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On the Side Effects of 'Pain' and 'Dehydration' in the Top 20 Selling Pharmaceuticals of 2017

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

Aims: To critically review the potential side effects relating to pain and dehydration symptoms from the top 20 selling pharmaceuticals.
Methodology: The Physicians' Desk Reference medication guide and drugs.com website was used to review medication side effects. The categories of 'pain' and 'dehydration symptoms,' were used to screen for possible side effects from the top 20 selling medications from the year 2017. A listing of likely symptom descriptions relating to pain and dehydration were first established and then used as the screening criteria.
Results: All medications had side effects; 100% (20/20) of the top selling medications caused pain as a potential side effect and 95% (19/20) caused symptoms related to dehydration as a potential side effect.
Conclusion: All medications have multiple potential side effects, and it is alarming that virtually 100% of the top 20 selling drugs may cause both pain and symptoms of dehydration. Since co-morbidities are very prevalent among ailing patients, pain syndromes and symptoms related to dehydration likely progress because of continued use of top pharmaceuticals. It is recommended that physicians routinely practice poly-de-prescribing and practice the simple prescription of physiologic treatments such as 'drink more water' and 'drink less alcohol/caffeine.'

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Keywords: Pharmaceuticals; medication; side effects; adverse drug reactions; pain; dehydration.

1. INTRODUCTION

Population growth and ageing is driving up the numbers of disability-adjusted life years (DALY), or the burden of disease from mortality and morbidity [1]. Although according to reports analyzing the Global Burdon of Disease Study (2013) (GBD 2013), worldwide life expectancy has increased from 1990 to 2013, this has caused a shift from YLLs (years of life lost due to premature mortality) to YLDs (years lived with disability) [1]. Comorbidity, or the presence of two or more diseases/conditions has also increased substantially from 1990 to 2013 [2]. Contemporary medical practice remains a challenge in the management of symptoms.

Regardless of specific condition(s), patients require treatments for their disease(s), and the use of pharmaceutical medication is ubiquitous within allopathic medicine. A quick review of the Physicians' Desk Reference (PDR) confirms the fact that all man-made pharmaceuticals have many potential side effects; there is no medicine without side effects [3]. The drawback from medication use and their potential side effects is the high rate of adverse drug reactions (ADRs); that is, when potential side effects become actual side effects.

Technically, ADRs are "any noxious, unintended, and undesired effect of a drug, which occurs at doses used in humans for prophylaxis, diagnosis, or therapy" [4]. ADRs are very common, affect millions of patients every year and represent one of the top leading causes of death in North America [5]. With so many pharmaceuticals, and their corresponding potential side effects, one wonders how often a patient being pharmaceutically treated for one condition may suffer an ADR of either developing a new condition, or experiencing a worsening of a pre-existing comorbidity from the associated side effects.

Since sixty percent of the US population has a chronic medical condition, and forty-two percent have more than one condition (comorbidities) [6], exigent demands are placed upon the practitioner to appease the patient and modulate existing symptoms by prescribing appropriate medications. The addition of multiple patient complaints, multiple medications (i.e. polypharmacy), and redundant drug side effects, the web of complexity certainly creates a rising level of uncertainty as one wonders which drugs may be necessary versus those that are not.

Two of the most common reported symptoms in primary care are 'pain' (i.e. back pain, stomach pain, headache, etc.) and 'dehydration symptoms' (i.e. constipation, dizziness, fatigue, hypertension, etc.) [7-9]. The purpose of this study was to critically review the potential side effects relating to the symptoms of pain and dehydration within the top 20 selling pharmaceutical medications of 2017.

2. METHODS

Screening criteria for 'pain' and 'dehydration symptoms' were created. Pain was considered any symptom associated with 'pain' (i.e. muscle pain) or a diagnosis known to be associated with pain (i.e. headache). Dehydration symptoms were gathered from both WebMD.com [10] and the Mayo clinic website [11] (Table 1). Both signs and symptoms of dehydration and causes of dehydration are listed. It is rationalized that a medication may cause dehydration both directly (i.e. dry mouth; thirst) or indirectly (i.e. fever; vomiting); therefore any side effect correlating to either signs and symptoms or causes were included to be related to dehydration.

Table 1. Signs, symptoms, and causes of dehydration [10-12]

Signs/Symptoms	Causes*
Dry mouth/tongue	Diarrhea
Sunken eyes	Vomiting
Irritability	Fever
Thirst	Excessive sweating
Less frequent urination	Increased urination
Dark-colored urine	Increased menstrual flow**
Hypertension	Bleeding**
Dyspnea**	
Fatigue	
Dizziness	
Confusion	
Dry skin	
Headache	
Muscle cramps	
Sleepiness	
Lack of energy	
Fainting	

**Causes of dehydration may elicit any of the listed signs/symptoms; **Self-explanatory*

The top twenty selling pharmaceutical medications were chosen to be a representative numerical sample of commonly used medications. Further, because it was the top 20 selling drugs, then the majority of medicated patients would likely be using at least one of these. The top 20 selling medications were identified from internet searches (www.igeahub.com), and were screened for potential side effects (PDR [3] and www.drugs.com) related to both pain and dehydration; only side effects having designations of 'very common' (>10%), and 'common' (1-10%) were included.

3. RESULTS AND DISCUSSION

Of the 20 top sold drugs from 2017, 100% (20/20) caused some sort of pain experience as a potential side effect, and 95% (19/20) directly or indirectly, caused potential side effects related to dehydration (Table 2). Most drugs studied had multiple listings of potential side effects for pain and dehydration.

Table 2. Top 20 pharmaceuticals (2017): purpose, pain-related side effects, and dehydration-related side effects

Rank	Drug	Purpose	Side effects of Pain	Side effects of Dehydration
1	Humira (Adalimumab)	Autoimmune	body aches stomach pain low back pain muscle pains face pain	stomach pain thirst wrinkled skin sunken eyes hypertension
2	Harvoni (Ledipasvir/sofosbuvir)	HCV/HIV	headache muscle pain	diarrhea irritability loss of strength
3	Enbrel (Etanercept)	Autoimmune	sore throat abdominal pain mouth ulcers headache pain in throat pain at injection site	fever diarrhea vomiting dizziness
4	Rituxan (Rituximab/MabThera)	Cancer	stomach pain body aches chest pain headache low back pain side pain mouth ulcers sore throat painful urination face pain joint pain migraine ear pain	sweating tiredness confusion dyspnea dry mouth dry skin increased thirst noisy breathing dizziness vomiting increased urination fever night sweats hypertension constipation
5	Remicade (Infliximab)	Autoimmune	stomach pain chest pain headache muscle pain sore throat joint pain back pain pain at injection site	dyspnea fever dizziness tiredness vomiting diarrhea constipation dry skin

Rank	Drug	Purpose	Side effects of Pain	Side effects of Dehydration
6	Revlimid (Lenalidomide)	Myeloma	chest pain low back pain side pain muscle pain sore throat painful urination mouth ulcers tooth ache oropharyngeal pain joint pain bone pain extremity pain headache	increased sweating decreased urine dyspnea dry mouth fever increased thirst vomiting tiredness night sweats irritability diarrhea constipation dry skin dizziness hypertension dehydration
7	Avastin (Bevacizumab)	Cancer	body aches chest pain pain pain in arm/leg painful urination sore throat stabbing pain headache heartburn stomach pain bone pain skin ulcer	dizziness cracks in skin decreased urine dyspnea fatigue sunken eyes thirst fever sweating wrinkled skin diarrhea dry mouth vomiting hypertension
8	Herceptin (Trastuzumab)	Cancer	headache muscle pain sore throat bone pain joint pain back pain chest pain pain oropharyngeal pain abdominal pain	vomiting weakness fever diarrhea dyspnea constipation dizziness vomiting tiredness hypertension dry skin dry eye
9	Januvia/Janumet (Sitagliptin)	DM	body aches muscle aches sore throat headache	dyspnea fever diarrhea constipation hypertension
10	Lantus (Insulin glargine)	DM	headache sore throat pain at injection site	cold sweats difficulty thinking tiredness fever confusion dizziness weakness hypertension

Rank	Drug	Purpose	Side effects of Pain	Side effects of Dehydration
11	Prevnar 13/Prevener (Pneumococcal 13-valent congugate vaccine)	Pneumococcal vaccine	headache muscle pain joint pain pain at injection site	fever fatigue irritability vomiting diarrhea
12	Xarelto (rivaroxaban)	anti-coagulant	back pain headache toothache abdominal pain joint pain extremity pain oropharyngeal pain	constipation diarrhea bleeding dyspnea dizziness increased menstrual flow vomiting hypertension fever fatigue weakness
13	Eylea (Aflibercept)	Macular degeneration	eye pain pain at injection site	
14	Lyrica (Pregabalin)	Epilepsy	headache stabbing pain low back pain chest pain cervical spasm leg cramps painful urination pain in extremities muscle pain joint pain cervical spasm pain otitis media	dyspnea shortness of breath fever dry mouth confusion constipation diarrhea dizziness irritability sleepiness vomiting
15	Neulasta (Pegfilgrastim/filgrastim)	Neutropenia	sore throat bone pain headache joint pain muscle soreness back pain neck pain mouth ulcers heartburn pain at injection site extremity pain	fever constipation diarrhea vomiting weakness cracked lips
16	Advair/Seretide (Fluticasone/Salmeterol)	Asthma	burning in extremity painful urination sore throat eye pain headache stabbing pains back pain	fever dryness of throat noisy breathing dizziness vomiting diarrhea dyspnea

Rank	Drug	Purpose	Side effects of Pain	Side effects of Dehydration
			myocardial infarction abdominal pain muscle cramps joint pain muscle pain bone pain painful urination mouth ulcers migraine dental pain	
17	Copaxone (Glatiramer acetate)	MS	pain at injection site chest pain joint pain low back pain neck pain painful urination painful lymph glands headache migraine pain	increased sweating tiredness weakness vomiting dyspnea hypertension
18	Sovaldi (Sofosbuvir)	HCV	low back pain mouth ulcers headache muscle pain pain chest pain migraine muscle spasms joint pain abdominal pain	fever tiredness weakness irritability diarrhea dizziness dry mouth dyspnea constipation
19	Tecfidera (Dimethyl fumarate)	MS	low back pain painful urination abdominal pain	fever diarrhea vomiting
20	Opdivo (Nivolumab)	Melanoma	back pain headache joint pain muscle pain muscle cramps sore throat mouth ulcers	constipation diarrhea dry skin fever hoarseness vomiting dyspnea tiredness weakness

Note: Drugs listed as 'Trade name (Generic name)'; 'Purpose' indicates the primary condition drug is prescribed for; The symptom of 'headache' is related to both pain and dehydration, but to avoid redundancy, if mentioned as a potential side effect, was listed only under the pain category; HCV=hepatitis C virus; HIV=human immunodeficiency virus; DM=diabetes mellitus; MS=multiple sclerosis

Pain as a symptom is listed on all of the top medicines and included diverse body areas, such as headache, abdominal pain, low back pain, extremity pain etc. Dehydration as experienced in various signs and symptoms was also discovered as a side effect in all but one

medicine. The finding that pain and dehydration are omnipresent is probably not coincidental. In fact, the link between pain and dehydration is an unappreciated one [12,13], and likely plays an interrelated role.

Headache, for example, is a sign of dehydration (Table 1) that is also a direct cause of pain. Headache, as a potential side effect was listed in 85% (17/20) of the medications and is a common ADR. Batmanghelidj has discussed the essential contribution of body hydration as a central role in pain production as cellular 'free water' deficiency and states that "the regulatory physiological effect of water has not received sufficient attention when evaluating disease processes, and that the body's response and reaction to simple water deficiency had led to confused trends in medicine [12]." The latter is in reference to the practice of prescribing medicine for the treatment of symptoms of dehydration.

Self-induced dehydration, or more appropriately 'inadvertent chronic dehydration' is essentially a silent epidemic, as 75-90% of people do not drink enough water [14,15]. Because water is essential for virtually every bodily process, its deficiency in the diet will promote disease processes. Many common as well as serious medical conditions are directly related to the inadequate consumption of water for example, asthma [16], cancer [17,18], headache [10], hypertension [13], pain [12,13], myocardial infarction [19], peptic ulcer [13], and stroke [20].

Is it possible that patients treated with popular selling pharmaceutics are suffering from dehydration-induced signs and symptoms including pain syndromes? Based on the evidence it seems likely. More concerning is the fact that most people do not drink enough water in the first place, thus when placed on a medication having a side effect of dehydration, this will only worsen the patients physiologic stress and further challenge their body to compensate. This may lead to more pains/discomforts and a worsening of the patient's disease burden.

An alarming notion is that comorbidity leads to polypharmacy. Polypharmacy, the use of multiple medications simultaneously, points to the scenario of patients who are taking several medications are highly likely to suffer from the common side effects of pain and dehydration. A patient suffering with pain and dehydration symptoms will not likely recover from these conditions if continuing to take several medications having side effects of these same symptoms. This is the 'pharmaceutical trap.'

ADRs and polypharmacy are of great concern in modern medical practice. This issue is being investigated, for example, 'potentially inappropriate medication' (PIM) is the term coined in 1991 by Mark H. Beers used primarily in geriatrics to eliminate unnecessary medications. The practice of poly-de-prescribing (PDP) is being investigated, and has been found to be a safe and effective practice to reduce medication use [21].

Since dehydration is so common, it is suggested that a physician recommends water intake over polypharmacy in the initial management of patient comorbidity. In patients already burdened with polypharmacy, continued implementation of PDP practice and inquiry about our patients water-drinking habits (and its recommended increase) should help reduce medication over-prescription and improve the quality of our patients lives. Another possible solution to address the dehydrated status of our patients is to have physicians routinely inquire about a patients dietary intake of diuretics (caffeine and alcohol), and to advise their minimization or abstinence.

The limitations to the current study include the limitation to only the top 20 pharmaceuticals versus a greater number, and the fact that only pain and dehydration symptoms were screened versus more varied symptom investigation. Further investigations could evaluate more medications and evaluate condition-specific side effects and common comorbidity patterns.

4. CONCLUSION

All medications have multiple potential side effects, and it is alarming that virtually 100% of the top 20 selling drugs may cause both pain and symptoms of dehydration. Since co-morbidities are very prevalent among ailing patients, pain syndromes and symptoms related to dehydration likely progress because of continued use of common pharmaceuticals. It is recommended that physicians routinely practice poly-de-prescribing and practice the simple prescription of physiologic treatments such as 'drink more water' and 'drink less alcohol/caffeine.'

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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