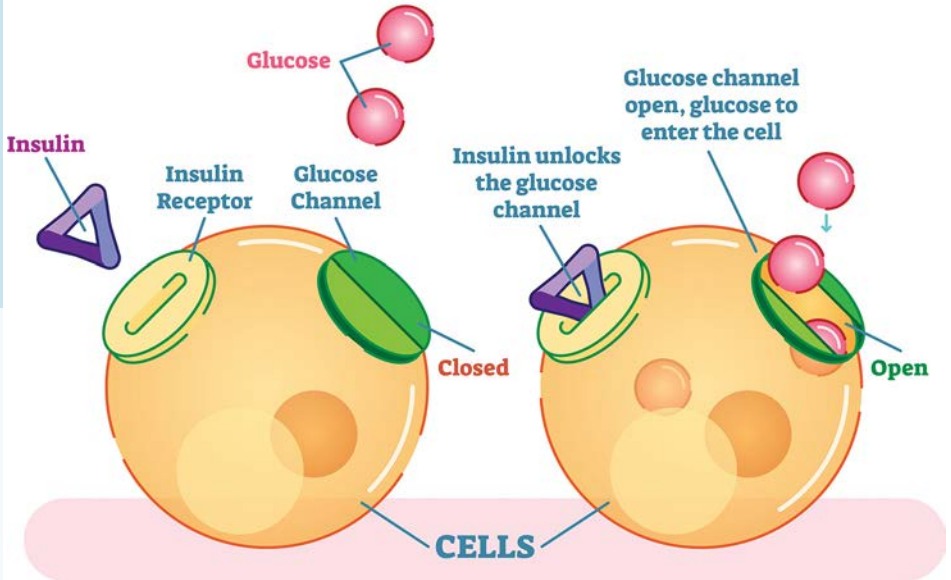


Photo credit: Shutterstock.com

References available in the online issue


Photo credit: Shutterstock.com

How to manage antidepressant-related sexual dysfunction

The primary treatment for major depressive disorder (MDD) often involves the use of antidepressant medications. However, there is a significant issue associated with these medications that often goes unnoticed and unaddressed – sexual dysfunction.

This treatment-emergent sexual dysfunction (TESD) is a side effect that can lead to distress for patients and their partners. It remains underestimated in clinical practice and in the technical data sheets for antidepressants.

Understanding the prevalence of TESD

TESD is a common problem among those who are actively engaged in sexual activity and are prescribed antidepressant medications. This issue often remains hidden, as patients may not readily report it to their healthcare providers due to its intimate nature. As a result, TESD is frequently underestimated both in clinical practice and in the technical information provided for antidepressant drugs.

The underestimation of TESD is due, in part, to the way its prevalence is reported. Many of the incidence rates are derived from controlled drug trials and short-term efficacy studies, which may not accurately reflect the real-world experiences of patients. These studies often exclude sexually inactive patients and rely solely on spontaneous reports, leading to an inaccurate picture of the issue. In actual clinical practice, TESD is believed to be much more prevalent than indicated in the official documentation, with estimates suggesting that it affects a significant portion of patients using antidepressants.

It is important to recognise that

TESD is not an isolated concern but is closely linked to depression itself. Depressed individuals are more likely to experience sexual dysfunction, which is why it is crucial for clinicians to screen for TESD when evaluating individuals with depressive symptoms.

MDD is a severe and debilitating mental illness that affects millions of people worldwide

The impact of TESD on patient adherence

TESD can have a profound impact on a patient's ability to tolerate and adhere to antidepressant treatment. This often leads to distress for the patient or their partner, creating a significant barrier to treatment adherence. The discomfort and dissatisfaction associated with TESD can result in patients discontinuing their medication or choosing not to initiate long-term treatment, particularly if the dysfunction persists beyond a certain duration.

It is important to note that not all patients are affected in the same way by TESD. Some individuals, such as post-menopausal women, may tolerate it without significant distress. However, for those who consider preserving their sexual function as crucial, clinicians have an ethical obligation to discuss the potential sexual side effects of antidepressant medication before prescribing it. This ensures that patients can make informed decisions about their treatment.

Psychotherapy may also be considered as an alternative for individuals who are unwilling to take antidepressants due to the risk of sexual dysfunction. This underscores the importance of a patient-centred approach to treatment.

Strategies for minimising TESD

To address TESD effectively, clinicians should consider several strategies. First and foremost, they should prioritise primary prevention by initiating treatment with antidepressants that have a low incidence of TESD. Some of the recommended antidepressants for this purpose include agomelatine, mirtazapine, and bupropion. Bupropion, in particular, has a substantial body of scientific evidence supporting its low incidence of TESD and is often considered the first choice for individuals who are sexually active.

Switching to bupropion

Bupropion stands out as one of the most widely used antidepressants with a minimal impact on sexual function. It primarily affects the release of dopamine and norepinephrine, without significantly influencing serotonin. Several controlled studies have demonstrated its effectiveness in minimising TESD, with some cases even showing improvements in sexual functioning, including enhanced sexual desire. In situations where switching medications is not possible, combining bupropion with an selective serotonin reuptake inhibitors (SSRI) can help reduce TESD.

Bupropion's effectiveness is further supported by clinical experience, which indicates that transitioning from bupropion to an SSRI can lead to SSRI discontinuation syndrome. To minimise these effects, a washout period is recommended before starting bupropion treatment.

It's important to note that while bupropion is a valuable option for minimising TESD, it may not be suitable for all patients.

As noted by Montejo *et al* (2019), there is a delicate balance between prescribing an effective drug that improves depressive symptomatology and has a minimum impact on sexuality. The suggested recommendations include the following: for low sexual desire, switching to a non-serotoninergic drug, lowering the dose, or associating bupropion or aripiprazole, for unwanted orgasm delayal or anorgasmia, dose reduction, 'weekend drug holiday' or switching to a non-serotoninergic drug or fluvoxamine, for erectile dysfunction, switching to a non-serotoninergic drug or the addition of an antidote such as phosphodiesterase 5 inhibitors, and for lubrication difficulties, switching to a non-serotoninergic drug, dose reduction, or using vaginal lubricants. A psychoeducational and psychotherapeutic approach should always be considered in cases with poorly tolerated sexual dysfunction.

Clinical recommendations and future directions

Currently, there is a consensus among healthcare professionals that TESD is frequently underestimated, and clinicians often fail to inquire about their patients' sexual activity and function. This oversight can have a significant impact on patient adherence to antidepressant treatment, potentially leading to relapses and recurrences of depression.

To address this issue, clinicians should make an effort to gather a comprehensive psychosexual history from patients before initiating antidepressant medication. This includes assessing the frequency of intimate relations, sexual satisfaction, and the patient's and their partner's perspective on the relevance of these aspects. Regular monitoring of sexual function is essential, and a personalised strategy for managing TESD should be devised if it arises and is poorly tolerated by the patient or their partner.

Given the diverse nature of human sexuality, there is no one-size-fits-all approach to alleviating TESD. The management of TESD remains dependent on clinicians' professional judgment, which often results in an incomplete assessment of the patient. Nevertheless, the primary focus should always be on primary prevention, utilising antidepressants with minimal impact on sexual function.

In conclusion, TESD is a significant concern in the treatment of MDD. Bupropion, along with other antidepressants like agomelatine and mirtazapine, offers a promising avenue for minimising this issue. However, the approach should be individualised, considering the specific needs and tolerances of each patient. By addressing TESD effectively, clinicians can improve treatment adherence, enhance patient quality of life, and achieve better overall treatment outcomes.

Overall, the awareness and understanding of TESD are crucial for improving the quality of life of individuals with MDD. Through continued research and a patient-centred approach, healthcare providers can help patients effectively manage depression without sacrificing their sexual well-being. SF

References available in the online issue

NEW

PROLONG THEIR POSITIVITY

PRODYNA 150 mg 300 mg XR

BUPROPION HYDROCHLORIDE

PATIENTS EXPERIENCING SYMPTOMS OF **LOSS OF POSITIVE AFFECT** CAN BE RETURNED TO NORMAL FUNCTIONING WITH AN AGENT THAT HAS A **DOPAMINERGIC** AND/OR **NORADRENERGIC** COMPONENT.[1]

For further product information contact **PHARMA DYNAMICS**
Email info@pharmadynamics.co.za **CUSTOMER CARE LINE** +27 21 707 7000

pharma dynamics
EFFECTIVE AFFORDABLE HEALTHCARE

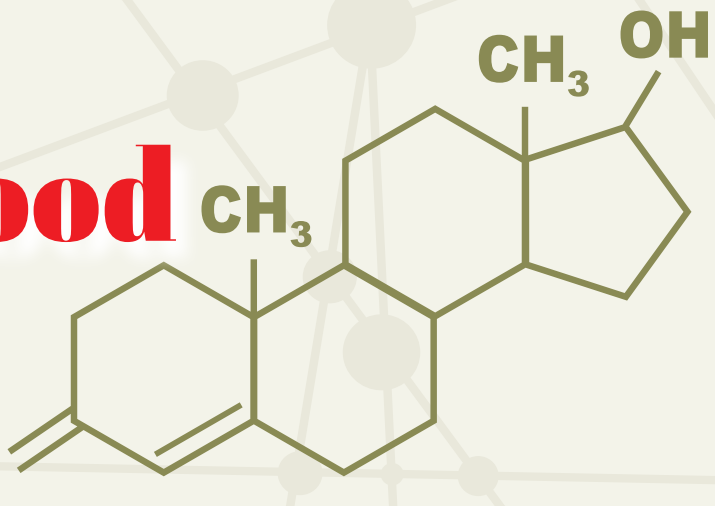
www.pharmadynamics.co.za

PRODYNA 150, 300 mg XR. Each tablet contains 150, 300 mg bupropion hydrochloride respectively. S5 A54/1.2/0181,0182. For full prescribing information, refer to the professional information approved by SAHPRA, March 2023. **1)** Nutt, D.J., 2008. Relationship of neurotransmitters to the symptoms of major depressive disorder. *The Journal of clinical psychiatry*, 69, pp.4-7. **PDAA914/10/2023**

November 2023 | Vol. 23 No. 11
www.medicalacademic.co.za

Photo credit: Shutterstock.com

The 'most misunderstood molecule in medicine'



This article highlights the significance of testosterone therapy (TTh) for men with testosterone deficiency (TD) or hypogonadism. It emphasises that while many people are aware of the role of testosterone in male sexual desire and muscle mass, the broader medical community often overlooks its vital importance in addressing various general medical conditions.

Testosterone is a ubiquitous molecule among vertebrates, leading to tens of thousands of research studies exploring its effects in animals. The effects of castration on muscle, fat, and sexual behaviour have been recognised in humans and domesticated animal species for millennia. The androgen receptor, a key molecule that mediates the effects of androgens in most human tissues, has been identified in a remarkably broad range of tissues, including but not limited to muscle, bone, bone marrow, the peripheral and central nervous system, adipocytes, liver, kidney, skin, and testis. It is no wonder that a deficiency of testosterone has been shown to have numerous negative effects in men, which may be improved or reversed with normalisation of serum testosterone through TTh.

Although healthcare providers (HCPs) may have a general awareness that testosterone is important for male sexual desire and muscle mass, it is not widely appreciated that TD is associated with several of the most important general medical conditions facing our society, including type 2 diabetes (T2DM), obesity, osteoporosis, and cardiovascular (CV) disease, and TTh has shown compelling health benefits for those conditions, among others. Testosterone levels have been associated with the most urgent global medical issue of the past several years, namely Covid-19 infection, and TTh has even been shown to reduce the rate of severe infection. Mortality has been shown to be associated with low levels of testosterone, and observational studies have shown a two-fold decrease in mortality among men with TD that received TTh.

Referring to the 'most misunderstood molecule in medicine', Morgentaler *et al* (2022) emphasise that there has been little recognition within the medical community of the health impact of T, TD, and the substantial benefits of TTh on health and quality of life despite high-level clinical evidence.

"TD negatively impacts human health and quality of life and is associated with increased mortality. Several studies have demonstrated that TTh in men with TD reduced all-cause and CV mortality. The longstanding belief that TTh is associated with increased prostate cancer risk is contradicted by recent evidence, including multiple studies showing that TTh is associated with reduced risk. Similarly, the weight of current evidence indicates the purported concern that TTh is associated with increased CV risk is incorrect," the authors stated.

Lines of evidence argue strongly for the need for greater awareness in the medical community of the impact of TD on health, and of the health benefits of TTh.

Testosterone deficiency and its impact

Testosterone plays a crucial role in various aspects of male health, including metabolism, sexual function, and vascular health. A deficiency in testosterone can have negative effects on physical, psychological, and cognitive well-being. Numerous studies have demonstrated the therapeutic value of TTh, showing improvements in sexual function, mood, bone density, and prevention of prediabetes progression to T2DM. Additionally, low testosterone levels have been linked to increased incidences of dementia and Alzheimer's disease.

Challenges with FDA and age-related TD

In terms of 'age-related' hypogonadism, there is no scientific basis for distinguishing between known causes of TD and age-related TD, as the problem in both cases is a deficiency of testosterone. The safety profile of TTh is considered acceptable, and since classical TD cases are rare, most research studies involve men with age-related TD.

TTh may be protective and therapeutic for prostate cancer

Morgentaler *et al* highlight studies that suggest TTh may have protective and therapeutic effects on prostate cancer. Research shows reduced recurrence rates and delayed recurrence in men receiving TTh after radical prostatectomy. A study on the combination of TTh and metformin shows a reduction in prostate cancer incidence. These findings challenge the historical belief that TTh increases the risk of prostate cancer.

TTh in diabetes and obesity

A significant portion of men with T2DM have TD, and obesity is a common cause of TD in the community. Studies indicate

S5 Androgel®
Testosterone 1% gel

HELP YOUR PATIENT PERFORM AT HIS LEVEL BEST

Indication: [1]

- Testosterone replacement therapy for male hypogonadism in adult men when testosterone deficiency has been confirmed by clinical features and biochemical tests

Pharmacokinetic properties:[1]

- Androgel® provides rapid effects, with no ups and downs in effectiveness, reaching steady state on Day 2
- Testosterone levels are maintained within the physiological range with a daily application
- Testosterone concentrations return to baseline 72-96h after the final dose

In men with hypogonadism Androgel® is associated with a range of benefits such as: [2,3,4]

- Improved mood
- Improved libido and sexual function
- Improved metabolic parameters
- Increased lean muscle mass
- Reduced body fat mass

Androgel® has been shown to significantly improve overall health-related quality of life in men with low testosterone.[4]

Nappi Code	Medicine Schedule	Active ingredient	Strength	Dosage Form	Quantity
3000765-001	S5	Testosterone	50mg/5g	Gel in sachet	30 per box

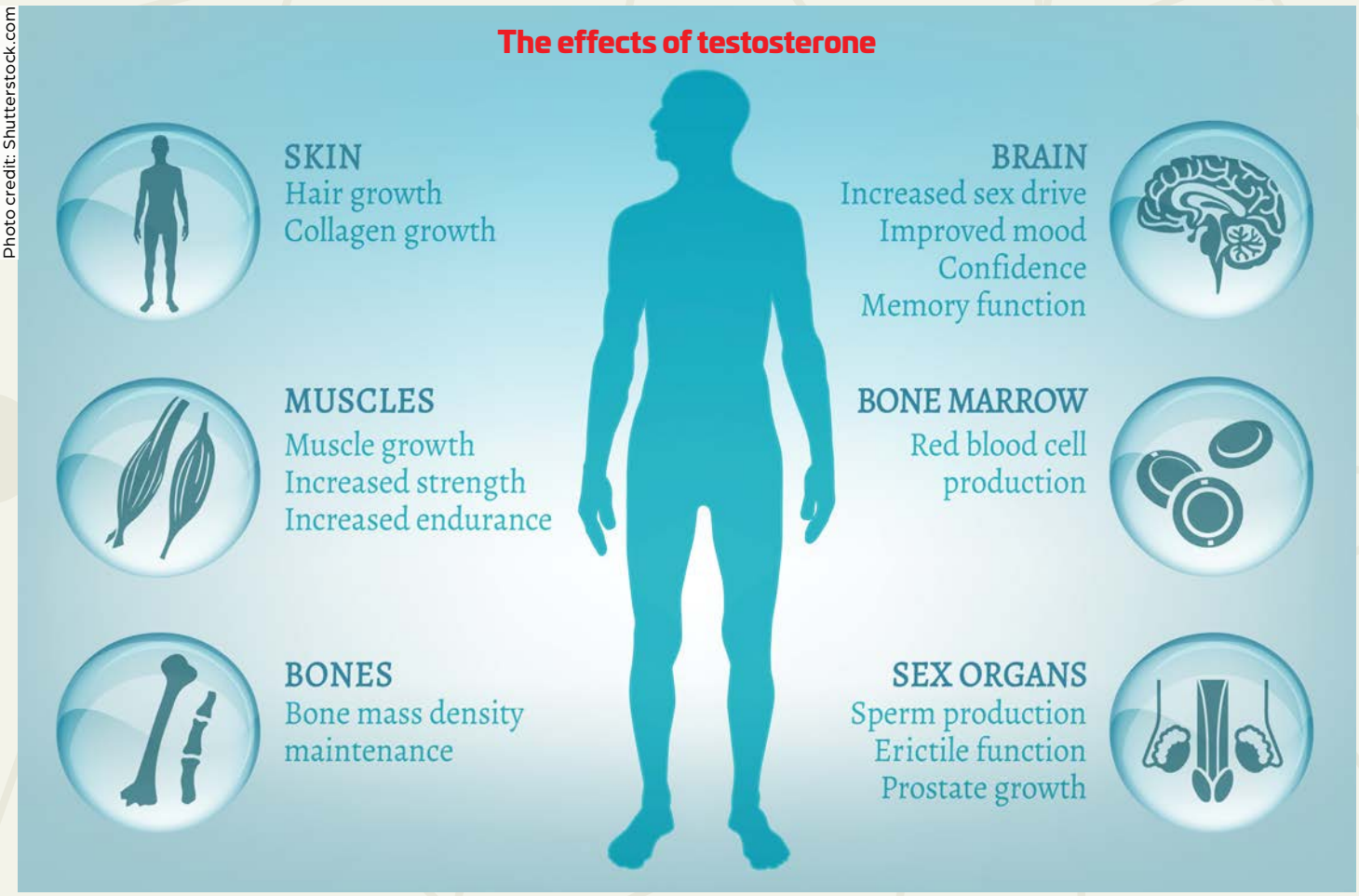
References: 1. Androgel® Package Insert; 2. Wang C et al.J Clinc Endocrinol Metab 2000;85:2839-2853; 3. Wang C et al.J Clinc Endocril Metab 2004;89:2085-2098; 4. Behre HM et al.Aging Male 2013;15:198-207

MEDI CHALLENGE (PTY) LTD
Innovating for Well-being BESINS HEALTHCARE

MEDI CHALLENGE (PTY) LTD
493 de Jonge Street Elarduspark,
Pretoria 0181
www.medichallenge.co.za

For more information on **Androgel®** or to obtain full Product Information please contact Medical Department at **denitza@medichallenge.co.za**

Photo credit: Shutterstock.com



that body weight strongly influences testosterone levels. Therefore, healthcare practitioners should measure testosterone in all T2DM and obese patients and consider TTh not only for sexual function but also for its metabolic benefits.

Long-term benefits of TTh

Long-term studies to understand the lasting effects of TTh are important. A 13-year follow-up study showed substantial weight loss, improved glycaemic control, and remission of T2DM in the TTh group. Adverse CV events were less frequent in this group, indicating a potential cardioprotective effect of TTh. A meta-analysis of TTh trials found no significantly increased risk of CV events. It also points out that active smoking can nullify the beneficial effects of TTh.

CV benefits of TTh

There is a link between low testosterone levels and increased mortality and CV events. Normalisation of serum testosterone with TTh is associated with reduced mortality, heart attacks, strokes, and atrial fibrillation, particularly in men without prior CV events. However, the protective effect of TTh is diminished in men with a history of myocardial infarction. SF

References available in the online issue

HELP YOUR PATIENTS WITH TYPE 1 DIABETES ENJOY MEALTIMES

For the 1
who has just turned one

For the 1
who has a busy lifestyle

For the 1
who never grew up

FIASP® - for all types of one[1]

Fiasp® can be dosed up to
2 minutes before the start of a meal[1†]

Fiasp® can be dosed up to
20 minutes after the start of a meal[1†]

† Fiasp® can be taken up to 2 minutes before the start of a meal, with the option to dose up to 20 minutes after starting a meal if needed. In children, Fiasp® can be administered up to 2 minutes before the start of a meal, with the option to administer up to 20 minutes after starting a meal, when there is uncertainty about the meal intake.[1]

Reference: 1. Fiasp Professional Information, February 2022.

Abbreviated Professional Information

Scheduling status: S3 **Name of the medicine:** Fiasp® **Qualitative and quantitative composition:** Contains insulin aspart 100 *U/ml*. **Therapeutic indications:** Maintenance treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above, used alone or in combination with other insulins or metformin. **Posology and method of administration:** Fiasp® is a mealtime insulin for subcutaneous administration at the start of a meal or post-meal (within 20 minutes after starting a meal). Dosing with Fiasp® is individual and determined in accordance with the needs of the patient. The individual total daily insulin requirement in adults, adolescents and children may vary and is usually between 0,5 and 1,0 *unit/kg/day.* Fiasp® should be used in combination with intermediate-acting or long-acting insulin given at least once a day. Blood glucose monitoring and insulin dose adjustment are recommended to achieve optimal glycaemic control. Converting from another mealtime insulin can be done on a unit-to-unit basis. Close glucose monitoring is recommended during the transfer from other mealtime insulins and in the initial weeks thereafter. Fiasp® can be used for continuous subcutaneous insulin infusion (CSII) in pumps. If necessary, Fiasp® can be administered intravenously by health care professionals. **Contraindication:** Hypersensitivity to the insulin aspart or any of the excipients and during episodes of hypoglycaemia **Special warnings and precautions for use:** The safe use of Fiasp® in treatment of ketoacidosis has not been established. Omission of a meal or unplanned, strenuous physical exercise may lead to hypoglycaemia. Patients, whose blood glucose control is greatly improved, e.g. by intensified insulin therapy, may experience a change in their usual warning symptoms of hypoglycaemia, and should be advised accordingly. Usual warning symptoms may disappear in patients with longstanding diabetes. In Paediatric population close monitoring of blood glucose levels is recommended if administering Fiasp® after the start of the last meal of the day, in order to avoid nocturnal hypoglycaemia. The fast onset of action should be considered in patients with delayed gastric emptying. Cases of congestive heart failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of congestive heart failure. Patients should be observed for signs and symptoms of congestive heart failure, weight gain and oedema. The use of inadequate doses or discontinuation of treatment, especially in patients requiring insulin, may lead to hyperglycaemia and diabetic ketoacidosis. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs. Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between Fiasp® and other insulin medicines. Concomitant diseases in the kidney, liver or affecting the adrenal, pituitary or thyroid gland may require changes in the insulin dose. Insulin administration may cause insulin antibodies to form. The presence of such insulin antibodies may necessitate adjustment of the insulin dose in order to correct a tendency to hyper- or hypoglycaemia. Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. **Pregnancy and lactation:** Safety in pregnancy and lactation has not been established. There are no restrictions on treatment with Fiasp® during breastfeeding as insulin aspart does not cross into breast milk. **Undesirable effects:** *Very common:* Hypoglycaemia; *Common:* Allergic skin manifestations, injection/infusion site reactions; *Uncommon:* Hypersensitivity, lipodystrophy, eruptions, refraction, diabetic retinopathy, oedema; *Rare:* Peripheral neuropathy; *Very rare:* Anaphylactic reactions; *Unknown:* Cutaneous amyloidosis. **Overdose:** Hypoglycaemia may develop over sequential stages if a patient is dosed with more insulin than required: **Reg. No.:** 51/21.1/0733 For full prescribing information, refer to the Professional Information approved by the Regulatory Authority.

novo nordisk®

Novo Nordisk (Pty) Ltd. Reg. No.: 1959/000833/07. 150 Rivonia Road, 10 Marion Street Office Park, Building C1, Sandton, Johannesburg, 2196, South Africa.
Tel: (011) 202 0500. Fax: (011) 807 7989. www.novonordisk.com.
22458T. ZA23FSP00002 July 2023.

Fiasp® fast-acting insulin aspart

INTRODUCING OUR

NEW

GLICLAZIDE MR
RANGE

MORE CHOICE
MORE **SUSTAINED**
CONTROL[1]

A compelling choice in sulphonylurea treatment: [2]

- Once daily formulation
- Improved compliance

Dynacaz MR
30 mg 60 mg 90 mg GLICLAZIDE

For further product information contact **PHARMA DYNAMICS**
Email info@pharmadynamics.co.za **CUSTOMER CARE LINE** +27 21 707 7000

pharma dynamics
EFFECTIVE AFFORDABLE HEALTHCARE

www.pharmadynamics.co.za

DYNACAZ 30, 60, 90 mg MR. Each tablet contains 30, 60, 90 mg gliclazide respectively. S3 A42/21.2/0249 , A48/21.2/1194, A53/21.2/0083. For full prescribing information, refer to the professional information approved by SAHPRA, 15 June 2021. **1)** McGavin JK, *et al.* Gliclazide modified release. *Drugs* 2002;62(9):1357-1364. **2)** Crepaldi G and Fioretto P. Gliclazide modified release: Its place in the therapeutic armamentarium. *Metabolism* 2000;49(10)supplement 2:21-25. **DCZB933/05/2023.**