Built Environment and Preterm Birth

Nikki Keene Woods, Ph.D., M.P.H.[1], Linda Watson[1], An-Diep T Nguyen[2]
Wichita State University, Wichita, KS
[1]Department of Public Health Sciences
[2]School of Nursing

Abstract

Background. Preterm birth affects approximately 500,000 babies a year in the United States. One out of nine babies born in the United States deliver before 37 weeks gestation. Preterm birth can cause lifelong neurological problems, cerebral palsy, vision and hearing impairments, and developmental delay. The estimated $26 billion a year in preterm birth related costs are staggering to the health care system. Preterm-related causes of death in 2008 together accounted for 35% of all infant deaths.

Methods. This paper is a review of the literature published (2006-2012) on the relationship between neighborhood environment and preterm birth.

Results. Neighborhood deprivation and the neighborhood environment were associated with low-birth weight and preterm birth. Examples of neighborhood deprivation include economic deprivation, social disorder, and lack of health resources. Neighborhood environment can be described as neighborhood physical deterioration, violent crime, and group density.

Conclusions. A significant association exists between the neighborhood environment and birth outcomes. More research is needed to explore interventions with a systems approach to promote healthy maternal behavior, reduce stress, and improve care for expecting mothers living in stressful neighborhood environments in order to reduce preterm births.

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Introduction

For many years, public health officials have known the environment impacts a person's health. According to the Centers for Disease Control and Prevention, life expectancy since 1900 in the United States has increased by approximately 40 years.[1] Only seven of those years can be attributed to improvements in disease care while the other years are the result of improved prevention efforts (such as immunizations) and improved environmental conditions, including sanitation and water. The link between the nation's health and the environment is unmistakable. Several factors can create disparities in a community's health status such as socioeconomic status,[2] land use and the built environment,[3] race/ethnicity segregation,[4] and environmental injustice.[5]

The built environment includes all physical aspects of the areas people live and work and influences a person's level of physical health and well-being.[6] Neighborhood characteristics such as sidewalks, aesthetics, low crime, and access to affordable food promote a healthier lifestyle than neighborhoods without these characteristics. Studies have shown neighborhoods with walkability features have a direct and specific relation to the health of residents.[7] Neighborhoods without sidewalks or a safe area to walk without heavy traffic restrict opportunities for physical activity. Individual personal health depends on having clean air and water, nutritious food to eat, access to healthcare, and areas free from crime and violence in which to engage in physical activity.[7]

Social capital is defined as a "community pool of human resources that is available."[6] Circumstances that prevent or limit the availability of social capital for a community and its members can have a negative effect on the health and well-being of individual community members. Neighborhoods where social cohesion is lacking can cause individuals to have social deprivation, a lack of social support and social capital, and increased frequency of violence. These neighborhood characteristics can contribute to a lower health status in general for the community. Both expected length of life and physical quality of life are influenced by the conditions in which one is born, lives, works, ages, and dies.[8]

Preterm birth affects approximately 500,000 babies a year and one out of nine babies born in the United States deliver before 37 weeks gestation.[9] Preterm birth can cause lifelong neurological problems, cerebral palsy, vision and hearing impairments, and developmental delay. Babies born prematurely have high risks of disability and poor health outcomes. The costs of preterm birth is staggering to the health care system. Decreasing preterm births have the potential to improve health outcomes for infants and generally improve the quality of life for families and society.

The environment in which a pregnant women lives can influence risks for preterm birth and impact pregnancy outcomes.[10] Adverse birth outcomes, such as low birth weight and its determinants, preterm births, and intrauterine growth retardation, have been associated with indicators of socioeconomic status and physical environment.[11] Neighborhood characteristics can affect maternal behavior and increase stress leading to complications in pregnancy and poor birth outcomes such as preterm birth.[12]

Previous reviews have been conducted related to the environment and adverse birth outcomes. A review and meta-analysis was conducted on articles from 1900-2010 involving observational studies on neighborhoods and pregnancy birth. This review focused on neighborhood income and low birth weight.[13] Additional reviews have been completed on other aspects of the environment including epidemiological studies and health effects (including low birth weight) from 1983-2008,[14] ambient air pollution and pregnancy outcomes (1981-2004),[15,16] and risks of living near landfill sites (1982-1997).[17] No previous reviews were found on the built environment and birth outcomes.

Methods

Studies for this systematic review were identified from 2006-2012 using the keywords: built environment, environment, neighborhood, low birth weight, and preterm birth. Nine databases were searched from January through May 2013, including: CINAHL, Academic Search Complete, Health Source, Social Sciences Citation Index, Science Direct, MasterFILE Premier, Proquest Nursing and Allied Health Source, and PubMed. To identify additional articles, the bibliographies of included articles were hand-searched.

Study selection. Two reviewers independently conducted a practical screen (reviewed titles and abstracts) to identify potential studies.[18] A methodological screen (full text review) was completed by the same two reviewers. Inter-rater reliability was 100%. Articles were reviewed if they included birth outcomes (low birth weight, preterm birth) and studied the built environment (physical characteristics). Studies were excluded if they had an international setting, focused on environment air quality or toxins, or only included psychosocial or socioeconomic factors in analysis (i.e., did not include physical characteristics of the environment). Articles on neighborhood deprivation were included

because the definition includes a physical environment component. Reviewers extracted specific study elements including study design, environment definition, effects/conclusions, limitations, and setting (Table 1).

Results

There were 1,973 research papers originally identified using the search terms, three additional articles were identified through the hand-search. After duplicates were removed 141 articles remained; 112 were excluded after reviewing the title and/or abstract. Twenty-nine full-text articles were assessed for eligibility and 18 were excluded for not meeting inclusion criteria (e.g., related to environmental conditions, such as air quality). Eleven articles on the relationship between the built environment and birth outcomes were included (Figure 1). Ten articles were retrospective cross-sectional studies and one was prospective study (Table 1).

Neighborhood disorder. Three studies reported that neighborhood environment had an impact on preterm birth and birth weight by way of physical disorder. Women who reported higher levels of perceived social and physical disorder and perceived crime also reported higher levels of psychological distress.[12] Women who reported more experiences of racial discrimination also had higher levels of psychological distress. Objective social disorder (i.e., activities involving people, such as drug dealing, prostitution, and gangs) and perceived crime predicted psychological distress. Objective physical disorder (i.e., physical conditions of neighborhood, such as vacant housing, vacant lots and vandalism) and psychological distress predicted preterm birth. Psychological distress mediated the effect of objective social disorder and perceived crime on preterm birth. The researchers concluded that women's neighborhood environments and racial discrimination were related to psychological distress, and these factors may increase the risk for preterm birth.[12]

Miranda, Messer, and Kroeger[10] studied the association between the quality of the residential built environment and pregnancy outcomes among women in North Carolina. Their research found that five built environment indices (housing damage, property disorder, tenure, vacancy, and nuisance count) were associated with each of the five outcomes: preterm birth, small for gestational age, low birth weight, continuous birth weight, and birth weight percentile for gestational age.

Schempf, Strobino, and O'Campo[19] examined the impact of the physical structure of neighborhoods on birth weight and evaluated mediation by psychosocial and behavioral factors. Neighborhood factors may influence birth weight by shaping maternal behavioral risks. Authors concluded neighborhood level interventions should be considered to address multiple maternal and infant health risks (e.g., tobacco use).

Neighborhood disorder and socio-economic status. Two studies reported poorer neighborhood conditions in lower socio-economic areas were linked to preterm birth and low-birth weight. One study found after controlling for various known individual-level risk factors, pregnant women living in neighborhoods of lower median incomes lived in poorer neighborhood conditions (i.e., boarded-up housing) and had infants with both lower birthweight-for-gestational-age and shorter gestations.[3]

Messer et al.[2] developed socio-economic indices, defined domains of education, employment, housing, occupation, poverty, and residential stability, and using maternal age and education adjusted models. Mothers living in tracts with high unemployment,

Table 1. Relationship between neighborhood environment and birth outcomes.

Study (year)	Study Design (N)	Environment (Setting)	Effects/conclusions	Limitations
Messer et al., 2008[2]	Retrospective, cross-sectional (231,912)	Neighborhood socioeconomic effects (Wake County, North Carolina)	Specific neighborhood-level socioeconomic features may be especially influential to health outcomes	Use of census data; no information on length of residence
Farley et al., 2006[3]	Retrospective, cross-sectional (105,111)	Neighborhood environment and adverse birth outcomes (Louisiana)	Measures of neighborhood economic conditions associated with both fetal growth and length of gestation independent of individual-level factors	Cross-sectional study; lack of actual data on retail outlets
Vinikoor-Imler et al., 2011[7]	Retrospective, direct observation (39,000)	Physical incivilities (neighborhood degradation), social spaces, walkability, borders and arterial features (North Carolina)	Certain neighborhood conditions were associated with maternal health behaviors and pregnancy outcomes	Not generalizable to entire population; lack of minority women other than black
Miranda et al., 2012[10]	Retrospective, direct observation, cross-sectional (17,000)	7 indices of residential built environment (Durham, North Carolina)	Relationship between quality of built environment/birth outcomes	Data quality limitations; residential mobility; omitted maternal smoking; may lie on causal paths which would adjust away from effect researchers trying to observe; cross-sectional study
Giurgescu et al., 2012[12]	Prospective, cross-sectional (72)	Neighborhood environment, racial discrimination, psychological distress and preterm birth (Chicago, Illinois)	Objective physical disorder and psychological distress predicted preterm birth; neighborhood environment and racial discrimination were related to psycho-logical distress, these factors may increase risk for preterm birth	Small sample size; limited variability for the objective neighborhood measures; cross-sectional study

Schempf et al., 2009[19]	Retrospective, cross-sectional (726)	Neighborhood environment on birth weight (Baltimore, Maryland)	Neighborhood structures and processes may have impact	Inability to disentangle the effects of specific neighborhood structures and distinguish effects on fetal growth restriction versus gestational age; cross-sectional study
Debbink et al., 2011[20]	Retrospective, cross-sectional (109,238)	Influence of racial residential segregation (Michigan)	Increased odds of low birth weight	Lacked individual-level data; cross-sectional study
Kramer et al., 2010[21]	Retrospective, cross-sectional (6,180,544)	Residential isolation (231 US Metropolitan statistical areas)	Black women, isolation is associated with very preterm birth and moderately preterm birth	Lack of information on important variables; cross-sectional study
O'Campo et al., 2008[23]	Retrospective (102,377)	Neighborhood deprivation (Maryland, Michigan, North Carolina, Pennsylvania)	Significant but moderate-to-weak association between neighborhood deprivation and preterm birth	Limited ability to adjust for individual-level confounders; quality of maternal data on birth certificates; lack of length of residence data
Holzman et al., 2009[24]	Retrospective, cross-sectional (182,938)	Maternal age, neighborhood deprivation (Maryland, Michigan, North Carolina, Pennsylvania)	Support "weathering" hypothesis	Bias by self-selection; cross-sectional study
Janevic et al., 2010[25]	Retrospective, cross-sectional (492,332)	Neighborhood deprivation and preterm birth/birth weight (New York City)	Preterm birth and low birth weight was associated with highest quartile of deprivation	Limitations of birth certificate data may have over-adjusted by controlling individual-level characteristics (e.g., smoking)

low education, poor housing, low proportion of managerial or professional occupation, and high poverty were associated with increased odds of preterm birth for non-Hispanic white women at most sites. Among non-Hispanic black women, similar associations were noted for tract-level low education, high unemployment, low occupation, and high poverty, but the effect estimates were generally smaller than those seen for white women. The authors suggest that specific neighborhood-level socioeconomic features may be especially influential to health outcomes. These socio-economic

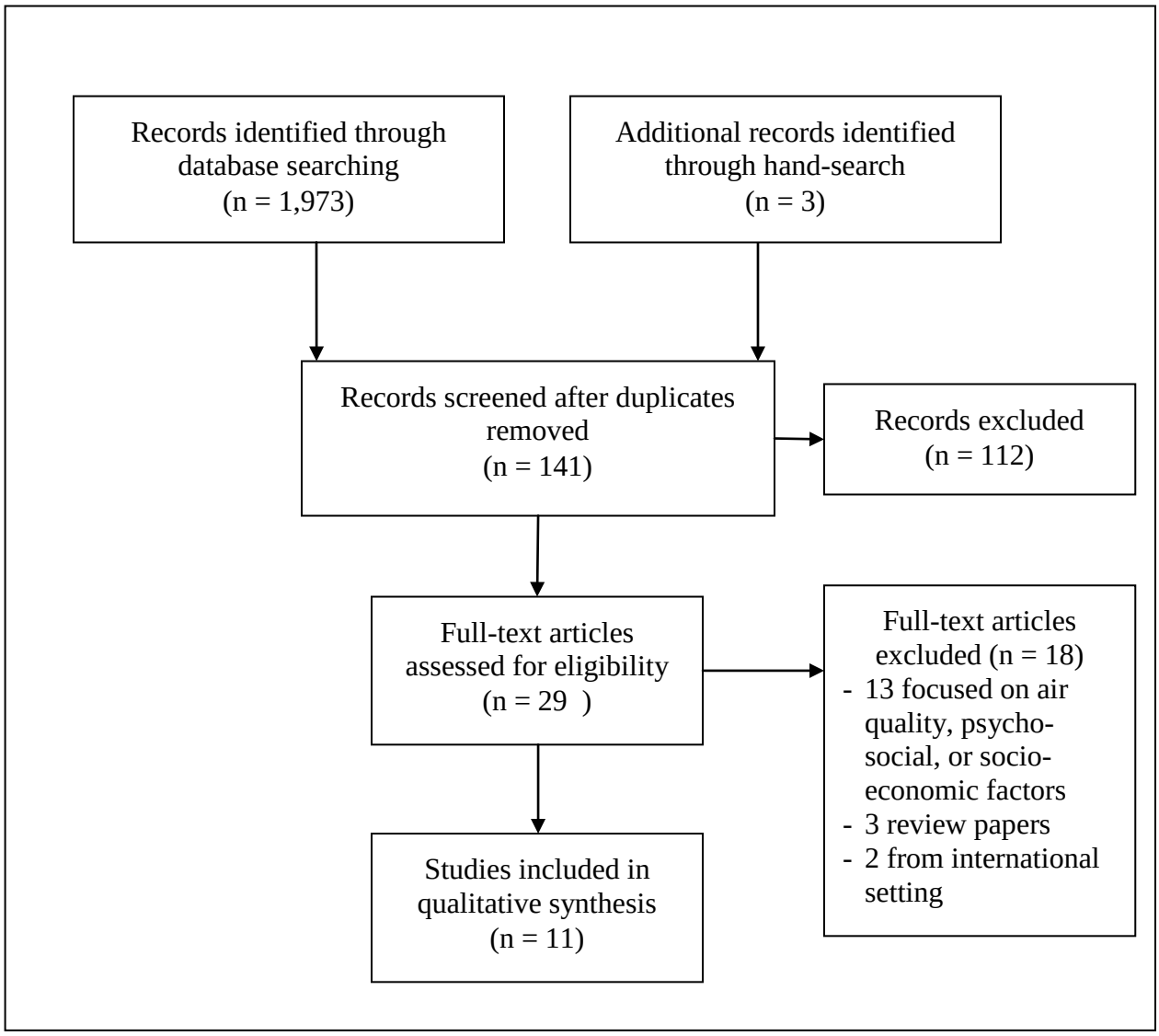

Figure 1. Flow diagram of study selection.

domains represent potential targets for intervention or policy efforts designed to improve maternal and child health and reduce health disparities.

Neighborhood diversity. Three studies reported an association between birth outcomes and whether an individual is a racial or ethnic majority in the local community. Debbink and Bader[20] studied racial residential segregation and low birth weight in Michigan's Metropolitan Areas. Living in a black segregated area was associated with increased odds (odds ratio [OR] = 1.15; 95% confidence interval [CI] = 1.03, 1.29; $p < 0.05$) of low birth weight after adjusting for individual- and tract-level measures. The authors suggested the association between low birth weight and racial segregation was attributable primarily to increased risk of intrauterine growth restriction. Similarly, residential isolation segregation (a measure of residential inter-racial exposure) was reported to be associated with rates of preterm birth experienced by black women.[21]

Messer and colleagues[22] reported non-Hispanic black women were more likely than non-Hispanic white women to deliver preterm (12.8% versus 6.7%), live in economically deprived block groups (42.2% versus 19.3% in the highest deprivation quartile), and experience more crime (32.0% versus 3.8% in the highest violent-crime-rate quartile). In unadjusted models, quartiles of violent, theft, property, and vice crimes were associated with preterm birth. In adjusted models, living in very high violent-crime-rate block-group quartiles was suggestive of increased odds of preterm birth for white and black non-Hispanic women. The authors concluded differential neighborhood exposures may contribute to racial disparity in preterm birth outcomes.[22]

Neighborhood deprivation. Five studies reported neighborhood deprivation was reported to be associated with low-birth weight and preterm birth. All studies included the same neighborhood deprivation index. Examples of neighborhood deprivation included economic deprivation, social disorder, and lack of health resources. O'Campo et al.[23] found deprivation at the neighborhood level was significantly associated with increased risk of preterm birth among both non-Hispanic white women and non-Hispanic black women.

Holzman, Eyster, and Kleyn[24] compared the association between advancing maternal age and risk of preterm delivery across four groups (black smokers, black nonsmokers, white smokers, and white nonsmokers) and within the context of neighborhood deprivation levels. For multiparous women, a significant age-related increase in preterm delivery was found. The adjusted odds ratio per five-year age increase was 1.31 for black smokers, 1.11 for black nonsmokers, and 1.16 for white smokers. For each group, the odds ratio increased as neighborhood deprivation increased. The results support the ''weathering'' hypothesis or accelerated aging, suggesting that black women, women with high-risk behaviors, and women living in high deprivation neighborhoods may develop ''accelerated aging'' that increases preterm delivery risk.

Janevic and colleagues[25] reported preterm birth outcomes were greater for the highest quartile of neighborhood deprivation. Preterm birth rates also varied by ethnicity where the greatest magnitude of preterm birth was reported for Hispanic Caribbean women and black women for low birth weight. Authors called for research to investigate birth outcome differences among individual ethnicity and cultures related to neighborhood deprivation.[25]

Discussion

Physical disorder, neighborhood deprivation, and neighborhood racial diversity impacted maternal health behavior and healthy birth outcomes. Mothers living in neighborhoods with a lower median income, low education, high unemployment and high poverty reported higher rates of infants with preterm birth and lower birth weight. Many factors of the environment the mother is exposed to during pregnancy can impact prenatal health, which also affects birth outcomes.[4,23,24] Despite efforts to reduce the gap between blacks and whites, racial disparities in adverse birth outcomes, specifically infant mortality, low birth weight, and preterm birth, continue to persist in the United States.[23] Confounding variables, such as socioeconomic status or maternal education, were identified in adjusted models of the evaluated studies based on theoretical associations.[21,25] Studies used stratification and multivariate analyses to control for these confounding variables.

Prior research established associations between pregnancy outcomes and specific neighborhood characteristics, including economic disadvantage, violent crime, and

racial/ethnic segregation.[4] Seven community factors of the built environment were identified previously as important in improving health outcomes for disadvantaged and vulnerable communities: transportation/business investments, access to food, access to health care, access to housing, air and water quality/ uncontaminated land, socioeconomic factors, and reduced residential segregation.[5] This review supplemented previous findings and highlighted the importance of the physical structure and quality of the built environment in relation to birth outcomes.

Clarifying ways that neighborhoods and the built environment influence health behaviors and outcomes is important for identifying policies and preventable care procedures needed to support efforts to reduce preterm birth.[7] Features of the built environment partially may explain the long-observed associations between socio-demographic conditions and adverse health.[10] Public health and environmental scientists are focused on the interdependent relationship between the built environment and health disparities.[5] Neighborhoods can influence individual-level behaviors that may influence the amount of stress a woman experiences during her pregnancy, which also may be associated with her decisions regarding the use of alcohol, tobacco, and other drugs, her ability to access adequate nutrition, and her sexual behavior.[13]

This type of research may be beneficial for healthcare workers to aid in identification of high-risk patients, providing an opportunity to connect mothers to community resources and part of a comprehensive solution needed to address the preterm birth rate in Kansas. According to Institute of Medicine, the annual societal economic burden associated with preterm birth in the United States was at least $26.2 billion in 2005, or $51,600 per infant born preterm.[26] Medical care services contributed $16.9 billion to the total cost and maternal delivery costs contributed another $1.9 billion. Lowering the number of preterm births will save healthcare dollars at both state and federal levels.

Interventions to reduce the morbidity and mortality related to preterm birth can be classified as primary (directed to all women before or during pregnancy), secondary (aimed at eliminating or reducing risk in women with known risk factors), or tertiary (initiated after parturition with a goal of preventing delivery or improving outcomes for preterm infants).[27] Iams et al.[27] reviewed preterm interventions and found that organized systems of perinatal care, commonly termed regional perinatal networks, in which mothers who are likely to deliver preterm are cared for by obstetric and neonatal specialists and appropriate equipment during labor, delivery, resuscitation, and newborn care, consistently have been associated with the greatest survival rates. Applying regional perinatal networks in Kansas with an emphasis on identifying women living in poor quality neighborhoods could address health disparities and improve preterm birth rates.

Communities should continue to connect high-risk pregnant women to social services through a public health network. These interventions may include support groups and mentoring programs to women living in poor quality built neighborhoods. Hobel, Goldstein, and Barrett[28] found that women who had multiple types of social support from difference sources had infants with the highest birth weights. The authors concluded social support may promote higher birth weights. In addition to direct material provisions, social support may encourage expectant mothers to adopt healthier lifestyles, reduce their stress levels, and pursue better prenatal care.

Conclusion

Additional research is needed to explore interventions with a systems-based approach to promote healthy maternal behaviors and improve care for expecting mothers living in poor quality neighborhood environments to reduce preterm births. One strategy is to increase the social capital of women living in poor quality neighborhood environments. Previous research reported those with high social capital are more likely to use adequate health care services.[29] Individuals of a community with high social capital may provide one another with greater instrumental and psychosocial support than those of a community with low social capital. The community's level of inter-connectedness and trust may reduce barriers to health care and mitigate negative health consequences associated with the built environment. A focus on the built environment with an emphasis on increasing the opportunities for healthy eating, physical activity, and early access to quality prenatal care has the potential to reduce maternal stress and improve birth outcomes of expectant mothers.[30]

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Satisfaction and Race Influence on Positive Health Choices among Patients at an Urban Community Health Center

Barbara S. Smith, Ph.D., P.T.[1], Richard D. Muma, Ph.D., M.P.H., P.A.-C[2,3,4],
Heather Brewster, M.P.A., P.A.[3], Charles Landers, M.P.A., P.A.[3],
Preston Schaffner, M.P.A., P.A.[3]
Wichita State University, Wichita, Kansas
Department of Physical Therapy[1]
Division of Academic Affairs [2]
Department of Physician Assistant[3]
Department of Public Health Sciences[4]

Abstract

Background. Promoting positive health choices is one way to lessen health care disparities in indigent populations. This pilot study investigated satisfaction with the health information received at an urban heath care center for the indigent and its effect on health behaviors. Such information will inform providers on their role in advancing the health center's quality improvement goals (i.e., goals used to measure the clinic's performance in providing preventive service information to patients).

Methods. A survey was used to determine respondent satisfaction with health care information and whether respondents would make positive health choices based on this information.

Results. Respondents (n = 185) were satisfied with the health information received; this was the most consistent predictor of making a lifestyle change. Minority respondents were more likely to get a vaccination, to not start smoking, and to start exercising than non-minority respondents.

Conclusion. The results suggested that, for the positive health choices examined, satisfaction with education is very important. For certain positive health choices, race also may play a role. Additional studies should be undertaken linking chronic health problems to patient responses.

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Introduction

Providing information on positive health choices to patients (e.g., offering information on breast cancer screening) is one goal of the Hunter Health Clinic (HHC), a federally funded community health center in Wichita, Kansas. It is also the state's only urban Indian health clinic. The clinic specializes in caring for those who are uninsured and under-insured. In 20ll, HHC had more than 84,000 patient encounters and 33,900 patients; 70% of whom were uninsured.[1]

The study's purpose was to investigate patient perceptions regarding the provider's ability to deliver health education that encourages behavior change in an urban indigent population and whether this information was influential in making positive health choices. The results were to be used by health center providers to measure clinic performance in providing preventive service information as required by their funders. Only patients from one of the five clinics under the HHC umbrella completed this pilot questionnaire. These results are expected to be used to enhance the survey for all clinics.

Methods

Wichita State University's Institutional Review Board approved this study.

Participants. For this pilot study, a convenience sample of only English and Spanish speaking patients, who had previously visited the clinic, were asked to participate. The survey was printed in Spanish and English. The appropriate survey was read to those who could not read. Exclusion criteria were first-time patients, refusal to participate, reading or speaking a language other than English or Spanish, and under 18 years of age. No data were collected on those who were excluded.

Materials. The survey consisted of demographics, patient perception regarding the provider's presentation of information about positive health choices, and patients' implementation of these changes. Statements used a 5-point Likert scale defined at opposite poles as strongly agree to strongly disagree. The survey is found in the appendix.

Prior to administration, HHC staff and members of its board of directors evaluated the perception statements for content. The statements were matched to quality improvement goals of HHC (i.e., goals used to measure the clinic's performance in providing preventive service material to patients such as education on cancer screening as required by federally funded grants).

Setting**.** The HHC provides medical, dental, and mental health services to individuals at five locations on a sliding payment scale. The Indian Health Service, one of this organization's funders, requires education on healthy behaviors. Medical staff is required to present positive health choice information verbally and in written form (language-appropriate) at each visit.[1]

Data analysis. Frequency distributions depicted respondents and their answers to Likert scale statements without regard for demographics. Logistic regression was used to determine if demographic variables and satisfaction with the information received about services to achieve healthy outcomes could predict changes in health behaviors. For analysis, minority respondents were those who chose the following race/ethnicities: African American, American Indian/Alaskan native, Asian, Native Hawaiian/Pacific Islander, or Hispanic. Non-minority respondents were non-Hispanic Caucasian. Data were analyzed with IBM SPSS Statistics (IBM Corp. 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.) and the alpha level was set at .05.

Results

The mean age of respondents (n = 185) was 41.4 (+/-13.5) years. The response rate was 61.6%. Sixty percent were female and 58.4% were minority (Table 1). Eighty-seven percent were satisfied (strongly agree/agree) with the health care information they received. Respondents were most satisfied with information received about smoking hazards (80.5%). Of all respondents, 77.0% began eating better. For female respondents, 81.8% indicated they had undergone breast cancer screening (Table 2).

Table 1. Demographic characteristics of respondents.

Sex	
Male	74 (40.0%)
Female	111 (60.0%)
Race/Ethnicity	
Non-minority[a]	77 (41.6%)
Minority[b]	108 (58.4%)
Spanish speaking only	
Yes	27 (14.6%)
No	158 (85.4%)

[a]Non-minority: Non-Hispanic Caucasian
[b]Minority: African American; American Indian/Alaskan Native; Asian; Native Hawaiian/Pacific Islander; Hispanic

Table 2. Frequency of responses in percent without regard to demographics (n = 185).*

Topic	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Generally satisfied with health education	52.5	35.6	6.7	2.8	2.8
Health care provider educated me about					
Smoking hazards	52.3	28.2	8.1	2.7	8.7
Getting a vaccine	37.0	37.6	13.3	6.1	6.1
Maintaining a healthy weight	45.1	32.3	10.4	4.3	7.9
Breast cancer screening	49.5	24.3	14.6	5.8	5.8
Cervical cancer screening	48.5	25.2	13.6	6.8	5.8
I made changes based on education I received					
Smoking cessation	38.7	26.9	22.7	5.9	5.9
Not starting to smoke	47.2	17.9	20.8	5.7	8.5
Getting a vaccination	39.5	28.7	19.1	7.6	5.1
Eating better	46.2	30.8	14.8	4.1	4.1
Starting regular fitness routine	38.2	30.9	21.8	3.6	5.5
Screening for cervical cancer	51.0	27.5	9.8	7.8	3.9
Screening for breast cancer	51.5	30.3	8.1	5.1	5.1

*Frequencies do not always add to 100.0% due to rounding.

A logistic regression analysis was conducted using patient satisfaction with race, age, and sex to examine their effect on making positive health choices. Patient satisfaction was the most significant predictor for all positive health choices. However, the effect was small. Being a minority was a statistically significant predictor for not starting to smoke (OR 4.9, 95% CI1.90-12.95), for getting a vaccination (OR 5.1, 95% CI 2.35-10.95), and starting a fitness program (OR 3.1, 95% CI 1.44-6.82). Being younger predicted starting an exercise program (OR 1.0, 95% CI 1.00-1.06; Table 3).

Discussion

This study examined predictors of seven health outcomes from among a convenience sample in a community health care center for the indigent. The results suggested patients are influenced most by satisfaction about education on healthy outcomes received from their provider. Satisfaction is one of the core outcome measures for health care. The most successful, competent treatment or program has limited usefulness if it does not fulfill the needs of patients receiving the service.[2] Many factors, such as ethnicity, socioeconomic status, age, and language barriers, affect patient satisfaction and compliance with medical advice.[3]

Race may be a significant predictor of making positive health choices. Being a minority predicted not starting to smoke in nonsmokers, getting a vaccination, and starting an exercise program. Shah et al.[4] categorized respondents as African American/Hispanic or Caucasian and found that race was not a factor in insured cardiology patients seen in an outpatient clinic in responses to statements about the quality of information received about lifestyle changes. No studies show race as an isolated factor in choosing positive health behaviors in indigent populations.

Table 3. Variables of significance in predicting positive health choices: satisfaction with information about healthy outcomes, race, and age (n=185 except as noted).

Health Outcome	Beta	Wald X^2	P^*	Odds Ratio	CI
Quitting smoking (n = 94)					
Satisfaction	1.792	4.94	.03	.167	.03-.81
Not starting to smoke (n = 91)					
Race	1.602	10.72	.00	4.963	1.90-12-95
Satisfaction	2.416	10.60	.00	.09	.02-.38
Getting a vaccine					
Race	1.624	17.09	.00	5.07	2.35-10.95
Satisfaction	1.669	7.95	.00	.19	.06-.60
Eating better					
Satisfaction	3.248	22.179	.00	.04	.01-.15
Start exercising					
Age	.030	3.99	.05	1.03	1.00-1.06
Race	1.141	8.27	.00	3.13	1.44-6.82
Satisfaction	3.04	14.00	.00	.05	.01-.24
Screen cervical cancer					
Satisfaction	4.095	11.86	.00	.02	.00-.17
Screen breast cancer					
Satisfaction	3.314	12.50	.00	.0	.00-.2

*P $\leq$ 0.05 indicates that variable had significant association with health outcome based on Wald Chi-square.

At HHC, patient satisfaction with education appeared to influence self-reported changes. Cooper et al.[3] linked patient-centered care to improvements in patient adherence and health outcomes. A systematic review, however, found no substantial documented changes in pro-motion of lifestyle change in general practice.[5] However, when specific populations were targeted (e.g., those with hypertension, diabetes, or post-acute coronary syndrome), more patients implemented changes.[3,6-8] In any case, HHC provider education appeared to make an impact.

Few studies evaluated satisfaction with information about health outcomes and patients' undertaking of such outcomes. Lam and Chung[9] found that the more satisfied patients were with their interaction with a pharmacist, the more likely they were to receive a flu vaccination. Almost 70% of their sample received a vaccination. However, the most important reason for vaccination was insurance coverage. Our results agreed, in part, with Lam and Chung. Satisfaction with health information may predict getting a vaccination, however, race appeared to be a more important predictor. Lam and Chung's respondents were Asian American, so race was not an issue.[9] Gold et al.[10] reported that insurance coverage and having diabetes were important in a patient's decision to have a flu vaccination. Patients at HHC received vaccines through their insurance coverage or, more commonly, paid on a sliding scale. Reasons for disagreement about vaccination were not explored in this sample.

Minority respondents were less likely to start smoking than non-minority respondents. While study results were available on smoking cessation programs in many populations, no literature was found on prevention of starting to smoke in an indigent population.

Only satisfaction with health information was a predictor for having a pap test. Eighty percent of female respondents indicated they had undergone a pap test. Most of these women were probably eligible for cervical cancer screening services through the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). Fewer than 10% of those eligible received NBCCEDP-funded Pap tests from analysis of 2004-2006 data.[11] Eligible women were 18 years and old, had not undergone a hysterectomy and did not have health insurance. Sadler et al.[12] found that encouragement to have an annual physical exam, including Pap test and mammogram, was the most important message health educators needed to convey. HHC medical records were not accessed regarding hysterectomy. Regardless of this omission, HHC appears successful in encouraging women to have pap tests.

Only satisfaction with educational information appeared to predict undergoing mammography. Age was expected to be a predictive as well. The American Cancer Society's data showed that as age increases, incidence and death rates from breast cancer increase.[13] Ninety-five percent of breast cancer deaths occur in women older than 40. One half of the women in the sample were under 40. This could be one of reasons why age was not a significant predictor for having a mammogram.

Data on healthy outcomes regarding eating better and beginning a regular fitness routine are more difficult to find. Definitions of "eating better" and "fitness routine" vary widely. This study defined eating better as consumption of less fatty foods and more vegetables. An example of a regular fitness routine was walking 30 minutes each day. Crouch et al.[14] examined intervention programs' effects in a systematic review in rural Australian women. Studies targeting physical activity reported activity increased, and these increases were sustained at one year. Studies about dietary modification programs show less positive effects over time. An exception is Khare et al.[15], who found improvement in nutritional and physical activity behavior in middle-aged, disadvantaged, low-income women undergoing a 12-week enhanced intervention program. These improvements were maintained at the 1- year follow-up.

Limitations. No survey can account for all predictors for making positive health choices. The advice from the health care provider may prime patients to become more aware of and attentive to health information found in the media, friends/family, or from other services. Those who perceive themselves to be susceptible to some adverse health outcome sometimes can be prompted to undertake lifestyle changes by discussion with their health care provider.[16] One of this study's participation requirements was a previous visit. A return visit may indicate some respondents felt more vulnerable due to a health issue. In addition, it is not possible to know how many respondents were more compliant or had a higher sense of volunteerism than nonrespondents.

Another limitation was not matching patient history to the survey results. Most studies on lifestyle changes in indigent populations use a common chronic condition as one of the inclusion criteria.[3,6,7] Health and socioeconomic status are inversely related: the lower the socioeconomic status, the higher the risk of morbidity and mortality from chronic disease.[17,18] Using presence/absence of a chronic disease may have changed the results of the regression

analyses. Assuming that a chronic condition such as diabetes may have been a significant predictor, HHC may wish to consider targeting information about positive health choices specific to the patients' conditions.

Future research. Follow-up on adherence to the changes reported by the respondents would be important way to meet the clinic's goals. Long-term maintenance of healthy outcomes is difficult for anyone. It is more complicated to keep primary prevention behaviors a regular focus when many participants are dealing with day-to-day challenges due to limited income, health concerns, and often multiple family responsibilities.[12] Use of technology such as internet tablets to capture patient-reported outcomes prior to seeing their health care provider may be one way for HHC to match patients tor the most appropriate or desirable positive health choices.

Conclusion

Promoting healthy outcomes is one avenue to eliminate pervasive health disparities in minority and indigent communities. Based on our data, it appears that the HHC is making a difference in assisting indigent patients in making decisions to promote healthy outcomes. Whether these changes can be continued needs to be investigated.

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Keywords: community health services, community health centers, health communication, quality improvement, lifestyle risk reduction

Appendix

1. What is your gender (or sex)? ☐Male ☐Female

2. Your age: _____

3. Race/Ethnicity ☐ African American
☐ American Indian/Alaskan Native
☐ Asian
☐ Native Hawaiian/Pacific Islander
☐ Hispanic
☐ Non-Hispanic Caucasian
☐ Other (please specify) _____

Please rate the following statements according to your satisfaction with your health care provider and the education you receive from them at Hunter Health Clinic. (*Please check only one box* for each response).

	My health care provider at Hunter Health Clinic educated me about these topics:	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree	N/A
4.	Smoking hazards						
5.	Getting a vaccine (for example, shots to prevent flu and/or pneumonia)						
6.	Maintaining a healthy weight						
7.	Breast cancer screening (only females answer this question)						
8.	Cervical cancer screening (only females answer this question)						
9.	I am generally satisfied with the health care education I receive from my provider?						
10.	***I have made changes in my life based on the education I received from my health care provider at Hunter Health Clinic, including***						
	a. Quitting smoking.						
	b. Not starting to smoke.						
	c. Getting a vaccine (for example, shots to prevent flu and/or pneumonia).						
	d. Eating better (for example, less fatty foods and more vegetables).						
	e. Starting a regular fitness routine (e.g., walking 30 minutes each day, etc.)						
	f. Getting screened for cervical cancer (only females answer this question)						
	g. Getting screened for breast cancer (only females answer this question)						

Integrating Health Literacy Questions into a Statewide Behavioral Risk Factor Surveillance System (BRFSS) Questionnaire

Amy Chesser, Ph.D.[1], Jared Reyes, M.Ed.[1], Kyle Smothers, B.S.[1],
Nikki Keene Woods, Ph.D., M.P.H.[2]
[1]University of Kansas School of Medicine-Wichita
Department of Family and Community Medicine
[2]Wichita State University Department of Public Health Sciences

Abstract

Objectives. The purpose of this pilot study was to evaluate the feasibility of adding health literacy questions to a state health assessment questionnaire.

Methods. Researchers conducted a series of telephone interviews (N = 20) to test the telephone administration of three health literacy screening questions with a convenience sample. Feedback obtained during the telephone interviews was used to revise the questions for clarity. The revised questions were proposed as an addition to the Kansas Behavioral Risk Factor Surveillance System (BRFSS).

Results. Pilot data included minor modifications to the language of the questions to broaden their interpretation outside of a hospital setting. Most participants (90%, n = 18) had adequate health literacy. The proposed questions were approved for addition to the BRFSS questionnaire. Prompts were added to a telephone script to aid BRFSS survey administrators.

Conclusion. As one of the first statewide health literacy assessments, this study has demonstrated one method for collecting baseline data. This new methodology has the potential to impact both patient care and broad public health efforts.

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Introduction

Low health literacy is associated with the inability to access available health information,[1,2] decreased use of preventive health services,[3,4] patients reporting more barriers to following health recommendations,[5,6] decreased ability to reach treatment goals,[7] and increased depression when dealing with chronic conditions.[3,8] Low health literacy may contribute to the inappropriate use of healthcare services and increased healthcare spending.[9,10]

Recent data on the prevalence of limited literacy, as reported by the Centers for Disease Control and Prevention (CDC),[11] come from the 2003 National Assessment of Adult Literacy (NAAL). In Kansas, an estimated 8% (n = 164,000) of the population lack basic prose literacy skills. At the county level, this estimate ranges from 4% to 32%.[12] Health literacy differs from prose literacy in that health literacy refers to "all the skills necessary to understand and communicate health information," including knowledge of the human body, health behaviors, and the healthcare system.[11] Prose literacy is "the knowledge and skills needed to perform prose tasks" (i.e., to search, comprehend, and use information from continuous text including editorials, news stories, brochures, and instructional materials).

A statewide assessment of health literacy would provide key information to support large-scale coordinated interventions to improve health literacy. Tailored and targeted efforts to improve health literacy have been successful with individuals and populations, respectively.[13,14] Therefore,

identifying a feasible method for reaching the long-term goal of assessing health literacy at the state level was important. The primary objective of this study was to evaluate the feasibility of using a brief screening tool to assess population health literacy using the Behavioral Risk Factor Surveillance System (BRFSS).

Methods

Health screening questionnaire. The Behavioral Risk Factor Surveillance System is a state-based, randomized digit dialing, telephone survey coordinated annually by the CDC.[15,16] BRFSS field operations, however, are managed by state health departments to collect self-reported information including health risk behaviors, clinical preventive health practices, and healthcare access that are associated with the leading causes of morbidity and mortality in the US. State survey data are transmitted to the CDC for editing, processing, weighting, and analysis, then returned to the state health departments for their own use.[17]

In Kansas, the BRFSS questions include core questions asked by every state, optional modules, and state-added questions. The core question topics include health status, health care access, healthy days, life satisfaction, emotional satisfaction, disability, tobacco use, alcohol use, exercise, immunization, HIV/AIDS, diabetes, asthma, and cardiovascular disease. Additional questions regarding topics such as hypertension awareness and men and women's health are alternated within the BRFSS from year to year. Optional question modules include questions about different topics that can vary from state to state. State-added questions are added based on the public health needs of the state, though they are not the responsibility of CDC for analysis.[16] Using response data from the BRFSS 2012, sample sizes for the health literacy questions could be 10,000 respondents with a target of 8,000 from landline and 2,000 from cellular phones (20% of the state's total landline and cell phone sample).[16]

Health literacy screening tool. The most feasible health literacy screening tool to implement into the BRFSS was a validated three question health literacy tool. The three question tool was validated for use in both inpatient and outpatient settings.[18,19] Questions for the screening tool are based on six themes which emerged from a qualitative study, including navigation, completing forms, provider-patient interactions, following medication instructions, appointment slips, and coping strategies.[20,21] Questions were designed to assess problems with understanding written medical information, such as "How often do you have someone help you read hospital materials?" and "How often do you have problems learning about your medical condition because of difficulty understanding written information?" Both questions are scored using a 5-point Likert scale ranging from 1 = "Always" to 5 = "Never." One question was designed to assess patient comfort with filling out medical forms by asking, "How confident are you filling out forms by yourself?" This question is scored using a 5-point Likert scale ranging from 1 = "Not at all" to 5 = "Extremely".

For the purposes of this study, risk for low health literacy was determined by a calculation from a cumulative score. Respondents with scores of 3-8 indicated low health literacy; scores of 9-14 indicated moderate health literacy; and a score of 15 indicated high health literacy.

Procedure. In October 2011, research staff from the Department of Family and Community Medicine (DFCM) at the University of Kansas School of Medicine-Wichita (KUSM-W) conducted a series of telephone interviews (N = 20) with a convenience sample to test the administration of an amended version of the three

question health literacy screening tool.[21] The interviews were standardized, including a protocol and script. The script was piloted with a sample of two. The convenience sample was accessed through acquaintances of the interviewers which included access to their telephone numbers. The proposed questions were not asked in previous BRFSS, either nationally or by the state of Kansas. The three question screening tool was used regionally by the authors as a component of previous research conduction in Saline and Sedgwick counties.[22,23]

Four investigators (two research associates and two Ph.D. social science researchers) contacted individuals in the state of Kansas via telephone and conducted independent telephone interviews. Phone calls to participants were made during the work day and evenings over one week. Notes of each call were logged and documents were issued to the principal investigator for qualitative feedback.

Participants were told they would be asked three questions to assess health literacy skills. Each respondent was asked one of the three questions and encouraged through a series of short prompts to assess their understanding of the question. Respondents also were asked what they would add or modify for each question to ensure clarity.

At the completion of the pilot study, modifications to the language in the original questions were made when necessary. Results were presented to the Kansas Department of Health and Environment (KDHE) for approval and addition to the 2012 BRFSS questionnaire. The KDHE adopted the pilot study recommendations and used the suggestions with additional prompts for the addition of health literacy questions to the 2012 BRFSS questionnaire.

The study was approved by the KDHE Institutional Review Board and received approval for future data analysis from the University of Kansas School of Medicine-Wichita Institutional Review Board.

Results

The principal investigator presented the proposed addition of the health literacy questions to the optional/state-added module during the Kansas BRFSS Annual Planning Meeting in August 2011. The board accepted the addition of the health literacy questions and notified the study team (see Figure 1). Table 1 displays the demographic information of participants. In general, participants were mostly female, well educated, and employed in wage-earning occupations.

Question 1 was: "How often do you have someone help you read hospital materials?" Responses for Question 1 indicated the majority "never" (40%; n = 8) or "rarely" (40%; n = 8) needed help reading hospital materials. Results showed four "sometimes" (20%) responses and only one (5%) "often" response.

Question 2 was: "How often do you have problems learning about your medical condition because of difficulty understanding written information?" Responses for Question 2 showed three respondents were unclear of the term "medical condition". Several participants also asked to have this question repeated. The investigators recommended changing the word "medical" to "health" condition. The majority of respondents indicated "never" (30%; n = 6) or "rarely" (45%; n = 9) followed by "sometimes" (20%; n = 4) and "often" (5%; n = 1).

Responses for Question 3, "How confident are you in filling out medical forms by yourself?", indicated less than half of the sample had inquiries for the survey administrator. However, three participant inquiries were aimed at which "medical

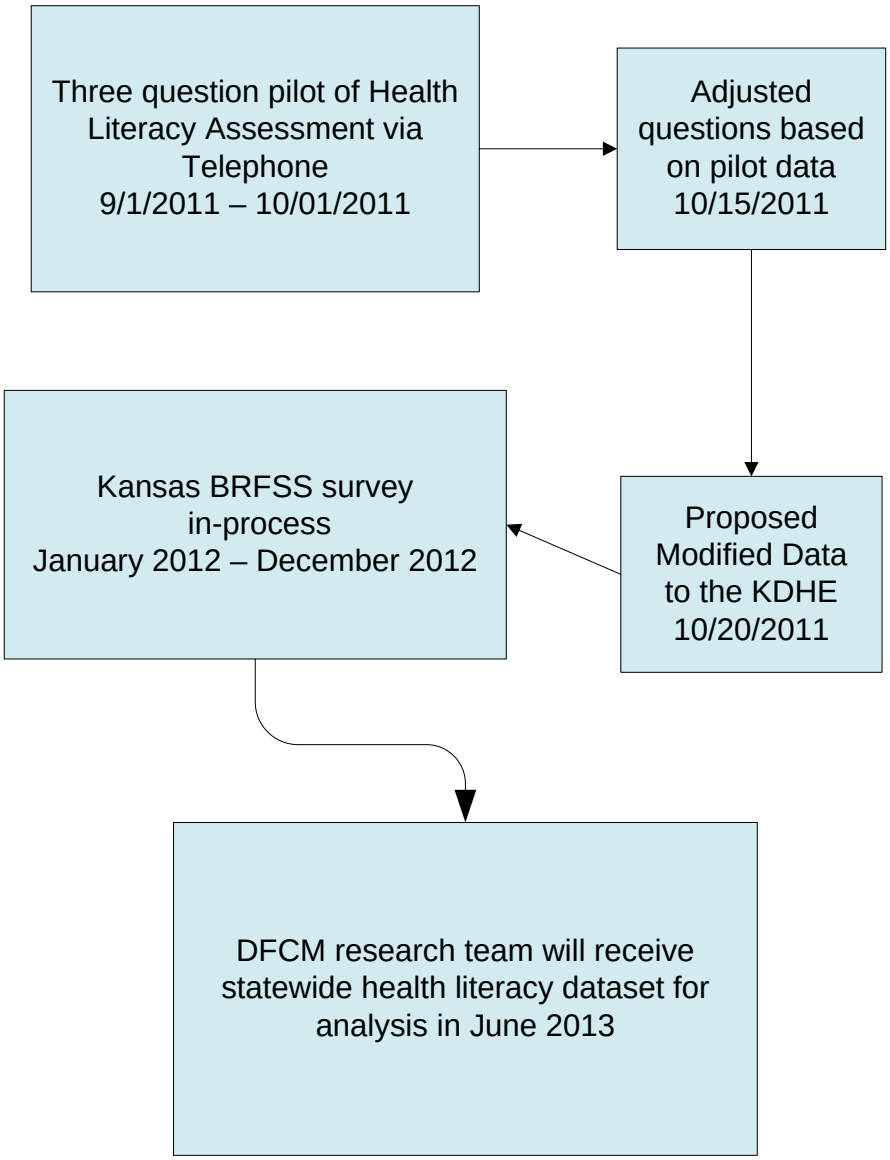

Figure 1. Kansas health literacy assessment development timeline.

forms" were referred to by this question. The research team recommended the addition of examples to describe "medical forms" such as: insurance forms, questionnaires, and doctors' office forms. For Question 3, 40% (n = 8) responded "extremely"; 35% (n = 7) responded "quite a bit'; 20% (n = 4) responded "somewhat"; and 5% (n = 1) indicated "a little".

Overall, participants had little trouble understanding questions or choosing from the multiple choice selection of words. Some questions were understood easily with no flaws in structure or content. Pilot subjects with questions were able to respond appropriately to each of the three questions following clarification by the study team member or repetition of the question. Amended questions that were added to the 2012 BRFSS for the state of Kansas are in Table 2.

Discussion

Pilot testing of a three question health literacy screening tool, modification of questions, and addition of modified question

Table 1. Participant demographics (N = 20).

Gender	
Male	6 (30%)
Female	14 (70%)
Age	
18-25	5 (25%)
26-35	6 (30%)
36-45	1 (5%)
46+	8 (40%)
Race/Ethnicity	
Caucasian	20 (100%)
Marital Status	
Married	7(37%)
Divorced	4 (21%)
Widowed	1 (5%)
Never Married	7 (37%)
Education Level	
Some high school	1 (5%)
Grade 12 or GED	4 (20%)
College 1-3 years	5 (25%)
College Graduate	10 (50%)
Employment Status	
Employed for wages	15 (75%)
Self-employed	1 (5%)
Homemaker	1 (5%)
Student	1 (5%)
Retired	2 (10%)
Health Literacy Level	
Adequate	18 (90%)
Low Health Literacy	2 (10%)

Table 2. Amended three question health literacy assessment.

Question 1	How often do you have someone help you read medical materials? For example: family member, friend, caregiver, doctor, nurse, or other health professional.
Possible Answers	□ Always □ Often □ Sometimes □ Rarely □ Never
Question 2	How often do you have problems learning about your health condition because of difficulty in understanding written information?
Possible Answers	□ Always □ Often □ Sometimes □ Rarely □ Never
Question 3	How confident are you in filling out medical forms by yourself? For example insurance forms, questionnaires, and doctor's office forms.
Possible Answers	□ Not at all □ A little □ Somewhat □ Quite a bit □ Extremely

to the Kansas BRFSS statewide health assessment were essential first steps toward meeting our long-term objective of a statewide health literacy assessment. Data from the 2012 Kansas BRFSS survey will be analyzed by DFCM research staff and results will be disseminated. Results at the population-level will be reported to KDHE and key stakeholders for research purposes and program planning and implementation. Key stakeholders include public health entities, researchers, clinical providers, and healthcare professionals. The addition of a health literacy screening tool to a large health assessment survey may set a precedent for other states to emulate or modify to conduct similar population-level assessments.

While this study provides a novel approach for assessing health literacy across the state of Kansas, it is not without limitations. The sample size used to pilot the screening questions was small and not demographically representative of the Kansas population. The possibility exists that modifications to the three health literacy screening questions were not substantial enough to clarify the meaning of each question to demographics not represented in our sample. Thus, it is possible that some selection bias may have influenced the clarification of questions. Health literacy levels of each participant may have influenced the clarifications that were needed to understand each question. Even with these limitations, the overall impact of the study is not diminished.

To our knowledge, this is the first time these questions have been piloted for a telephone issued, statewide survey. The addition of the three question health literacy screening tool to an already existing statewide health assessment survey may be a feasible and inexpensive option for assessing health literacy in the state of Kansas and building collaboration between university researchers, academic faculty, federal, state, and local governments. Since the tool can be administered over the phone in a short period of time, the cost for administering this tool in a large population study may be significantly less than with another health literacy assessment tool.

The addition of questions to the 2012 BRFSS required collaboration between the CDC, KDHE, local health departments, and public health professionals. A key strength of this study is that it facilitated a first step in collaboration between these agencies for addressing health literacy in Kansas, and working toward goals set out in the CDC's National Action Plan to Improve Health Literacy.[11]

Conclusions

Addressing health literacy requires engagement from multiple healthcare sectors. University and state-run agencies should continue to collaborate to support the assessment of health literacy levels. Both public health and medicine may benefit from exploring health literacy rates using the BRFSS questionnaire.

Future research should focus on identifying risk factors associated with low health literacy and developing targeted interventions for improving health literacy in areas marked by low health literacy. Future studies should utilize the population-level health literacy data in Kansas to analyze trends and identify individuals with the highest risk for poor health outcomes. These data provide the opportunity for scientists and practitioners alike in Kansas to be the health literacy research pioneers.

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Keywords: health literacy, behavioral risk factor surveillance system

Emphysematous Cystitis: An Unusual Imaging-based Diagnosis

Giordano Alves, M.D.[1], Bruno Hochhegger, Ph.D.[2], Edson Marchiori, Ph.D.[1], Klaus L. Irion, Ph.D., F.R.C.R[3]
[1]Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
[2]Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil
[3]Liverpool Heart and Chest Hospital NHS Foundation Trust, Liverpool, United Kingdom

Introduction

Emphysematous cystitis (EC) is defined by an acute gas-production bacterial infection, affecting the urinary bladder.[1,2] In this rare situation, gas is identified within the bladder walls, with or without associated with free gas in the lumen of this organ. However, there are other causes for the presence of air inside the urinary tract, such as instrumentation, fistulae, and abscesses. Early diagnosis and treatment are crucial to avoid urinary sepsis, which could be fatal.

We describe a case of an elderly woman who developed EC during her admission for treating a small bowel obstruction. The imaging findings on the abdominal x-rays and multidetector computed tomography (MDCT) of the abdomen are described and illustrated.

Case Report

An 86-year-old female patient was admitted with complaints of nausea, anorexia, lethargy, and weight loss. The past medical history was otherwise irrelevant, except for an uneventful cholecystectomy, performed ten years earlier. She was found to have a small bowel obstruction, which was caused by an adenocarcinoma of the proximal ileum. The patient was submitted to ileostomy and resection of the tumor.

The patient presented symptoms of major depression after the intervention and was kept institutionalized awaiting clinical improvement. In the course of her post-operatory period, an abdominal x-ray demonstrated the presence of gas in the walls of the urinary bladder (Figure 1). The patient was neither diabetic nor immuno-suppressed. She had no significant urinary symptoms, except for occasional episodes of urinary incontinence.

Figure 1. The frontal radiograph of the pelvis shows the presence of air within the urinary bladder walls, outlining its anatomy.

MDCT assessment (Figure 2) confirmed the emphysematous cystitis and showed no ureteral or renal involvement. The urine samples analysis and culture indicated the presence of *Escherichia coli* as the infective agent. A transurethral urinary bladder catheter was inserted to reduce the urinary

bladder pressure and the treatment with broad-spectrum antibiotics was prescribed.

The patient evolved well from the EC perspective, with no signs of urinary sepsis or local complications. The patient remained depressed, despite the resolution of the infectious process.

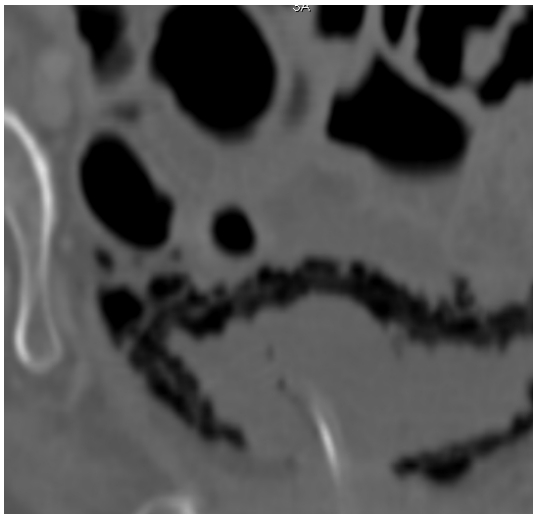

Figure 2. MDCT coronal reformat shows the presence of gas within the urinary bladder walls. No other signs of complication are noted. The transurethral catheter also can be identified inside the bladder.

Discussion

Patients with EC generally present with a predisposing underlying disease. Diabetes and immunosuppressive disorders are the most commonly reported associations.[1,3] Other conditions, such as recurrent urinary tract infection (UTI), neurogenic bladder, and long-term urinary catheterization also are considered as risk factors.[2,4] Similar to other types of UTI, EC is more prevalent in female patients. In the case reported, the catheterization during the gastro-intestinal operation and the advanced age of the patient were believed to be the precipitating factors for the EC.

The precise pathophysiology of EC has not been elucidated. In diabetic patients, most authors suggest that the exceeding urine glucose, which is present in the majority of patients, would be fermented, resulting in an abnormal production of CO_2.[5] The gas progressively would lead to higher intramural and intraluminal pressures, causing tissue ischemia and necrosis. *Escherichia coli* is the causative agent of EC in approximately 60% of cases, followed by *Klebsiella pneumonia*, *Proteus mirabilis*, *Candida albicans* and other micro-organisms.[6] Symptoms often include abdominal pain, dysuria, but might vary between asymptomatic and septic scenarios. The diagnosis is based on the demonstration of emphysematous walls of the urinary bladder on imaging studies, and the infection generally is confirmed on urinary tests. MDCT is also important for ruling out other complications, such as intra-abdominal collections and fistulae.

The abdominal x-ray frequently is diagnostic showing hyperlucent dots aligned on the shape of the bladder walls.[2] However, MDCT is more sensitive and can detect earlier cases, also showing gas within the bladder walls. Moreover, MDCT also provides relevant information for establishing differential diagnosis, especially fistulae and pelvic abscesses.

The isolation of the causal organism should not delay the treatment, and broad-spectrum antibiotics should be initiated as soon as the diagnosis of EC is suspected radiographically, especially in patients with predisposing conditions. Association of antifungal therapy also should be considered in severely immunosuppressed patients.[7] The insertion of a transurethral catheter usually provides an improvement of tissue perfusion, by reducing the pressure on the bladder walls. Finally, an appropriate control of the glycemia is crucial, and may have significant prognostic implications. Surgery may be required in patients with necrosis of the bladder walls due to delayed diagnosis and in cases that have not

responded to a conservative treatment.[8] Even with the appropriate management, the mortality rate is high, reaching 7-10% of all cases.[3]

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Keywords: cystitis, infection, urinary tract, radiography, diagnosis

Unusual Cause of Hypocalcemia: Regorafenib-Induced Hypocalcemia

Maharshi Bhakta, M.D.
Rudruidee Karnchanasorn, M.D.
University of Kansas
School of Medicine-Kansas City
Department of Internal Medicine

Introduction

Hypocalcemia is a known side effect of regorafenib, however, the mechanism is poorly understood. Regorafenib is a new tyrosine kinase inhibitor approved by the US Food and Drug Administration (FDA) for treatment of metastatic colorectal cancer.[1] This report describes a case of profound hypocalcemia potentially related to the use of regorafenib in a patient with metastatic colon cancer. The etiology of hypocalcemia is not clearly published in the English literature. This case illustrated the importance of monitoring calcium and phosphate levels in patients who are on a tyrosine kinase inhibitor to avoid potential lethal toxicity.

Case Report

A 65-year-old woman with a history of hypertension, diabetes, and metastatic colon cancer presented with progressive weakness, fatigue, and postictal symptoms at an oncology clinic. She had profound hypocalcemia (corrected Ca 5.5 mg/dl, baseline of 8.3 mg/dl) and was admitted to the hospital (see Figure 1 for lab results). She recently had been started on regorafenib approximately 15 days prior to presentation.

Her parathyroid hormone (PTH) level was elevated at 541 pg/ml (reference 10-65 pg/ml) and her phosphorus level was 4.5 mg/dl. Her 25-hydroxy vitamin D level was low at 4 ng/ml (reference 30-80ng/ml). Urine studies showed a random urine calcium less than 2 mg/dl/24-hour. There was normal urinary excretion of phosphate, sodium, potassium, and cyclic adenosine monophosphate (AMP). Her admission echocardiogram revealed a prolonged QTc of 487 msec.

On admission, regorafenib was discontinued and the patient was admitted to the telemetry unit. Her hypocalcemia was managed with intravenous calcium infusion to maintain serum calcium above 6 mg/dl. She required approximately 22 g of calcium gluconate infusion over the first four days of hospitalization. On day 5 of admission, ergocalciferol as well as calcitriol was initiated, and she was transitioned from parenteral calcium to oral calcium citrate as her serum calcium levels improved. On day 10, her calcium levels stabilized close to baseline and she was discharged on calcium citrate 3800 mg TID AC, ergocalciferol 50,000u q48h, and calcitriol 2 mcg PO TID. Follow-up laboratory studies demonstrated stability of her calcium and phosphorus levels.

Discussion

Regorafenib is a multi-kinase inhibitor that targets kinases involved with tumor angiogenesis and oncogenesis.[2] It may cross-react with other receptors involved in both calcium and phosphate homeostasis. We hypothesized that the degree of profound hypocalcemia in our patient may have been due to severe vitamin D deficiency and possible PTH resistance type 2.

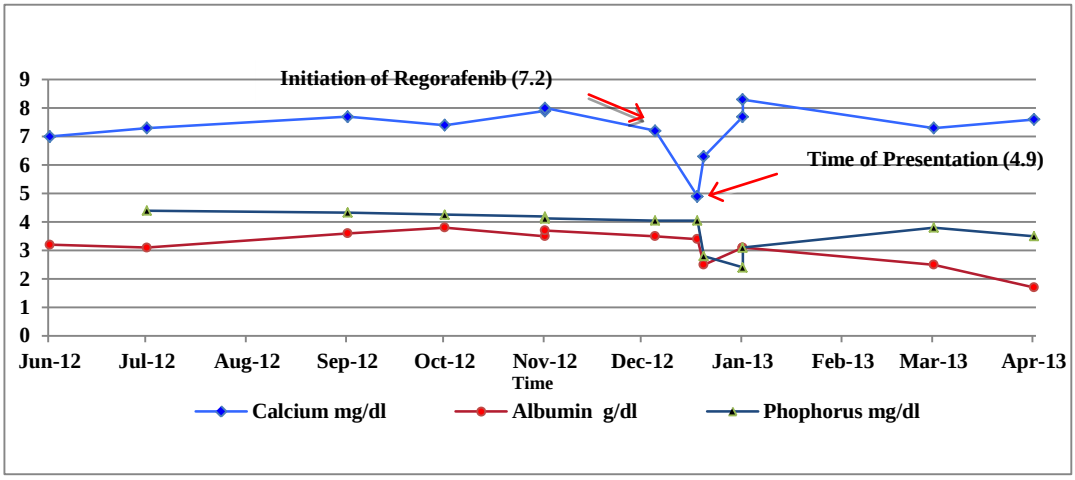

Figure 1. Serum calcium, albumin, and phosphorus levels over time.

Proposed mechanisms of action for regorafenib included: 1) increased metabolism of vitamin D in the liver by inducing P 450 enzyme activity or inhibiting hydroxylation of vitamin D to 25-hydroxy vitamin D or 2) induction of PTH resistance type 2 in which there is a defect downstream on the PTH receptor pathway allowing normal levels of urinary cyclic AMP but low calcium and Vitamin D levels.[3] Profound hypocalcemia can have very serious clinical consequences. This case suggested that serum calcium levels should be monitored closely among patients receiving tyrosine kinase inhibitor to avoid potential lethal toxicity.

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Keywords: regorafenib, tyrosine kinase inhibitor, hypocalcemia, colon cancer, chemotherapy

Young Boy with Abdominal Pain

George Sarin Zacharia, M.D.
Thazhath Mavali Ramachandran, D.D.M.
Government Medical College,
Department of Medical Gastroenterology
Calicut, Kerala, India

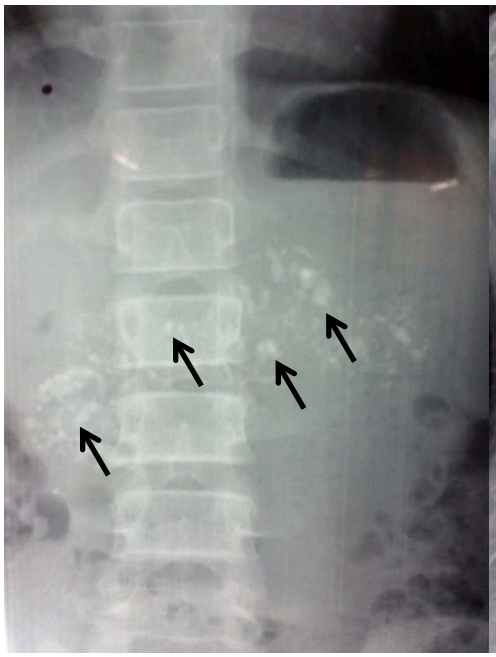

Figure 1. Plain x-ray of the abdomen shows calcifications (arrows) on either side of midline across the midline.

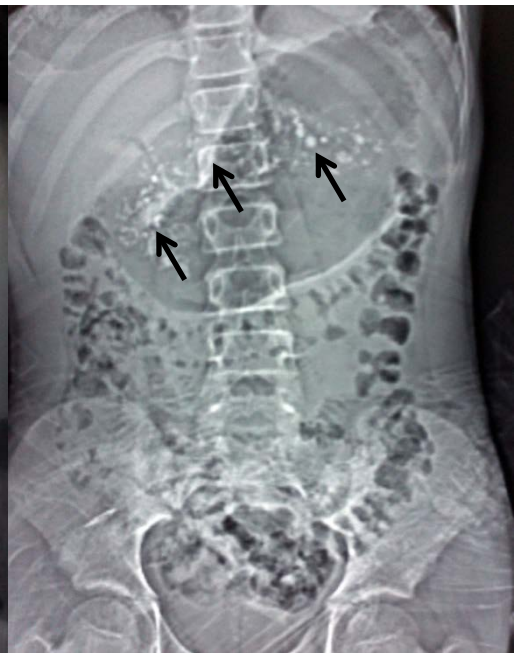

Figure 2. CT skiagram showing calcifications (arrows) across the midline.

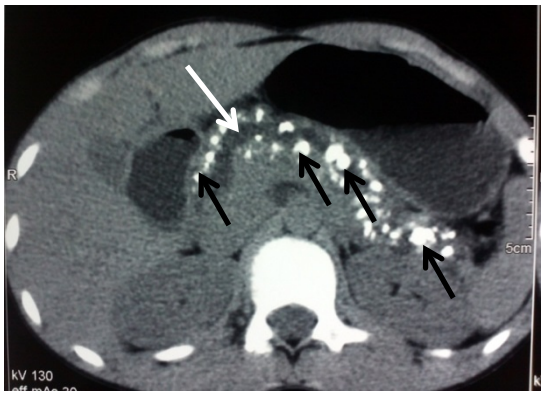

Figure 3. CT of the abdomen showing diffuse pancreatic calcification (black arrows) and dilated pancreatic duct (white arrow).

A 12-year-old boy presented with abdominal pain of three days duration. Pain involved the epigastrium and radiated to the back. He had history of multiple similar episodes of abdominal pain over the past six months. Parents noticed the boy sitting up and leaning forward during the episodes of pain and he reported to have pain relief. He had no significant comorbid illnesses, had neither addictions nor any chronic drug abuse including complementary and alternative medications. He had no significant family history. Physical examination was non-contributory except for emaciation and epigastric tenderness. Hemogram was normal. Blood sugar, amylase, and lipase levels were elevated and the rest of the biochemical parameters were normal.

Plain x-ray of the abdomen revealed calcification in the upper abdomen on either side of midline (Figure 1). Contrast computed tomography revealed diffuse pancreatic calcification and a dilated pancreatic duct suggestive of calcific pancreatitis (Figures 2 and 3). The diagnosis of chronic calcific pancreatitis with acute exacerbation was made. The patient was treated with intravenous fluids, analgesics, pancreatic enzyme supplements, and other supportive measures. He improved with treatment.

Discussion

Intra-abdominal calcification on plain x-ray of the abdomen can be due to pancreatic calcification, renal calculi, biliary stones, calcified mesenteric nodes, tumor calcifications, fecaliths, vascular calcifications, and calcified costal cartilages.[1-3] The location of calcification helps in differentiating the organ of involvement. Pancreatic calcification typically occurs at the level of T9-T12 vertebrae, may cross the midline or overlies the spine, and can be diffuse or focal.[2] Pancreatic calcification most often is due to chronic pancreatitis and rarely due to calcified tumors or cysts.[1,2] Chronic pancreatitis is characterized by irreversible inflammatory damage of the pancreas with or without loss of exocrine and endocrine functions. Etiologies include alcoholism, gall stones, hereditary, autoimmune, tropical, and idiopathic causes.[3] Advanced cases of chronic pancreatitis may be associated with varying degrees of pancreatic calcification. Calcification is reported commonly with tropical, idiopathic, and alcoholic variants of chronic pancreatitis. Being a youth from southwest India, presenting with diffuse pancreatic calcification and ductal dilatation with early onset of endocrine deficiency, the most probable diagnosis in our case was tropical pancreatitis. Treatment options include medical management with analgesics and pancreatic enzyme therapy, endoscopic therapy, and surgery.[4]

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Keywords: tropical calcific pancreatitis, physiological calcification, case report

Tricuspid Valve Mass: Think beyond Vegetation

Mahmoud Farhoud, M.D.[1]
Wassim Shaheen, M.D., F.A.C.C.[1,2]
[1]University of Kansas School of Medicine-Wichita
Department of Internal Medicine
[2]Heartland Cardiology, P.A., Wichita, KS

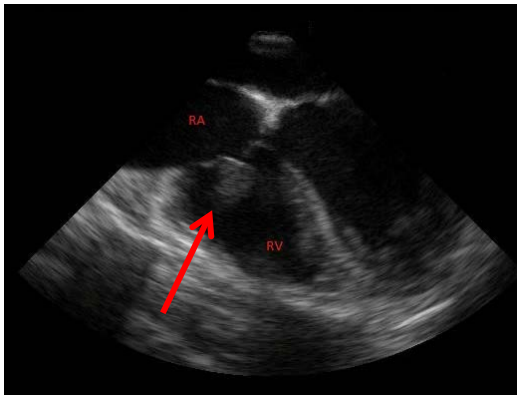

Figure 1. Transesophageal echocardiogram shows the mass. RA: right atrium; RV: right ventricle.

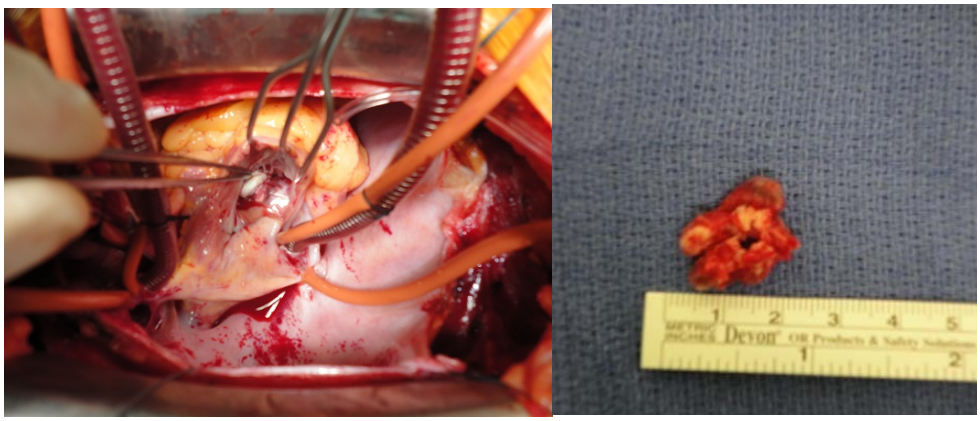

Figure 2. Operative finding of thrombus.

A 38-year-old female with a past medical history of autoimmune hemolytic anemia and two spontaneous abortions, presented to the hospital for sudden onset blindness, headache, and vomiting. The patient had been having joint pain for six months. A magnetic resonance imaging (MRI) of the brain showed abnormal signals within the posterior bilateral cerebral hemispheres suggestive of posterior reversible encephalopathy syndrome. An echocardiogram showed a tricuspid valve (TV) mass and a transesophageal echocardiogram revealed the mass

measuring 2.0 x 2.5 cm (see Figure 1). She was started on antibiotics empirically. Three sets of blood cultures were negative. Anti-Smith antibody, anti-double stranded DNA, and Lupus anti-coagulant antibodies were positive. She underwent cardiopulmonary bypass surgery to resect the mass and prevent pulmonary embolism. A fleshy irregular-shaped mass was attached to the septal leaflet (see Figure 2). Histopathological examination of the mass revealed an organized thrombus without any evidence of malignancy (Figure 3). The patient was diagnosed with secondary antiphospholipid syndrome (APS) due to systemic lupus erythematosus. Her post-operative course was uneventful. She was started on warfarin, steroids, and intravenous cyclophosphamide.

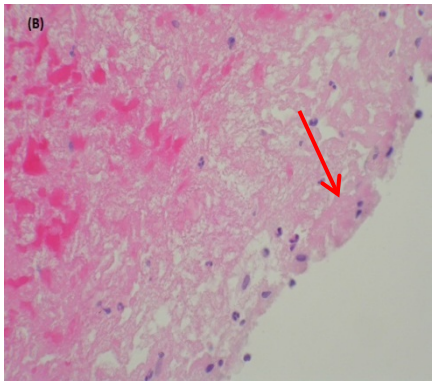

Figure 3. Fibrin material with scant inflammatory cells indicative of thrombus.

Discussion

Antiphospholipid syndrome (APS) is characterized by venous or arterial thromboses, morbidity during pregnancy, and/or antiphospholipid antibody (APL)-related clinical manifestations, such as livedo reticularis, thrombocytopenia, cardiac valve disease, or APL-nephropathy.[1] Intracardiac thrombi have been reported with APS, but involvement of the tricuspid valve is rare.[2] There are three basic types of tricuspid valve masses: tumor, thrombus, and vegetation.[3] Vegetation is the most common. Isolated thrombi of the tricuspid valve may mimic vegetations or tumors and lead to fatal pulmonary embolism.[4] APL antibodies activate endothelial cells to create a hypercoagulable state.[5]

In patients with APS, careful use of anticoagulant therapy is necessary to prevent pulmonary embolization. There is a high risk of recurrence after discontinuation of oral anticoagulant therapy.[6]

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Keywords: antiphospholipid syndrome, antiphospholipid antibodies, thromboembolism, tricuspid valve

CLINICAL INQUIRY

Steroid Use in Prevention of Recurrent Migraine

Zita Magloire, M.D.[1], Sylvester Domme, M.D.[1], Paul Cleland, M.D.[1], Heather Myers Cooper, D.O.[1], Jennifer Esau, D.O.[1], Camilla Gentry, M.L.S.[2], Ryan Lasota, M.D.[1], Samuel Todd Stephens, M.D.[1], Nicholas Tomsen, M.D.[1]
[1]University of Kansas School of Medicine-Wichita, Via Christi Family Practice Residency, Wichita, KS
[2]Via Christi Health, Wichita, KS

Clinical Question

Does administration of intravenous dexamethasone as part of standard acute migraine treatment reduce migraine recurrence?

Evidence-Based Answer

Addition of intravenous dexamethasone to standard abortive therapy in the acute management of migraines reduces recurrence at 48-72 hours. Strength of Recommendation [SOR] is A, based on consistent results of three meta-analyses. Migraine recurrence may be associated with incomplete relief of migraine symptoms at initial presentation. ([SOR]: B, based on one small randomized control trial).

Methodology

A systematic review was performed in the PubMed database using the keywords “migraine treatment”, “steroids and migraine treatment”, and “dexamethasone and migraine recurrence”. Only meta-analyses and randomized control trials (RCTs) were included. The bibliographies of the meta-analyses also were reviewed for RCTs fitting search criteria. Finally, only articles reporting patient-centered outcomes (including reduced morbidity, reported symptom improvement, improved quality of life, and lower cost) in the acute setting (24-72 hours) were included.

Evidence Summary

Migraine headache is a common medical complaint accounting for millions of emergency department visits annually. Standard treatment of acute migraine generally includes use of antiemetics, non-steroidal anti-inflammatory drugs (NSAID), opioids, triptans, ergots, and antihistamines.[1] There may be an inflammatory process linked to the occurrence of migraines, therefore, targeting the inflammatory cascade may be beneficial in treatment.

Three meta-analyses met inclusion criteria and all showed a decrease in migraine recurrence when dexamethasone was added to standard therapy. Colman et al.[1] showed a 26% relative risk reduction in recurrence of migraines when using dexamethasone versus placebo in addition to standard medical therapy. Adverse effects between treatment and control groups were not statistically significant, except that persons in the treatment group were more likely to report dizziness than the placebo group. Similar findings were reported by Singh et al.[2] who found that

moderate to severe recurrent headache could be prevented in 1 out of 10 patients who received dexamethasone along with standard anti-migraine therapy, while Giuliano et al.[3] also reported prevention of migraine recurrence in 10% of patients.

A total of seven randomized control trials (RCTs) were included in this review, with some conflicting findings. Innes et al.[4] randomized 98 patients presenting to the emergency room with migraine to receive either 24 mg of intravenous (IV) dexamethasone or placebo in addition to standard treatment. At 48-72 hour follow-up, patients in the dexamethasone group had a 59% relative risk reduction in recurrence of severe migraine (number needed to treat (NNT) = 4). Similarly, Baden et al.[5] showed a relative risk reduction of 84% in migraine recurrence at 48-72 hours in patients treated with 10 mg IV dexamethasone versus placebo (NNT = 1), while Jones et al. [6] reported a 37% relative risk reduction in migraine recurrence in patients treated with 20 mg IV or intramuscular (IM) dexamethasone.

Fiesseler et al.[7] randomized 173 patients getting standard therapy to receive either oral prednisone 40 mg, IV dexamethasone 10 mg, or placebo, and found no statistically significant difference in symptoms recurrence at 24-72 hours. In a slightly larger study, Friedman et al.[8] randomized 205 patients to receive either dexamethasone or placebo as adjunctive therapy and also did not find a significant decrease in migraine recurrence within 72 hours. However, migraine recurrence was decreased in the treatment group after 72 hours. Two other small RCTs, Donaldson et al.[9] and Rowe et al.[10], also failed to show a statistically significant decrease in recurrence at 72 hours, however, Rowe found that migraine recurrence was associated with incomplete relief of migraine symptoms at initial presentation.

Heterogeneity between the studies, including variation in standard medical therapy, dosage range, route and type of steroid, and time to presentation from onset of migraine requires further scrutiny. Although dexamethasone appears to reduce recurrence of migraines, further studies are needed to determine appropriate dose, time to administration, and other potentially confounding factors. Furthermore, the correlation between incomplete symptom relief and increased recurrence of migraines is an important finding for guiding future studies investigating predictors of migraine recurrence.

Recommendations from Others

A 2011 article published in the American Academy of Family Physicians gave a SOR A for using intravenous dexamethasone in the treatment of acute migraine based on results of two meta-analyses.[11] The International Headache Society and American Academy of Neurology websites were searched using the keywords “migraine” and “migraine treatment” and did not find any recommendations on specific therapies. We also searched the National Guidelines Clearinghouse using keywords “migraine treatment” and “steroids in migraine treatment” and did not return any results.

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Keywords: steroids, migraine disorders, dexamethasone, secondary prevention, systematic review

Appendix
(Adapted from American Family Physician*)

Strength of recommendation	*Basis for recommendation*
A	Consistent, good-quality patient-oriented evidence**
B	Inconsistent or limited-quality patient-oriented evidence**
C	Consensus, disease-oriented evidence** (usual practice, expert opinion, or case series for studies of diagnosis, treatment, prevention, or screening)

*http://www.aafp.org/dam/AAFP/documents/journals/afp/sortdef07.pdf

**Patient-oriented evidence measures outcomes that matter to patients: morbidity, mortality, symptom improvement, cost reduction, and quality of life.

Disease-oriented evidence measures intermediate, physiologic, or surrogate end points that may or may not reflect improvements in patient outcomes (e.g., blood pressure, blood chemistry, physiologic function, pathologic findings).

Commentary

Clinical Practice

Evaluating and Treating ADHD in Primary Care Settings with Updated AAP Guidelines

Raymond R. Chankalal, M.D., M.Sc.[1]
Rebecca S. Daily, M.D.[2]
[1]University of Kansas School of Medicine-Wichita
Department of Psychiatry and Behavioral Sciences
[2]Inasmuch Foundation Pediatric and Wellness Center
Oklahoma City, OK

The decision of primary care providers to initiate treatment for attention-deficit/hyperactivity disorder (ADHD) in child and adolescent populations is a difficult choice that will be encountered often. ADHD is the most chronic health condition affecting school-aged children, with a prevalence of 8% in children and youth.[1,2] Beyond academic underachievement and increased risk for accidental injury, children with ADHD may experience troublesome interpersonal relationships with family members and peers that contribute to the development of low self-esteem. More importantly, children left untreated for ADHD are at risk of developing substance abuse. Assessment, management, and treatment of ADHD can improve the educational and psychosocial development of most afflicted children and youth.[3,4]

The American Academy of Pediatrics (AAP) recognizes that younger ages, coexisting conditions, and other concerns make the decision to treat increasingly pertinent, yet difficult for outpatient providers to perform.[5] Specifically, intellectual disability, autistic spectrum disorder, moderate to severe sensory deficits, and physical, emotional, or sexual abuse, represent patient populations that would benefit from specialist referral or collaboration (see Table 1). There is also a high prevalence of coexisting conditions such as Oppositional Defiant Disorder (ODD) (35%), mood disorder (18%), anxiety disorder (25%), and learning disabilities (12-60%), which require evaluation, but do not preclude treatment for ADHD if diagnostically present.[6]

The aim of this article is to provide a synopsis of the recommended changes and process of care algorithm developed by the AAP Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management, recently developed to streamline the diagnosis and treatment of ADHD by either family physicians or pediatricians on an outpatient basis.[5]

Table 1. Coexisting conditions to be aware of when evaluating and diagnosis ADHD.

	Mood and Behavior	**Physical**	**Developmental**	**Situational**
Coexisting Conditions	Anxiety	Sleep Disorder	Learning Disorder	Adjustment
	Depression	Seizure Disorder	Language Disorder	Abuse
	Oppositional Defiance Disorder	Tics Disorder	Autism Spectrum	Stress
	Conduct Disorder	Hearing Deficits	Intellectual Disorder	Substance

Guideline Revisions

Previously, the American Academy of Family Physicians (AAFP) had utilized the set of guidelines established by the AAP for assessment and diagnosis of school-aged children with ADHD, most recently from 2001.[6] The former recommendations were applicable to an age range from six to twelve years, meeting the criteria of ADHD according to DSM-IV-TR,[7] evident in various settings documenting the degree of functional impairment, core symptoms and duration, assessment for coexisting conditions, and diagnostic tests not routinely indicated for diagnosis of ADHD but helpful with evaluation for comorbid disease.[6] The recommendations have been updated by the Subcommittee which is comprised of the AAP in collaboration with a subcommittee made up of primary care and developmental behavioral pediatricians, members of the American Academy of Child and Adolescent Psychiatry, Child Neurology Society, Society for Pediatric Psychology, National Association of School Psychologists, the Society for Developmental and Behavioral Pediatrics, the American Academy of Family Physicians, Children and Adults with Attention-Deficit/Hyperactivity Disorder, along with epidemiologists from Center for Disease Control and Prevention.[5] Most noteworthy is the effort given to provide evidence based updates to the guidelines focusing on current treatment approaches, safety concerns, and practicality in a busy outpatient setting. The key action statements are summarized below in Table 2. The key action statements of the new guidelines[5] are:

- Evaluation for any patient, 4-18 years of age, who has symptoms suggestive of ADHD is strongly recommended (quality of evidence B).
- The DSM-IV-TR[7] criteria for ADHD, regardless of subtype, must be satisfied based on reports from two settings, usually parents and teachers (strongly recommended; quality of evidence B).
- Assessment for coexisting conditions including physical, behavioral, developmental, and situational (stress, adjustment, abuse) is strongly recommended (quality of evidence B).
- Perception of ADHD must recognize affected patients as having special health care needs that qualifies as a chronic condition (strongly recommended; quality of evidence B).
- Age specific treatments exist, specifically preschool children, 4-5 years of age. Receive behavioral therapy as first line treatment is strongly recommended (quality of evidence A) while possible use of US Food and Drug Administration (FDA) approved medications is recommended (quality of evidence B). Elementary-aged children 6-11 years of age receive FDA-approved medications for treatment of ADHD (strongly recommended; quality of evidence A), along with parent and/or teacher administered behavioral therapy (quality of evidence B). Adolescents 12-18 years of age receive FDA-approved medications for treatment of ADHD (strongly recommended; quality of evidence A) and behavioral therapy is recommended (quality of evidence C).
- Primary care physicians should titrate FDA approved medications for treatment of ADHD to maximize benefits yet minimize adverse effects (strongly recommended; quality of evidence B).

Process-of-care Algorithm

The AAP has set forth a treatment and assessment algorithm to streamline the decision making process when working with school aged children with concerns of ADHD, with a summary provided in Figure 1. The sentiments of the process-of-care algorithm are paraphrased in Table 3. Of importance, the process outlined in the algorithm is not intended to be completed in one office visit, but correct application depends on the provider experience and comfort level,

Table 2. Strongly recommended key action statements for the new guidelines regarding evaluation, diagnosis, and treatment of ADHD, except for behavioral therapy in ages greater than 11 years, which is recommended with a quality of evidence C.

	Key Statement of Guideline	Additional Consideration
Expanded Age Range	Evaluation and treatment of ADHD is expanded to ages 4-18 years old, no longer limited to 6-12 years old.	ADHD must be diagnosed before 7 years, unless history prior to cutoff reveals symptoms fulfilling criteria for diagnosis.
Diagnostic Criteria	Identification of DSM-IV-TR[7] symptoms reported from two settings (parents and teachers).	Ensure validated DSM-IV-TR ADHD rating scales are utilized; consider mood and behavioral disturbances along with substance use.
Coexisting Conditions	Appropriately screen for conditions that coexist with ADHD (e.g., ODD, Tourette's).	Assess physical, behavioral, developmental, and situational conditions.
Clinical Perception of ADHD	Youth and children with ADHD have special health care needs.	Management of ADHD patients should follow the principles of the chronic care model and the medical home.
Age Determines First Line of Treatment	Children less than 6 years old: behavioral treatment and possible FDA-approved medication.*	First line medication is methylphenidate, with patient appropriate formulation.
	Children 6-11 years old: FDA-approved medication and behavioral treatment.	Second line medication is atomoxetine.
	Children and adolescents older than 11 years: FDA-approved medication and possible behavioral treatment.	Third line and adjunctive treatments include guanfacine ER and clonidine ER.
Titrate ADHD approved Rx for maximal benefit but minimize ADRs	70% of ADHD patients respond with continued systematic trials of different therapies given adequate titrations over 3 to 7 days prior to changing agents.	Headaches, reduced appetite, decreased sleep, and reduced growth velocity in first two years. Rare risk of sudden cardiac death. Guanfacine has risk of hepatitis.

*Decision to utilize FDA-approved medications in preschool children depends on severity of ADHD symptoms and duration.

existing office resources and infrastructure acquainted with mental health surveillance and screening.[8] All aspects of the diagnostic and treatment procedures must be documented in the patient's chart along with the use of rating scales at baseline to assess response to medications and provide objective reports to parents.[9] In the Subcommittee's development of the process-of-care algorithm for the assessment, diagnosis, and treatment of ADHD, occasionally there was

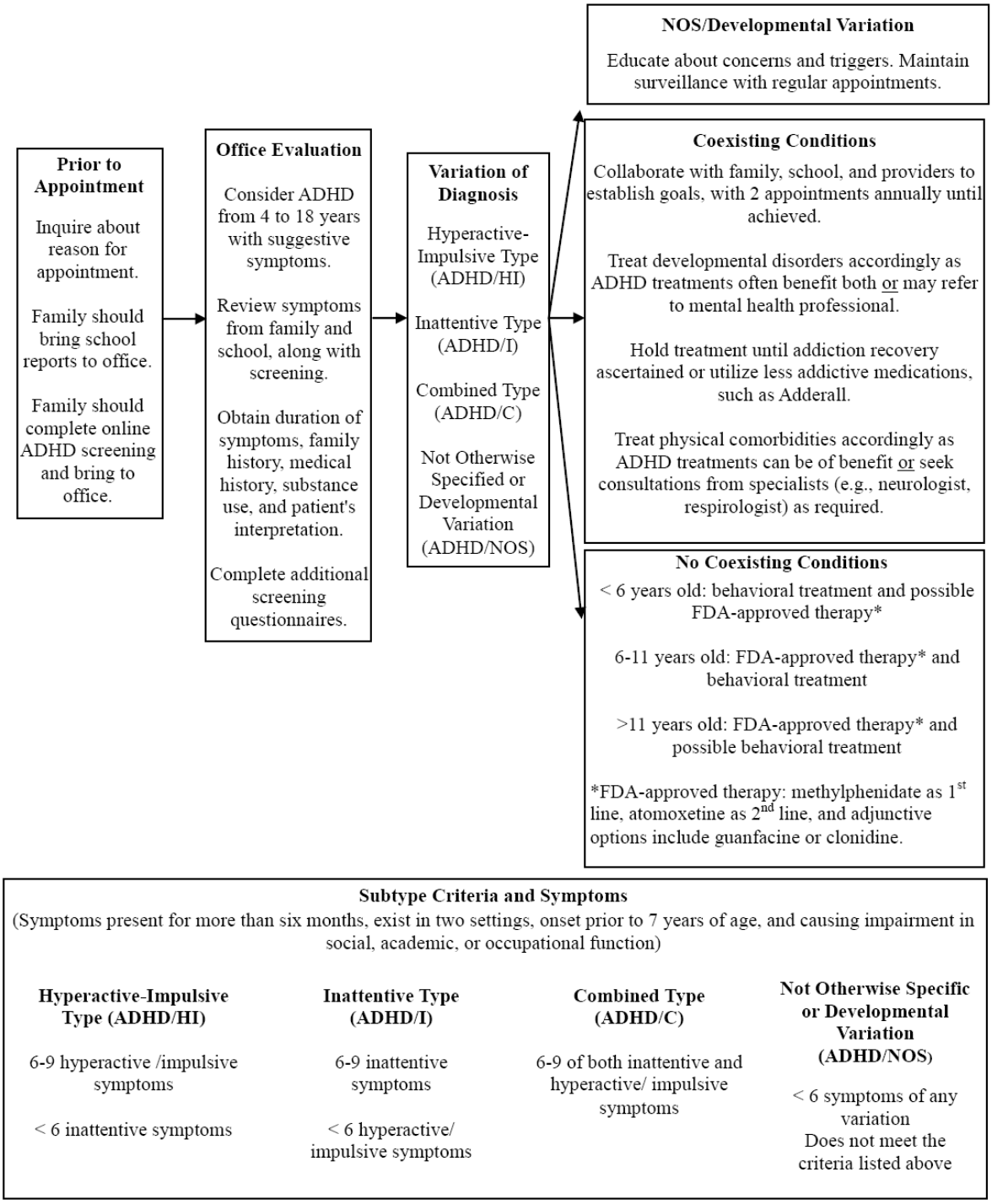

Figure 1. Modified ADHD process-of-care algorithm from the AAP.[9]

insufficient evidence based data to support parts of the approach but these were supplemented with the utilization of expert opinion.[5]

In a sensitive manner, office staff is recommended to inquire about the chief complaint to set an appointment that provides adequate time and resources to optimize the encounter. Prior to

Table 3. Outline of ADHD process-of-care algorithm from the AAP.[9]

Step	Recommended Approach
Before Appointment	Identify reasons for appointment and schedule adequate time. Pre-exam questionnaires by patient, teachers, and parents. Obtain consent for school data, reports, etc.
Evaluation	Consider ADHD in any patients 4 to 18 years old with symptoms. History from family and teachers, with validated ADHD scales. History to include: onset and duration of symptoms, past medical, family, psychosocial, coexisting conditions, substance abuse, and report of function. Interview patient to determine their self-impression of function; observe their mood symptoms and behaviors, and to assess neurological function. Administer self-report instrument of ADHD in adolescents.
Diagnosis	6-9 inattentive symptoms and < 6 hyperactive/impulsive symptoms suggestive of ADHD/I (inattentive type). 6-9 hyperactive/impulsive symptoms and < 6 inattentive symptoms suggestive of ADHD/HI (hyperactive-impulsive type). 6-9 symptoms of both inattentive and hyperactive/impulsive is suggestive of ADHD/C (combined type). Less than 6 symptoms and/or failing to satisfy below criteria is suggestive of ADHD/NOS or Developmental Variation. Symptoms need to be present > 6 months, must be present in two settings, must be present prior to age of 7, and must coincide with significant impairment in social, academic, or occupational functioning.
No Coexisting Conditions	Treat according to guidelines based on patient's age.
Coexisting Conditions	Establish management team with collaboration with family, school, child, and other health care providers to establish treatment goals and strategy, with follow-up a minimum of twice a year once goals obtained. Developmental concerns may be treated depending on provider level of comfort, as both can improve with therapy, or referral for collaboration with mental health professional can be beneficial Behavioral or situational concerns may be treated depending on provider level of comfort, as both can improve with therapy, or referral for collaboration with mental health professional can be beneficial. Hold treatment for coexisting substance use until addiction recovery is ascertained or utilize less addictive medications such as adderall. Physical co-morbidities may be treated depending on provider level of comfort or seek consultation from neurology or respirology as required.
Developmental Variation	Provide education regarding concerns and triggers; maintain surveillance with regularly scheduled appointments.

attending the first appointment to assess for ADHD, parents should be asked to complete questionnaires regarding symptoms and level of functional impairment, obtain information from academic settings such as report cards, standardized testing, and psychoeducational assessments, along with signing consent for primary treatment teams to obtain and share information with academic institutions.[9] Evaluation is required in any patient ages 4 to 18 years of age with symptoms suggestive of ADHD. Evaluation requires obtaining functional history of impairment from two settings, commonly parents and teachers, with use of validated ADHD scales whenever possible. These parties also should assist in provision of medical, family, developmental, psychosocial, and substance abuse history. To assess for coexisting conditions in adolescents, it is essential to be conscious of mood disorders, psychosocial stressors, or neurological conditions, and obtain the patient's self-impression, sometimes requiring the use of self-reported instruments.

In diagnosis of ADHD, the presence of core symptoms is essential.[9] The presence of 6-9 hyperactive/impulsive symptoms and less than six inattentive symptoms are required for ADHD/Hyperactive/Impulsive (HI) subtype diagnosis. The presence of 6-9 inattentive symptoms and less than six hyperactive/impulsive symptoms are required for ADHD/Inattentive (I) subtype diagnosis. Finally, the presence of 6-9 symptoms of both hyperactive/impulsive and inattentive features is indicative of ADHD/Combined (C) subtype. If there is presentation after age 7, years without symptoms in the history before this age, the duration of symptoms is less than six months, these features are not observed in two settings, or these symptoms do not provide functional impairment, then the diagnosis of ADHD cannot be made and the term of Developmental Variation is applied.[9] If there is the presence of less than six symptoms of either subtypes or the patient fails to meet the qualifier remarks above, then the diagnosis of ADHD/NOS may be applied. Table 4 includes a list of ADHD subtype symptoms based generated from the DSM-5.[10] Screening for coexisting conditions may be positive which could warrant the referral to appropriate services should the primary team feel uncomfortable treating ADHD under such circumstances. Beyond physical contributors such as hearing deficits or seizure, ADHD treatment may preclude treatment of anxiety or depression as these disorders often benefit from this approach.

Discussion

The new treatment guidelines[5] are an extension of the previous action statements in 2001[6], but have utilized evidence based material to update these practices and provide more guidance for practitioners in a demanding outpatient setting. There will be features of the new guidelines that may generate questions from family and providers; however, it is essential to consider the long term outcomes of untreated ADHD. Parents of young children may have concerns regarding the assessment and possible treatment of ADHD in preschool age ranges, but there is evidence to support the early presentation and the acute benefits of treatment.[11,12] For providers, it is important to note that most patients with ADHD will not display core symptoms during physical and mental status examinations placing significant weight on the description of features by family and teachers.[13] It is critical that screening for addiction be conducted and that appropriate treatment be provided prior to the management of ADHD.[14] To avoid long term consequences of ADHD, the chronic care model suggests ongoing care along with bidirectional communication with teachers, other mental health professionals, and the parents; an approach that has been validated in asthma patients.[15,16]

Table 4. ADHD subtype symptom requirements* adapted from DSM-5.[10]

Hyperactive/Impulsive	Inattentive
Fidgeting	Seems not to listen
Unable to remain seated	No sustained attention
Runs or climbs in inappropriate settings	Poor attention to details or careless mistakes
Difficulty with leisure activities	Fails to finish tasks
Seems to be "On the go"	Poor organization
Talks excessively	Avoids tasks requiring attention
Blurts out answers	Loses things for tasks
Unable to wait turn	Easily distracted
Interrupts or intrudes on others	Forgetful

*Symptoms must have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level. Symptoms must occur prior to age 7 years and must occur in two settings. The disturbance must cause clinically significant distress or impairment in social, academic, or occupational functioning.

The major concern with lack of treatment is the long term risks of poor academic achievements, inability to build beneficial relationships, poor executive function throughout life, substance abuse, and decreased self-esteem with risk of mood disorders.[9] Methylphenidate is strongly recommended with a quality of evidence A, followed by atomoxetine, extended release guanfacine, and extended release clonidine, in that order, with strong recommendation and the quality of evidence A.[5] Dextroamphetamine is the only ADHD medication approved for use in patients less than 6 years of age with insufficient evidence for safety, while there are more clinical studies with methylphenidate suggesting efficacy and safety.[5,17] Treatment of preschool children with FDA-approved medications has been targeted toward patients with moderate to severe ADHD that has persisted more than nine months, has been refractory to behavioral therapy, all of which has been observed in two or more settings.[17] A referral to a specialist for treatment of preschool children with moderate to severe symptoms would be reasonable should the primary care provider feel it warranted. Children of preschool ages have lower rates of metabolism thus lower dosages are recommended with regular titration as necessary. Guanfacine ER and clonidine ER are the only two medications that are FDA approved for adjunctive therapy in children 6 to 17 years old.[18,19]

Common adverse effects of medication approved for ADHD include headache, decreased appetite, sleep disturbance, and decreased growth velocity of about 1-2 cm on average.[20] There can be psychosis and hallucination with stimulant use, a rare occurrence, with one study showing a 1.48% rate of incidence.[21] In patients younger than 6 years of age, there are reports of greater mood lability and dysphoria.[17] Although there are case reports of stimulant-induced cardiovascular effects,[22] along with the non-stimulant drug-induced myocardial infarction,[23] ADHD specialists from the European ADHD Guidelines Group, the European Network of Hyperkenetic Disorders, and pediatric cardiovascular specialists came to the conclusion that the

overall risk of sudden death in young individuals using ADHD medications does not exceed that of the general population.[24] Children who suffer from ADHD had changes in heart rate variability that benefit from stimulant treatment.[25] Overall, most reports in children and adolescents indicated rare occurrence of stimulant-induced cardiovascular adverse effects.[26] The effect of stimulant use on sleep is not straightforward as it is multifactorial that includes the subtype of ADHD, the patient's pretreatment sleeping habits, the type of medication utilized, along with the duration, frequency, and formulation of the medication.[27] The most common adverse event with stimulant medication is delayed sleep onset latency that ranges from 30 to 50 minutes depending on the agent utilized.[28,29]

Behavioral modification therapy often helps parents and teachers devise reward systems that encourage desired behavior along with elimination of unwanted traits.[30-32] Beyond assisting parents to modify the home environment to benefit the child, it also builds parental awareness of triggers and helps children/patients regulate their own behaviors.[5] The long term effects of behavioral therapy remain to be evaluated but incorporation of such strategies is essential under the chronic care model.[33] Despite mixed reviews on the combined efficacy of medications and behavioral therapy, there is certainty that lower dosages are required, thus reducing the risk of adverse effects.[34]

Ultimately the evaluation, diagnosis, and treatment of ADHD will be conducted by outpatient providers and the aim of the new guidelines, and this article, is to assist these treatment teams in such roles. There continues to be shortcomings based on limited information such as long term effects of medications in preschool populations, comparisons of different medications in the different age ranges, validated diagnostic tools, effectiveness of collaborative efforts, timelines for follow-ups, and approaches to increase adherence to treatments.[5] However, there are advancements emerging such as computer aided evaluations[35] along with off label administration of safety established neurological agents, which could aid substantially in the diagnosis and treatment of ADHD.[36,37] More recently, electroencephalographic (EEG) studies showed fronto-central theta-to-beta band activity ratios that displayed consistent abnormalities in patients with ADHD.[38] Such neuro-feedback studies have shown application to ADHD in young adult populations.[39] Meta-analyses showing EEG to have some prognostic utility[40] leading the FDA to approve this three dimensional approach as a conjunctive tool in the diagnosis of ADHD in patients 6 to 17 years of age.[41]

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